Supporting Information

Applying pose clustering and MD simulations to eliminate false positives in molecular docking

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Table S1 RMSD values, distance values from the protein surface, and protein-ligand contacts of poses that drifted 2 Å from the known binding site during the course of the simulation.

System	Before MD	After MD				
	RMSDx[a] (Docking Score[b])	RMSDx[a] (Docking Score[b])	RMSDd[c]	ΔScore	Ligand Diffusion Distance[d]	Number of Contacts[e] Before/After
1M7D	7.6 (-6.5)	9.6 (-4.6)	1.2	+1.9	2.1	43/34
	7.3 (-6.5)	10.0 (-4.3)	2.7	+2.2	2.0	48/33
1MFA	14.8 (-5.0)	41.0 (0.0)	38.6	+5	-	40/0
1MFB	5.4 (-6.3)	9.4 (-6.3)	2.7	0	1.8	70/83
1OP3	6.0 (-5.6)	9.6 (-3.3)	7.6	+2.3	1.8	33/34
	18.7 (-5.5)	22.6 (-3.3)	4.0	+2.2	2.0	37/17
	11.4 (-5.4)	15.8 (-2.0)	6.4	+3.4	2.1	39/17
1M7I	12.1 (-7.2)	23.9 (-0.1)	24.7	+7.1	1.8	61/10
	11.2 (-6.7)	28.9(-0.1)	24.3	+6.6	2.2	73/6
1UZ8	3.2 (-6.1)	12.3 (-1.2)	12.6	+4.9	2.1	44/10
	5.9 (-5.8)	10.9 (-2.6)	6.2	+3.2	1.6	32/22
1S3K	5.0 (-6.5)	9.1 (-3.2)	6.3	+3.3	1.8	36/17
3TV3	6.7 (-5.6)	43.0 (-1.3)	42.0	+4.3	-	35/0
	22.1 (-5.6)	24.1 (-4.1)	3.7	+1.5	1.8	45/42

[a] RMSD relative to the crystal structure

[b] kcal/mol

[c] RMSD of the pose from MD relative to the docked pose before MD

[d] Shortest distance between any atom in the ligand and any atom in the protein from the last frame of the MD simulation.

[e] Total number of contacts between all atoms in the ligand with atoms on the protein surface.

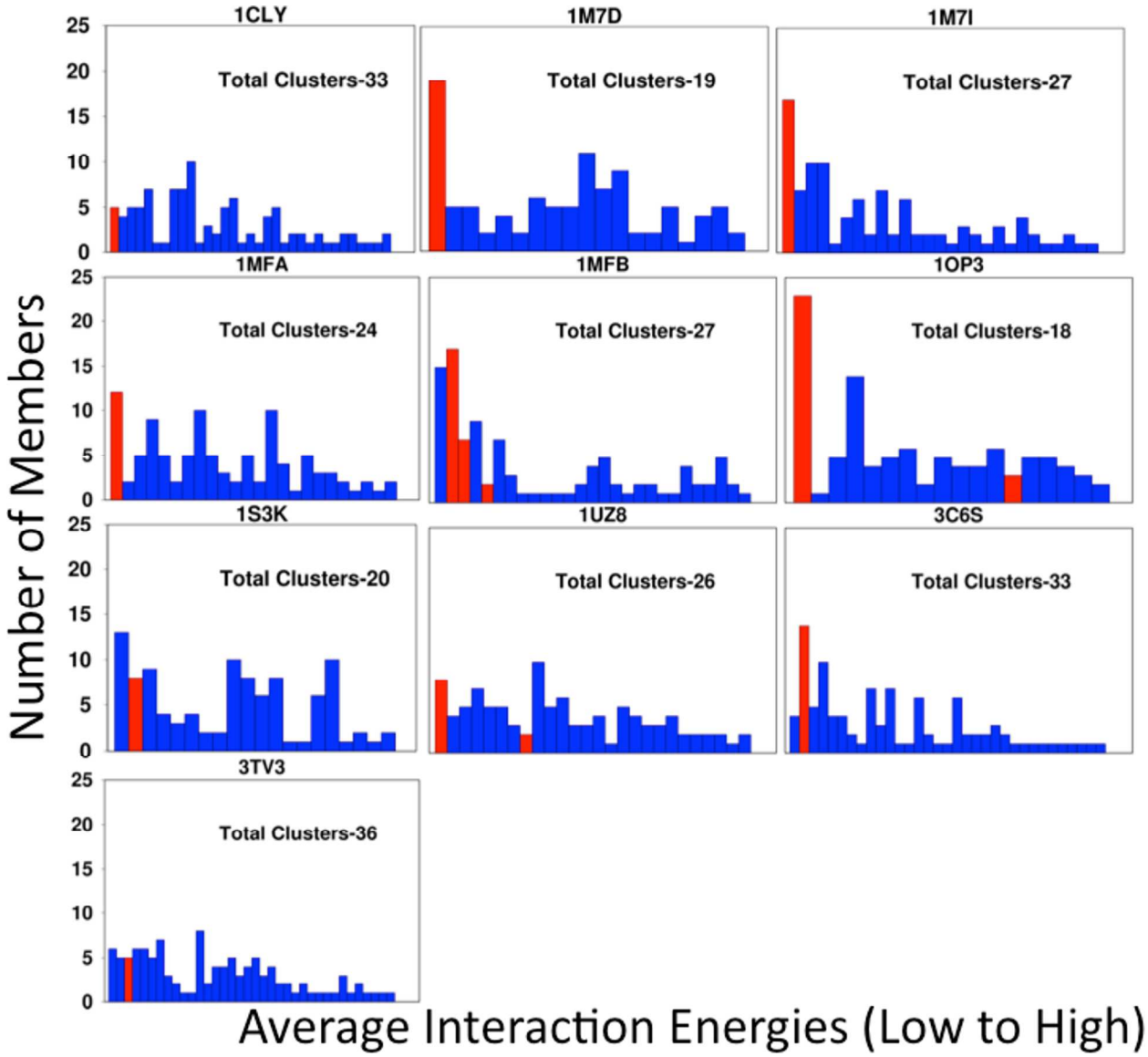

Figure S1. Clustering results for the 10 cognate systems, each ranked from most (left) to least (right) stable based on docking score. Clusters that contain an acceptable pose (RMSD < 2 Å) are colored in red.

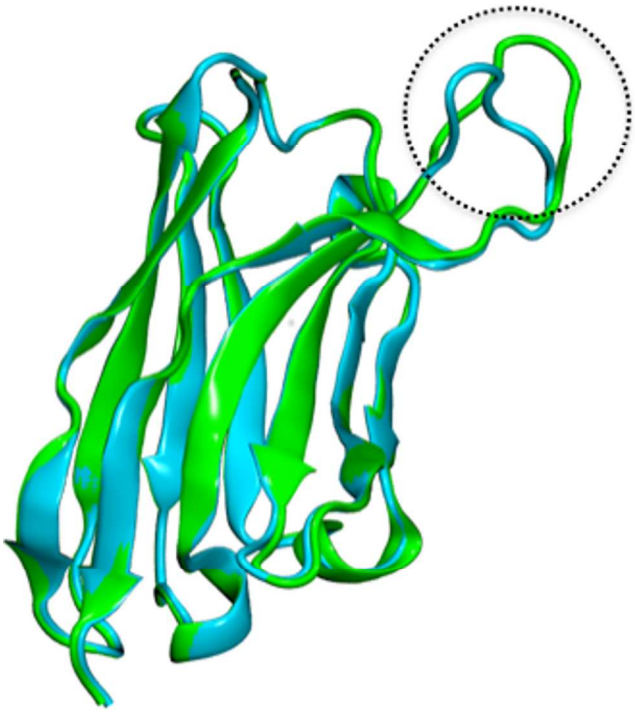

Figure S2 Heavy chain of 1OM3(green) superimposed onto 1OP3(blue) shows the difference in the conformation of the H3 loop between the apo and cognate structures.

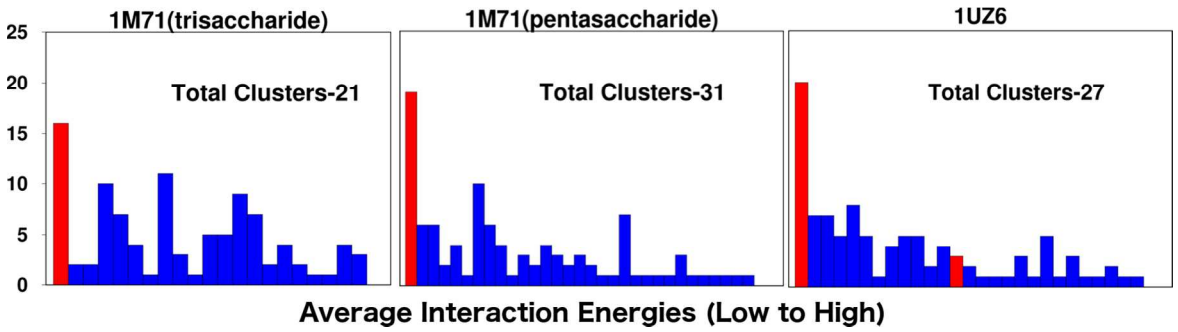

Figure S3 Clustering results for apo systems, each ranked from most (left) to least (right) stable based on docking scores. Clusters that contain an acceptable pose (RMSD < 2 Å) are colored in red.

Table S2 Ligand RMSD (Å) values of the top 10 poses after pose clustering, MD simulation, and post-MD rescoring for the cognate systems. Acceptable poses are shown in red. Poses that worsened by 2 Å from their initial position during MD are shown in green.

1M7D			1CLY		
RMSD Before MD (Sorted by Rank)	**RMSD After MD**	**RMSD After MD (Sorted by Rank)**	**RMSD Before MD (Sorted by Rank)**	**RMSD After MD**	**RMSD After MD (Sorted by Rank)**
0.4 (1)	**1.1 (1)**	**1.1 (1)**	**0.7 (1)**	**1.1 (1)**	**1.1 (1)**
2.2 (2)	**1.1 (2)**	**1.1 (2)**	6.0 (2)	7.7 (10)	**1.1 (2)**
7.9 (3)	7.8 (4)	5.7 (3)	5.3 (3)	5.3 (4)	5.7 (3)
6.6 (4)	6.9 (5)	7.8 (4)	**3.9 (4)**	**1.1 (2)**	5.3 (4)
7.6 (5)	**9.6 (9)**	6.9 (5)	7.0 (5)	7.1 (7)	5.5 (5)
8.4 (6)	7.0 (8)	6.9 (6)	7.0 (6)	6.7 (8)	7.2 (6)
7.3 (7)	**10.0 (10)**	8.9 (7)	6.9 (7)	7.2 (6)	7.1 (7)
6.3 (8)	6.9 (6)	7.0 (8)	6.5 (8)	5.7 (3)	6.7 (8)
5.9 (9)	5.7 (3)	**9.6 (9)**	6.6 (9)	7.5 (9)	7.5 (9)
8.7 (10)	8.9 (7)	**10.0 (10)**	5.5 (10)	5.5 (5)	7.7 (10)
1MFA			**1MFB**		
RMSD Before MD (Sorted by Rank)	**RMSD After MD**	**RMSD After MD (Sorted by Rank)**	**RMSD Before MD (Sorted by Rank)**	**RMSD After MD**	**RMSD After MD (Sorted by Rank)**
0.8 (1)	**1.1 (1)**	**1.1 (1)**	3.3 (1)	3.0 (3)	3.2 (1)
5.6 (2)	5.5 (3)	16.9 (2)	0.7 (2)	**2.1 (2)**	**2.1 (2)**
6.5 (3)	6.8 (5)	5.5 (3)	4.6 (3)	3.9 (7)	3.0 (3)
6.7 (4)	6.8 (7)	5.1 (4)	**3.0 (4)**	**5.1 (4)**	**5.1 (4)**
14.8 (5)	**41.0 (10)**	6.8 (5)	2.7 (5)	2.5 (8)	**9.4 (5)**
5.5 (6)	5.1 (4)	**16.5 (6)**	2.7 (6)	3.2 (1)	6.3 (6)
14.8 (7)	**16.5 (6)**	6.8 (7)	12.3 (7)	13.0 (10)	3.9 (7)
13.9 (8)	**15.7 (9)**	16.8 (8)	**5.4 (8)**	**9.4 (5)**	2.5 (8)
17.3 (9)	16.9 (2)	**15.7 (9)**	14.0 (9)	14.3 (9)	14.3 (9)
16.6 (10)	16.8 (8)	**41.0(10)**	5.9 (10)	6.3 (6)	13.0 (10)
1OP3			**1UZ8**		
RMSD Before MD (Sorted by Rank)	**RMSD After MD**	**RMSD After MD (Sorted by Rank)**	**RMSD Before MD (Sorted by Rank)**	**RMSD After MD**	**RMSD After MD (Sorted by Rank)**
0.9 (1)	**0.8 (2)**	**0.9 (1)**	**0.7 (1)**	**0.7 (1)**	**0.7 (1)**
5.2 (2)	6.0 (7)	**0.8 (2)**	4.7 (2)	5.3 (6)	**0.7 (2)**
13.4 (3)	13.8 (6)	**2.0 (3)**	5.4 (3)	4.9 (4)	5.1 (3)
3.3 (4)	4.2 (4)	4.2 (4)	4.5 (4)	5.2 (5)	4.9 (4)
6.0 (5)	**9.6 (8)**	13.0 (5)	4.9 (5)	5.3 (7)	5.2 (5)

13.0 (6)	13.0 (5)	13.8 (6)	**3.2 (6)**	**12.3 (10)**	5.3 (6)
18.7 (7)	**22.6 (9)**	6.0 (7)	4.5 (7)	5.1 (3)	5.3 (7)
1.6 (8)	**0.9 (1)**	**9.6 (8)**	**5.9 (8)**	**10.9 (9)**	6.3 (8)
2.4 (9)	**2.0 (3)**	**22.6 (9)**	4.9 (9)	6.3 (8)	**10.9 (9)**
11.4 (10)	**15.8 (10)**	**15.8 (10)**	**3.7 (10)**	**0.7 (2)**	**12.3 (10)**
	1M7I			**3C6S**	
RMSD Before MD (Sorted by Rank)	**RMSD After MD**	**RMSD After MD (Sorted by Rank)**	**RMSD Before MD (Sorted by Rank)**	**RMSD After MD**	**RMSD After MD (Sorted by Rank)**
0.6 (1)	**1.8 (1)**	**1.8 (1)**	8.1 (1)	8.5 (3)	**2.5 (1)**
11.9 (2)	11.8 (8)	4.7 (2)	**1.9 (2)**	**2.5 (1)**	**2.6 (2)**
12.1 (3)	**23.9 (10)**	6.7 (3)	8.0 (3)	8.5 (5)	8.5 (3)
5.4 (4)	6.7 (3)	7.2 (4)	8.3 (4)	8.4 (6)	6.6 (4)
4.9 (5)	5.8 (7)	10.9 (5)	3.9 (5)	3.9 (7)	8.5 (5)
4.4 (6)	4.7 (2)	12.0 (6)	7.2 (6)	6.6 (4)	8.4 (6)
11.2 (7)	**28.9 (9)**	5.8 (7)	**4.0 (7)**	**2.6 (2)**	3.9 (7)
11.6 (8)	10.9 (5)	11.8 (8)	5.2 (8)	5.1 (9)	5.6 (8)
11.6 (9)	12.0 (6)	**28.9 (9)**	**14.9 (9)**	**20.2 (10)**	5.1 (9)
8.1 (10)	7.2 (4)	**23.9 (10)**	5.9 (10)	5.6 (8)	**20.2 (10)**

Table S3. Differences in positions of residues (Å) in the heavy chain CDR loop regions in the apo- and co-complexes.

H1	1OM3	1UZ6	1M7D	1M7I	3C5S
26	0.2	0.3	0.5	0.8	1.5
27	0.1	0.4	0.3	0.3	--
28	1.1	0.9	0.3	0.4	--
29	0.0	0.3	0.6	0.5	--
30	0.1	1.1	0.2	0.3	1.8
31	0.1	0.2	0.3	0.4	1.4
32	0.2	1.4	0.3	0.4	5.3
33	0.2	0.3	0.4	0.4	0.5
34	0.2	0.2	0.3	0.3	1.6
35	0.2	0.2	0.3	0.3	0.4
H2	**1OM3**	**1UZ6**	**1M7D**	**1M7I**	**3C5S**
50	0.5	0.3	0.4	0.5	0.4
51	0.1	0.2	0.8	0.6	0.5
52	0.2	0.3	0.5	0.4	0.9
52A	N/A	0.3	0.5	0.5	--
52B	N/A	N/A	0.9	1.0	--
52C	N/A	N/A	0.3	0.4	--
53	0.4	0.4	1.1	1.1	--
54	0.5	0.3	1.3	1.5	--
55	1.3	0.3	0.4	0.4	--
56	4.5	0.1	0.6	0.4	--
57	0.3	0.3	0.5	0.4	0.5
58	1.6	0.3	0.4	1.2	0.5
H3	**1OM3**	**1UZ6**	**1M7D**	**1M7I**	**3C5S**
95	0.5	1.2	0.6	0.5	0.3
96	2.6	0.5	0.5	0.5	0.3
97	5.5	0.5	0.8	0.9	--
98	5.9	1.4	0.9	0.8	--
99	10.1	2.4	0.6	0.6	--
100	7.9	0.5	0.2	0.3	--
100A	3.7	N/A	N/A	N/A	N/A
100B	2.7	N/A	N/A	N/A	N/A
100C	1.2	N/A	N/A	N/A	N/A
100D	0.9	N/A	N/A	N/A	N/A
100E	0.4	N/A	N/A	N/A	N/A
100F	0.2	N/A	N/A	N/A	N/A
101	0.2	0.5	0.4	0.3	0.5

SI

102	0.2	0.4	0.3	0.3	0.4

-- Indicates missing residues in the apo sequence
N/A Indicates that the insertions do not exist