SUPPORTING MATERIAL

MOLECULAR DYNAMICS ANALYSIS OF ANTIBODY RECOGNITION AND ESCAPE BY HUMAN H1N1 INFLUENZA HEMAGGLUTININ

Pek Ieong[1], Rommie E. Amaro[1]*, Wilfred W. Li[2]*

Department of Chemistry and Biochemistry[1]

San Diego Supercomputer Center[2]

University of California, San Diego

La Jolla, CA 92093

*Corresponding Author Contact Info

Wilfred Li, Phone: 858 822 0974, Email: wilfred@ucsd.edu

Rommie Amaro, Phone: 858 534 9629, Email: ramaro@ucsd.edu

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Naming Scheme	Crystal Structure	Strain	Simulation Time (ns)	No. of atoms
18HA	3LZF	A/South Carolina/1/1918	69	475,554
09HA	3LZG	A/California/04/2009	69	539,569
06HA	3SM5	A/Solomon Islands/3/2006	69	467,368
09HA_mut	3LZG*	A/California/mutant*	69	565,969

Supporting Table S1: Description of each system. The four systems that were simulated in this experiment are shown above. Their system name, PDB ID, strain, simulation time and number of atoms are listed.

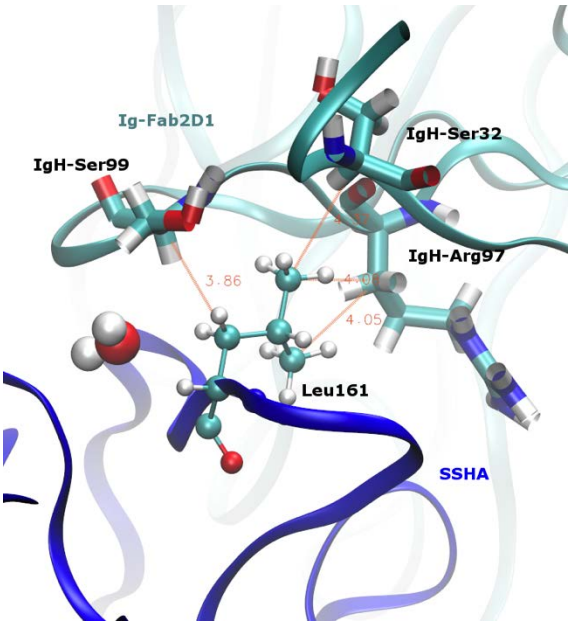

Figure S1. VDW interaction between L161 and R97 of IgH. Ig-2D1 residues are drawn in bonds style and L161 from 06HA is shown in CPK style using VMD. The rest of the Ig-2D1 and 06HA protein backbone are both displayed in ribbon. The 06HA is colored in navy blue and Ig-2D1 is in cyan.

S (125)	Hbond	IgL-W91^{+}
		IgL-D93^{+}
	Dipole	IgL-N95A^{+}
		IgL-G95B^{+}
S (126)	Hbond	IgL-D93^{+}
	Dipole	IgL-W91
P (128)	VDW	IgL-W91^{+}
K (158)	Salt	IgH-D54^{+}
	Hbond	IgH-R97
	Dipole	IgH-D54^{+}
		IgH-T56^{+}
		IgH-R97
	VDW	IgH-D54^{+}
G (159)	Dipole	IgH-D53^{+}
		IgH-R97
S (160)	Hbond	IgH-D53
		IgH-D53
	Dipole	IgH-R97
		IgH-S99^{+}
S (161)	Dipole	IgH-G33
		IgH-R97^{+}
		IgH-S99^{+}
Y (162)	Hbond	IgH-G100^{+}
	Dipole	IgH-V98
		IgH-S99^{+}
P (163)	Dipole	IgH-D100A^{+}
	VDW	IgH-R97^{+}
K (164)	Hbond	IgH-D100A
	VDW	IgH-Y100B^{+}
K (167)	Salt	IgL-D93^{+}
	Hbond	IgL-N31^{+}
	Dipole	IgL-S30^{+}
		IgL-N31^{+}
S (168)	Hbond	IgL-S30^{+}
	Dipole	IgL-S30^{+}
Q (197)	Hbond	IgH- S99
N (198)	Dipole	IgH- S99^{+}
		IgH- G100^{+}
T (249)	Dipole	IgH- G100^{+}
		IgH- G100

Supporting Table S2. Bond interactions between Ig-2D1 and 18HA. All the epitope residues (column I) and the corresponding Ig-2D1 residues (column III) are indicated according to the type of interactions (column II). The interactions that were also found in the crystal structure (PDB ID 3LZF) are marked with $^{+}$ next to Ig residues.

S (125)	Hbond	IgL-W91
S (126)	Hbond	IgL-D93
	Dipole	IgL-W91
P (128)	VDW	IgL-W91
	Dipole	IgH-R97
	VDW	IgH-D54
G (159)	Dipole	IgH-R97
		IgH-D53
S (161)	Dipole	IgH-R97
Y (162)	Hbond	IgH-G100
P (163)	Dipole	IgH-G100
		IgH-D100A
	VDW	IgH-R97
K (164)	Hbond	IgH-D100A
	Dipole	IgH-W100B or IgH-D100A or IgH-G100
	VDW	IgH-D100A
		IgH-W100B
K (167)	Salt	IgL-D93
	Hbond	IgL-N31
	Dipole	IgL-S30
S (168)	Hbond	IgL-S30
	Dipole	IgL-S30
T (249)	Dipole	IgL-G100

Supporting Table S3. Bond interactions between Ig-2D1 and 09HA. All the epitope residues (column I) and the corresponding Ig-2D1 residues (column III) are indicated according to the type of interactions (column II).

E (124)	Hbond	IgH-Y58
S (125)	Hbond	IgL-W91
	Dipole	IgH-Y58
S (126)	Dipole	IgL-W91
P (128)	VDW	IgL-W91
K (158)	Dipole	IgH-R97
N (159)	Hbond	IgH-R97
L (161)	VDW	IgH-R97
Y (162)	Dipole	IgH-G100
P (163)	Dipole	IgH-D100A
	VDW	IgH-V100C
N (164)	Hbond	IgH-D100A
	Dipole	IgH-V100C
		IgH-G100 or IgH-D100A
L (165)	VDW	IgH-Y100B
S (166)	Dipole	IgL-T32
K (167)	Salt	IgL-D93
	Hbond	IgL-N31
	Dipole	IgL-S30
S (168)	Hbond	IgL-S30
	Dipole	IgL-G29
		IgL-S30

Supporting Table S4. Bond interactions between Ig-2D1 and 06HA. All the epitope residues (column I) and the corresponding Ig-2D1 residues (column III) are indicated according to the type of interactions (column II).

S (125)	Hbond	IgL-W91
	Dipole	IgL-D93
		IgL-N95A
P (128)	VDW	IgL-W91
K (158)	VDW	IgH-D54
G (159)	Dipole	IgH-D53
		IgL-S24
S (161)	Dipole	IgL-G25
		IgH-S99
Y (162)	Hbond	IgH-S99
		IgH-G100
P (163)	Dipole	IgH-G100
		IgH-D100A
	VDW	IgH-R97
K (164)	Hbond	IgH-D100A
	VDW	IgH-D100A
		IgH-Y100B
S (168)	Dipole	IgL-S30
N (198)	Dipole	IgH-S99
		IgH-G100

Supporting Table S5. Bond interactions between Ig-2D1 and 09HA_mut. All the epitope residues (column I) and the corresponding Ig-2D1 residues (column III) are indicated according to the type of interactions (column II).

PB	18HA		09HA		06HA		09HA_mut	
Contribution	Mean	SE	Mean	SE	Mean	SE	Mean	SE
ΔE_{vdW}	-117.7	1.1	-112.2	1.1	-106.4	1.1	-112.2	0.8
ΔE_{elec}	-434.9	4.5	-521.6	4.9	-428.5	5.0	-305.3	5.7
ΔE_{PB}	490.4	4.6	577.2	5.0	479.6	5.0	451.0	5.4
ΔE_{cavity}	-12.2	0.1	-11.4	0.1	-12.3	0.1	-11.5	0.1
ΔG_{gas}	-552.7	4.8	-633.8	5.2	-534.9	5.2	-417.5	5.9
ΔG_{solv}	478.2	4.5	565.8	4.9	497.3	4.9	379.6	5.3
$\Delta G_{subtotal}$	-74.4	1.1	-68.0	1.2	-67.6	1.6	-37.9	1.6

Supporting Table S6. MM-PBSA energy breakdown of the four systems. All energies are reported in kcal/mol, averages from three independent calculations over a period of 69 ns. ΔE_{vdW} is the van Der Waal term and ΔE_{elec} is the electrostatic energy. ΔE_{PB} is the solvation energy estimated using the Poisson Boltzmann equation. ΔE_{cavity} is a repulsive nonpolar de-solvation energy term. ΔG_{gas} is the energy of the protein complex in vacuum and ΔG_{solv} is the energy takes to add solvent to a system in vacuum.

GB (igb2)	18HA		09HA		06HA		09HA_mut	
Contribution	Mean	SE	Mean	SE	Mean	SE	Mean	SE
ΔE_{vdW}	-117.7	1.1	-112.2	1.1	-106.4	1.1	-112.2	0.8
ΔE_{elec}	-434.9	4.5	-521.6	4.9	-428.5	5.0	-306.1	5.7
ΔE_{GB}	493.5	4.2	585.8	4.7	486.2	4.9	393.2	5.3
ΔE_{cavity}	-15.3	0.1	-14.6	0.1	-14.6	0.1	-14.1	0.1
ΔG_{gas}	-552.7	4.8	-633.8	5.2	-534.9	5.2	-418.3	6.0
ΔG_{solv}	478.1	4.2	571.1	4.7	471.5	4.9	379.2	5.3
$\Delta G_{subtotal}$	-74.5	1.0	-62.7	1.1	-63.4	1.5	-39.1	1.1

Supporting Table S7. MM-GBSA energy breakdown of the four systems. All energies are reported in kcal/mol, averages from three independent calculations over a period of 69 ns. ΔE_{vdW} is the van Der Waal term and ΔE_{elec} is the electrostatic energy. ΔE_{GB} is the solvation energy estimated using the Generalized Born equation. ΔE_{cavity} is a repulsive nonpolar de-solvation energy term. ΔG_{gas} is the energy of the protein complex in vacuum and ΔG_{solv} is the energy takes to add solvent to a system in vacuum.

Position		18HA		09HA		06HA		09_mut
124	T	-0.6±0.1		-1.1±0.1	E	0.4±0.1		-1.0±0.1
125	S	-3.4±0.1		-3.1±0.2		-2.6±0.1		-3.5±0.2
126	S	-3.1±0.1		-3.0±0.1		-3.5±0.2		-0.7±0.1
128	P	-2.7±0.1		-3.0±0.1		-2.6±0.1		-2.9±0.1
129	N	0.4±0.1		-0.9±0.1		-0.2±0.1		-0.1±0.1
157	K	0.3±0.0		0.5±0.0	G	0.2±0.0		0.6±0.0
158	K	-4.4±0.2		-2.3±0.2		-2.2±0.2		-1.9±0.2
159	G	-3.1±0.1		-2.2±0.1	N	-2.9±0.1		-1.8±0.1
160	S	-4.9±0.2	N	-0.5±0.1	G	-0.0±0.0	N	-0.9±0.1
161	S	-1.8±0.1		-1.8±0.1	L	-4.0±0.1		-2.0±0.1
162	Y	-2.3±0.1		-2.3±0.1		-0.7±0.1		-2.6±0.1
163	P	-4.5±0.1		-4.7±0.1		-3.3±0.1		-4.7±0.1
164	K	-3.9±0.1		-3.8±0.1	N	-2.7±0.1		-3.3±0.1
165	L	-0.6±0.1		-0.9±0.1		-1.4±0.1		-0.4±0.0
166	S	-0.6±0.1		-0.6±0.1		-1.0±0.1		-0.6±0.1
167	K	-6.6±0.2		-6.3±0.2		-6.6±0.2	E	2.9±0.1
168	S	-1.7±0.1		-1.1±0.1		-2.3±0.1		-0.4±0.1
170	V	-1.3±0.1	I	-1.5±0.1	A	-0.7±0.0	I	-1.3±0.1
197	Q	-0.7±0.1		-0.5±0.1	H	0.1±0.0		-0.6±0.1
198	N	-0.5±0.0		-0.5±0.1	T	-0.4±0.0		-0.4±0.1
247	E	0.8±0.0		1.0±0.0		0.7±0.0		0.8±0.0
249	T	-0.5±0.0		-0.6±0.0	N	-0.6±0.1		-0.6±0.0

Supporting Table S8. Energy decomposition breakdown of the four systems. All energies are reported in kcal/mol +/- standard deviation of the mean. The values are obtained from averaging three monomers over 69 ns. All the canonical epitope residues and the surrounding residues are shown for the 18HA. For other systems, only the mutations are listed.