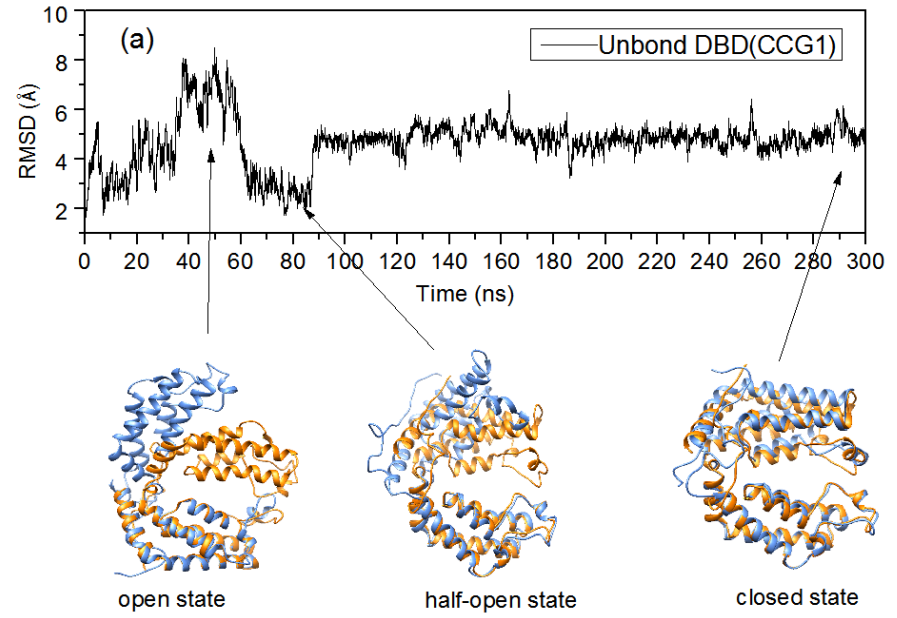
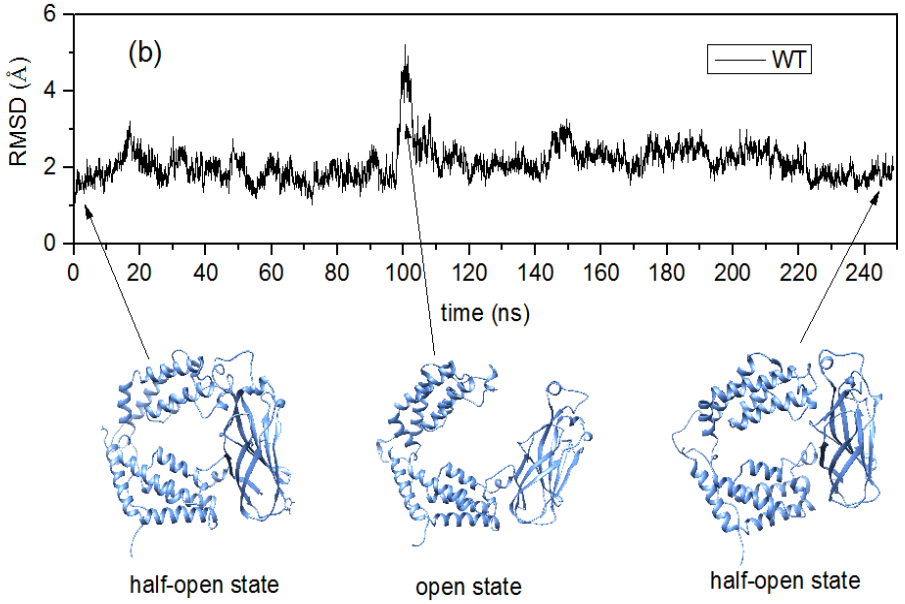
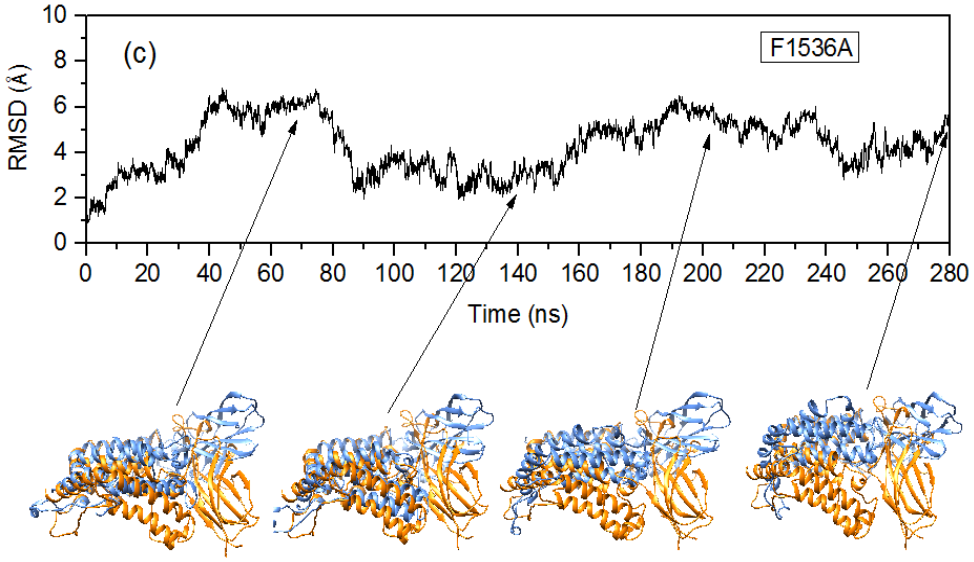
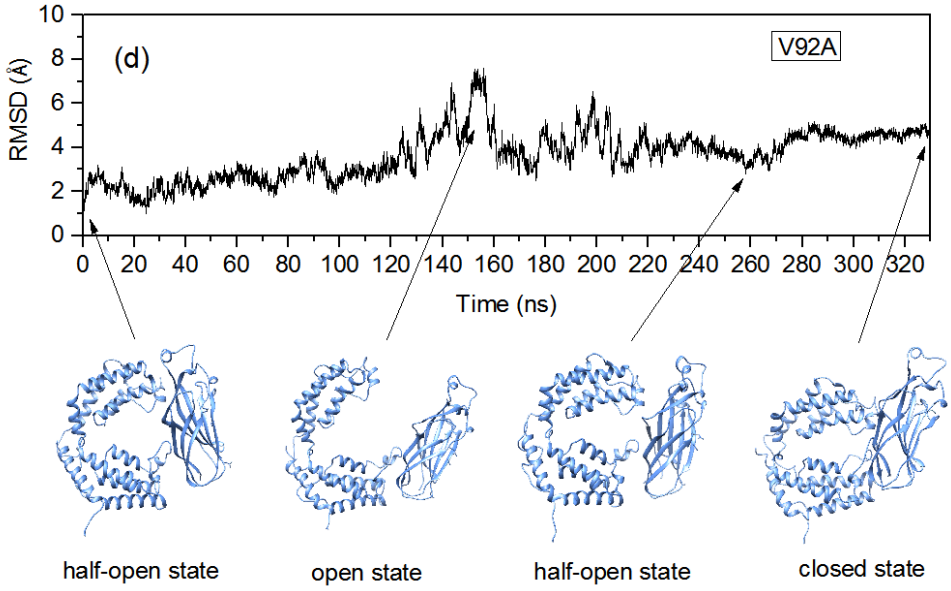

(a)
Unbond DBD(CCG1)
RMSD (Å)
Time (ns)
open state
half-open state
closed state


(b)
WT
RMSD (Å)
time (ns)
half-open state
open state
half-open state


(c)
F1536A
RMSD (Å)
Time (ns)


(d)
V92A
RMSD (Å)
Time (ns)
half-open state
open state
half-open state
closed state

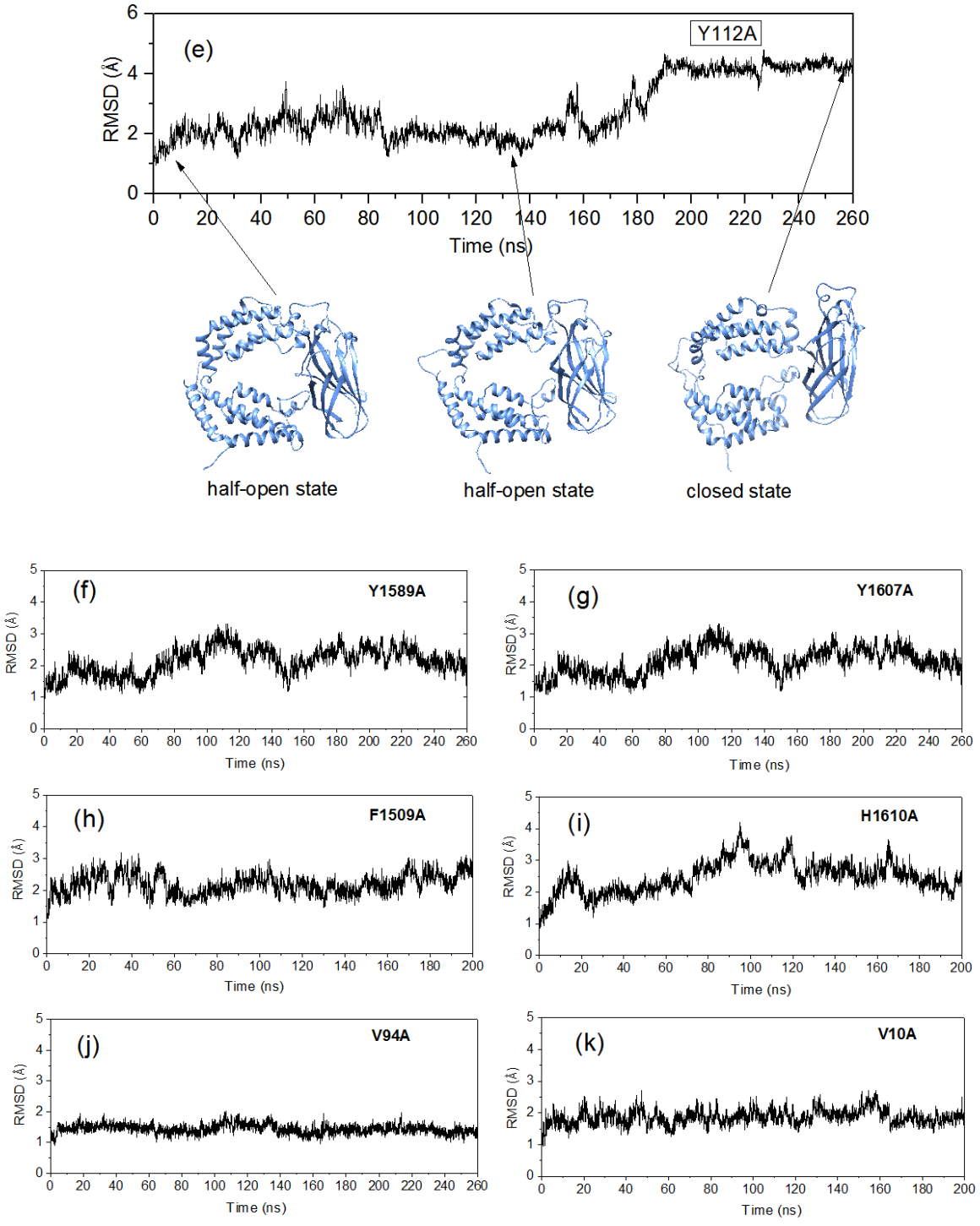


Figure S1. The RMSDs of all systems for C_α atoms relative to the starting structure. The corresponding structures of unbound DBD(CCG1), WT, F1536A, V92A, and Y112A systems, which show large fluctuation of RMSDs, were extracted from the MD simulations. The structures that were extracted from MD simulations were colored in cornflower blue, and the crystal structure of unbound DBD was colored in orange. The structures of F1536A were in upward view.

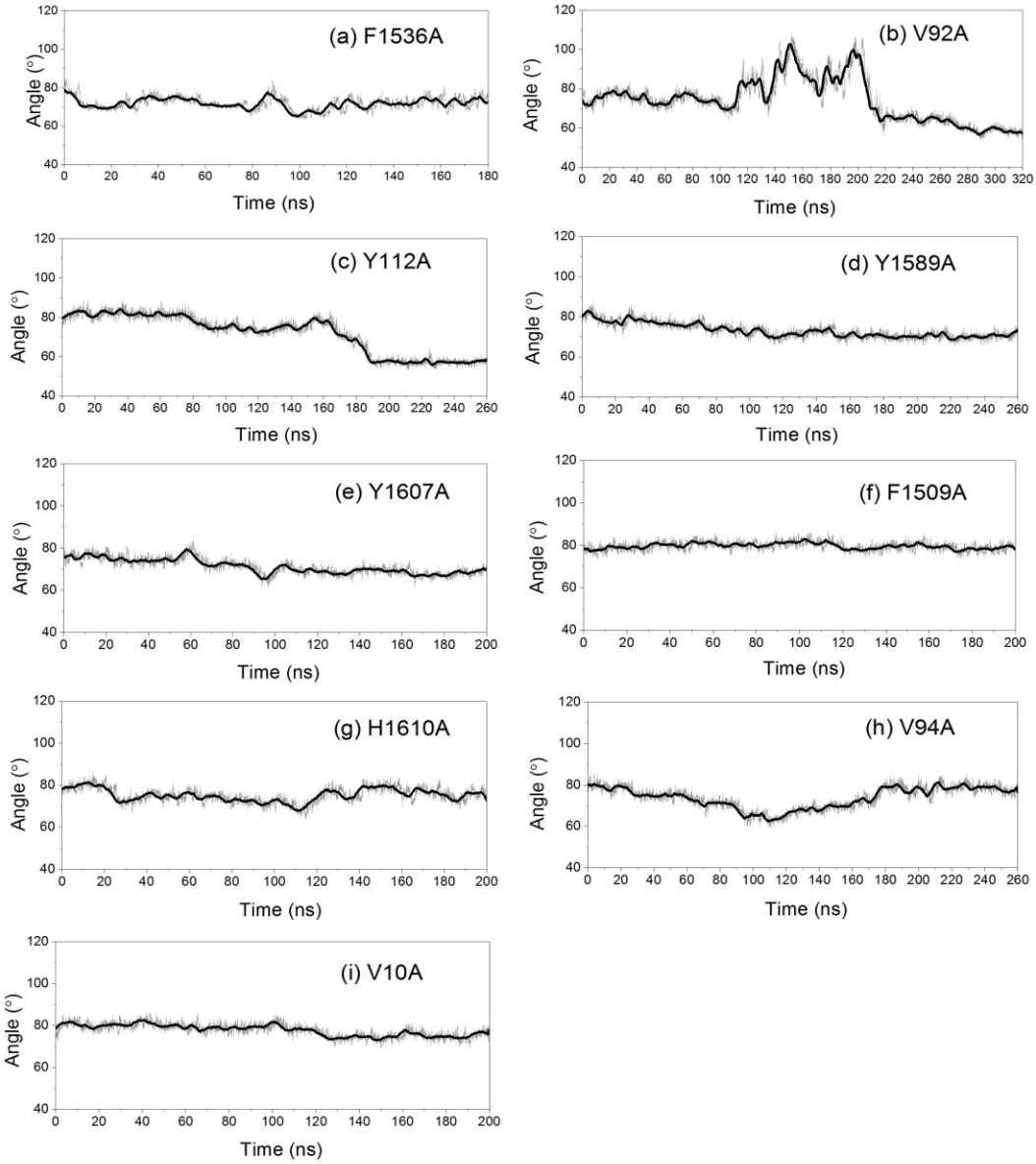


Figure S2. The angle curves between two domains of DBD(CCG1) for all mutant systems versus time. The mutations of V92A and Y112A have a great effect on the binding state, and their binding state finally located at the closed binding state.

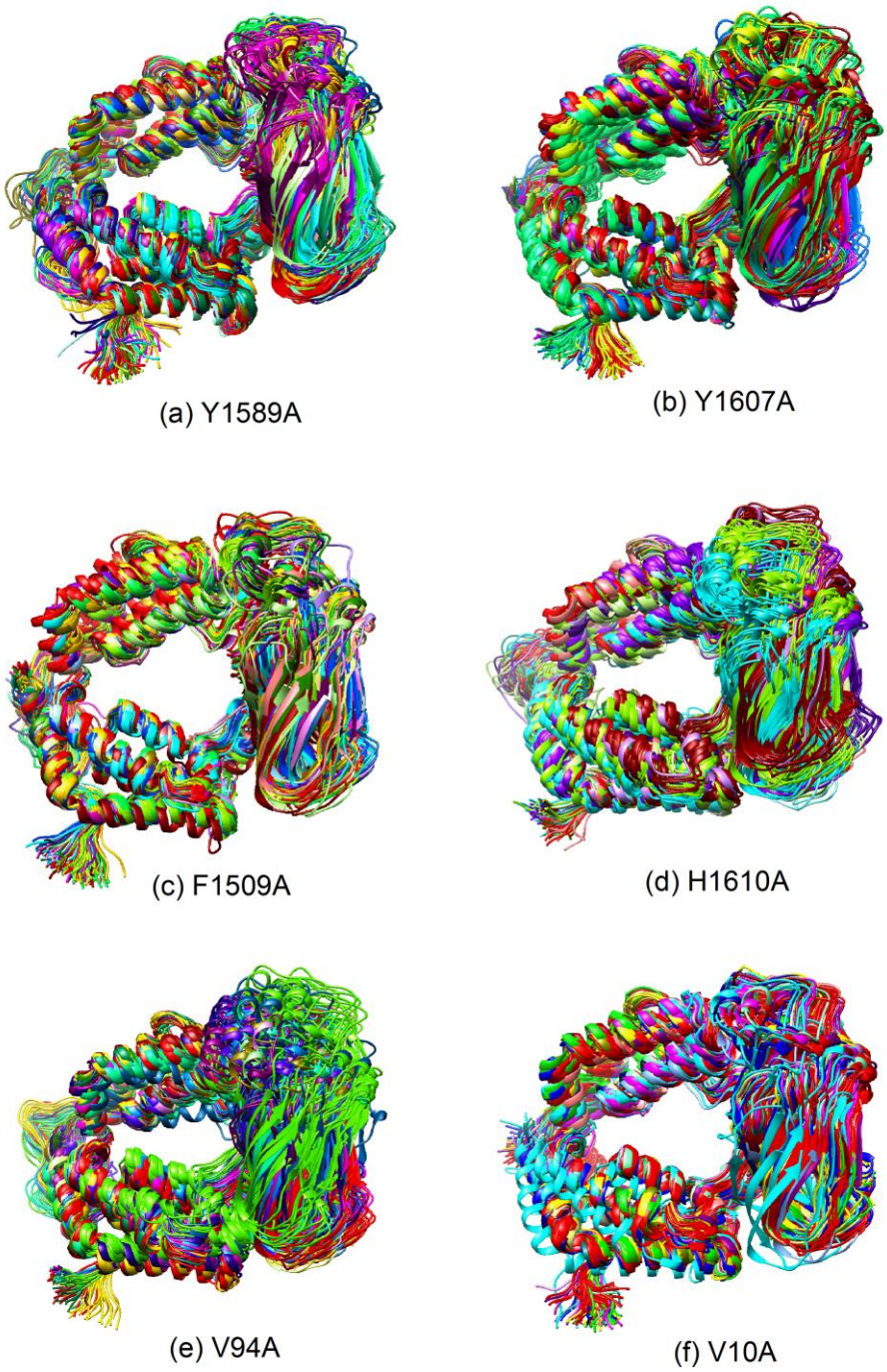
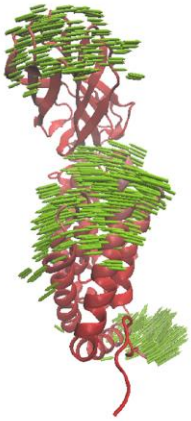
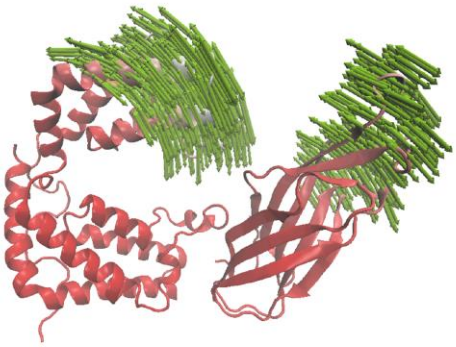


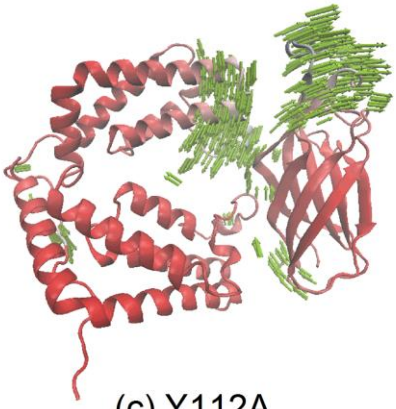
Figure S3. Ensemble cluster analysis of (a) Y1589A, (b) Y1607A, (c) F1509A, (d) H1610A, (e) V94A, and (f) V10A systems. These mutant systems do not show binding state change in the MD simulations.



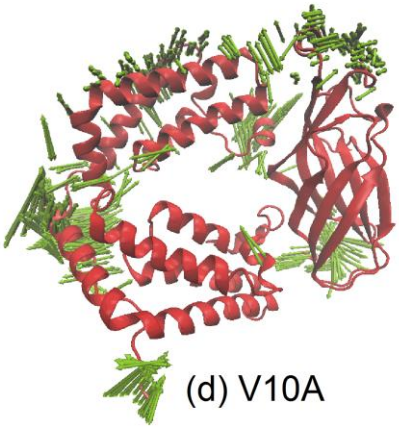
(a) F1536A



(b) V92A



(c) Y112A



(d) V10A

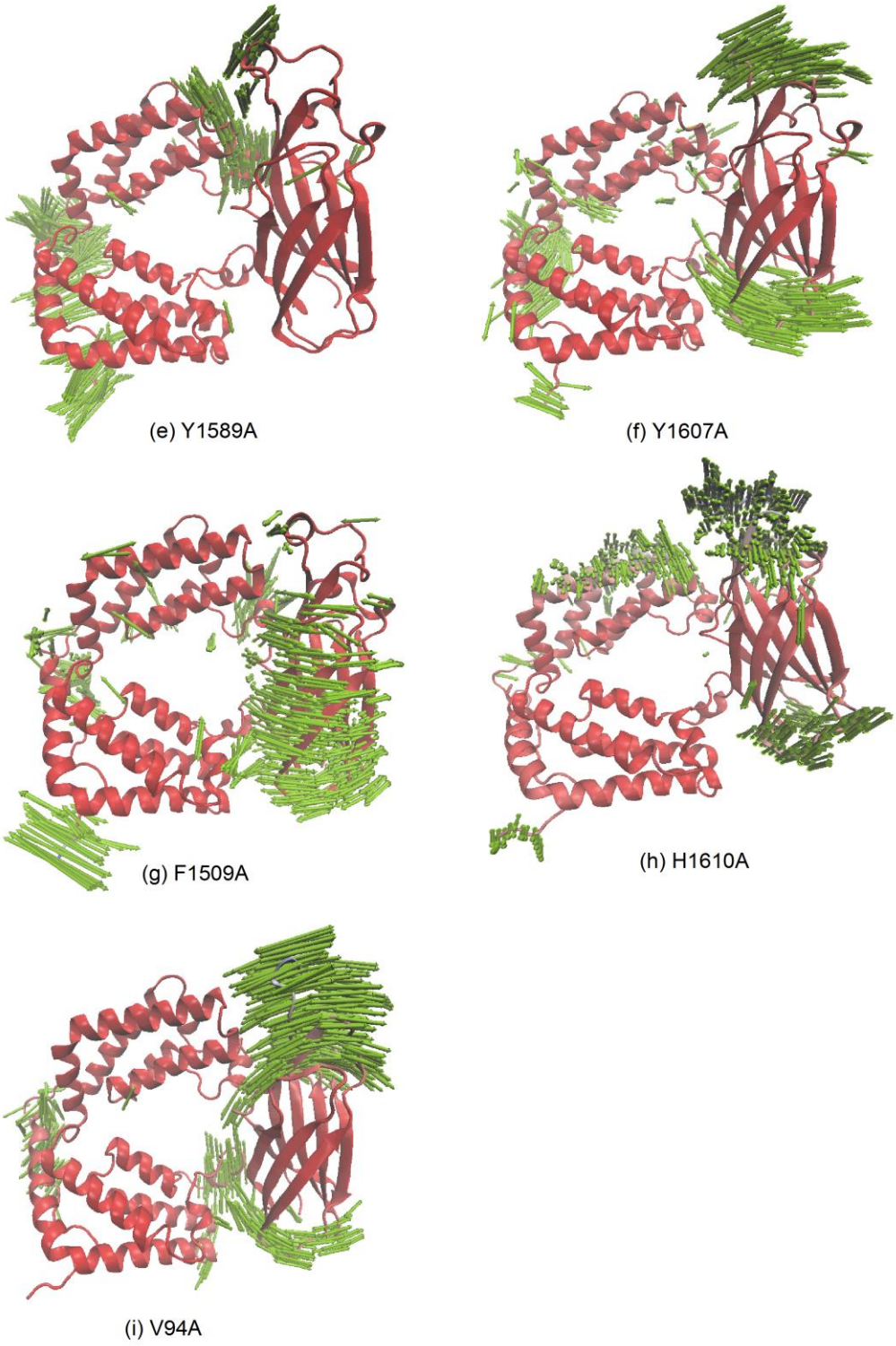


Figure S4. Principal component analysis of (a) F1536A, (b) V92A, (c) Y112A, (d) V10A, (e) Y1589A, (f) Y1607A, (g) F1509A, (h) H1610A, and V94A systems. The binding state changes of V92A and Y112A are mainly caused by the movement of domain 1 and the rotation of CIA/ASF1.

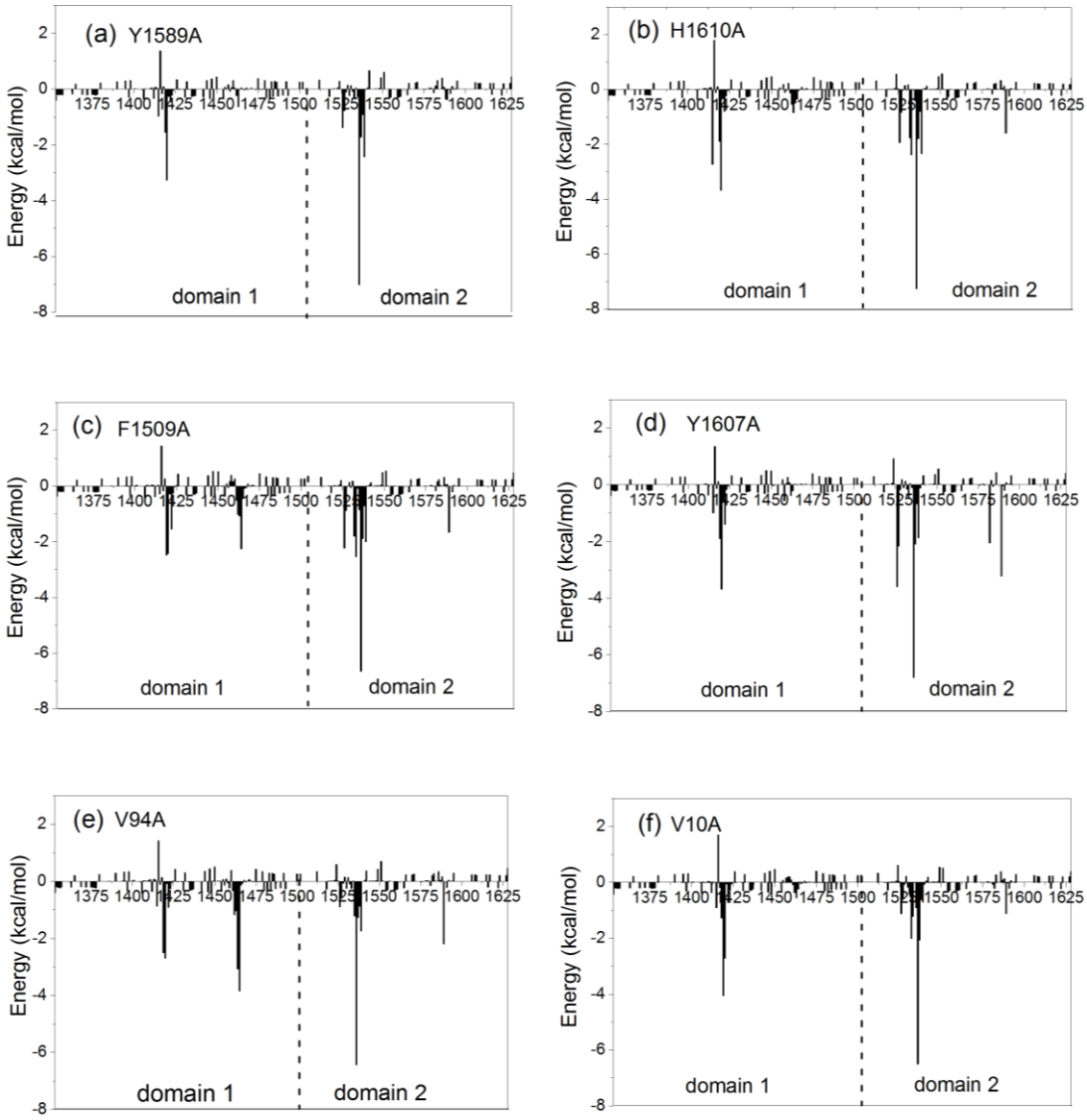


Figure S5. Decomposition of the binding free energy on the residue basis for (a) Y1589A, (b) H1610A, (c) F1509A, (d) Y1607A, (e) V94A, and (d) Y1607A systems. The left side of the dotted line shows the energy contribution of domain 1 and the right shows the energy contribution of domain 2. The interaction spectra of these systems are similar to the WT system with a few exceptions.

Table S1. The hydrophobic interactions and hydrogen bond analysis of crystal structure and average structure of last 20 ns of CIA/ASF1-DBD(CCG1).

Crystal structure of CIA/ASF1-DBD(CCG1)	
Hydrophobic Interactions	
Binding site 1a	
ILE1420-LEU140	ILE1420-VAL92
TYR1459-VAL92	TRP1526-VAL10
Binding site 1b	
PHE1536—ILE107	PHE1536-VAL109
PHE1536-VAL109	PHE1536-TYR111
PHE1536-PRO144	PHE1536-VAL146

PHE1536-VAL6		PHE1536-VAL9	
Hydrogen bond			
Acceptor	Donor		Distance (Å)
TRY1589	ARG69		3.42
Average structure of last 20 ns trajectory			
Hydrophobic Interactions			
Binding site 1a			
ILE1420-LEU140		TRP1526-MET71	
Binding site 1b			
PHE1536-ILE107		PHE1536-VAL109	
PHE1536-TYR111		PHE1536-PRO144	
PHE1536-VAL6		PHE1536-VAL9	
VAL1537-VAL6		PRO1538-VAL146	
Hydrogen bond			
Acceptor	Donor		Distance (Å)
ASN143@OD1	LYS1535@NZ		2.65
GLU29@OE1	TYR1589@OH		3.35
GLU29@OE2	TRY1589@OH		3.28
ASP1539@OD1	ARG148@NH1		2.92
ASP1539@OD1	ARG148@NH1		2.92
ASP1539@OD2	ARG148@NH1		2.86
ASP1539@OD2	ARG148@NH1		2.86
ASP1539@OD1	ARG148@NH2		2.91
ASP1539@OD1	ARG148@NH2		2.91
ASP1539@OD2	ARG148@NH2		2.83
ASP1539@OD2	ARG148@NH2		2.83

Table S2. The binding energy contributions of key residues for all systems. Vdw van der Waals energy; ele, electrostatic energy; GB, polar solvation energy; SA, non-polar solvation energy; S, side-chain atoms; B, back-bone atoms; T, total energy. All values are given in kcal/mol.

Residue	S_{VDW}	B_{VDW}	T_{VDW}	S_{ELE}	B_{ELE}	T_{ELE}	S_{GB}	B_{GB}	T_{GB}	T_{SUR}	T_{GBTOT}
WT											
K1415	-0.14	-0.07	-0.22	-50.58	-10.71	-61.29	49.39	10.8	60.19	-0.09	-1.41
K1419	-1.03	-0.74	-1.77	-48.11	-9.73	-57.84	47.43	10.91	58.34	-0.36	-1.63
I1420	-2.68	-0.68	-3.35	-1.41	-1.45	-2.87	1.34	1.62	2.96	-0.46	-3.72
K1535	-2.08	-1.05	-3.13	-37.85	-6.96	-44.81	38	9.03	47.03	-0.48	-1.39
F1536	-6.72	-1.29	-8	-1.9	-1.68	-3.58	2.81	3.19	6.01	-0.89	-6.46
V1537	-1.39	-0.39	-1.77	-0.52	1.61	1.09	0.49	-1.02	-0.54	-0.2	-1.43
P1538	-1.02	-0.22	-1.24	0.26	2.49	2.75	0.04	-2.46	-2.42	-0.17	-1.07
D1539	0.74	-0.17	0.58	-29.06	1.74	-27.32	26.62	-1.68	24.93	-0.18	-2
Y1589	-0.94	-0.03	-0.97	-6.33	0.57	-5.76	5.1	-0.54	4.55	-0.3	-2.47
N8	-1.27	-0.65	-1.92	-2.08	0.86	-1.21	3.42	-1.09	2.33	-0.14	-0.95
V9	-0.73	-0.69	-1.42	1.09	-3.02	-1.93	-1.12	3.43	2.31	-0.07	-1.11
Y112	-2.79	-0.13	-2.92	1.18	-1.93	-0.75	0.04	2.02	2.06	-0.32	-1.93
L140	-1.89	-0.24	-2.13	1.48	-2.78	-1.3	-1.31	3.24	1.93	-0.3	-1.8
N143	-2.21	-0.6	-2.81	-12.05	2.28	-9.77	11.89	-1.22	10.68	-0.46	-2.37
P144	-1.72	-0.34	-2.06	16.56	-26.38	-9.82	-16.18	25.02	8.84	-0.3	-3.34
V146	-2.08	-0.39	-2.46	1.23	-3.03	-1.8	-1.21	3.44	2.23	-0.3	-2.34
R148	-0.25	-0.04	-0.29	21.81	11.53	33.34	-25.95	-11.25	-37.2	-0.39	-4.54
F1536A											
V1414	-0.82	-0.4	-1.22	-0.9	-0.43	-1.34	0.92	0.72	1.64	-0.1	-1.01

K1415	-1.33	-0.4	-1.73	-49.3	-14.15	-63.45	49.6	14.51	64.11	-0.19	-1.26
D1416	-0.62	-0.85	-1.48	26.36	8.65	35.01	-28.22	-7.92	-36.14	-0.43	-3.04
K1419	-2.11	-0.37	-2.48	-65.73	-10.74	-76.47	66.07	11.4	77.47	-0.39	-1.88
I1420	-2.02	-0.22	-2.24	-1.17	0.7	-0.47	1.2	-0.53	0.67	-0.32	-2.36
Y1459	-2.62	-0.67	-3.29	-3.1	-1.18	-4.27	3.78	1.87	5.65	-0.31	-2.23
H1464	-0.74	-0.08	-0.81	-8.14	-2.98	-11.12	6.39	3.05	9.44	-0.24	-2.73
S47	0.82	-0.42	0.41	-11.03	-4.29	-15.33	4.44	2.9	7.34	-0.08	-7.66
A48	-1.46	-0.58	-2.04	2.33	-4.19	-1.86	-2.26	3.55	1.29	-0.21	-2.83
E49	-0.85	-0.19	-1.04	-63.37	-22	-85.37	63.31	20.05	83.37	-0.18	-3.24
A87	-0.89	-1.03	-1.92	2.76	-3.75	-0.99	-2.73	4.57	1.84	-0.31	-1.38
D88	-0.41	0	-0.41	-17.85	0	-17.85	13.5	0	13.5	-0.18	-4.93
V92	-2.45	-1.21	-3.66	1.32	0.25	1.57	-1.17	0.61	-0.56	-0.31	-2.95
N114	-1.55	-0.18	-1.73	-2.68	-0.62	-3.3	2.78	0.74	3.53	-0.22	-1.72
L140	-1.51	-0.11	-1.62	1.45	-1.66	-0.21	-1.37	1.87	0.5	-0.18	-1.5
Y1589A											
K1415	-0.11	-0.08	-0.2	-47.11	-10.33	-57.45	46.28	10.45	56.73	-0.07	-0.98
K1419	-1.76	-1.02	-2.78	-38.42	-7.95	-46.38	38.44	9.57	48.01	-0.41	-1.56
I1420	-2.52	-0.89	-3.41	-1.28	-0.91	-2.19	1.22	1.52	2.74	-0.41	-3.27
K1535	-2.27	-0.84	-3.11	-32.71	-7.55	-40.26	34.37	9.24	43.6	-0.51	-0.28
F1536	-6.86	-1.11	-7.97	-1.87	-2.88	-4.75	2.84	3.74	6.58	-0.89	-7.02
V1537	-1.66	-0.43	-2.09	-0.67	1.57	0.91	0.64	-0.96	-0.32	-0.22	-1.72
P1538	-0.92	-0.21	-1.12	-0.13	2.67	2.54	0.42	-2.63	-2.21	-0.13	-0.92
D1539	0.53	-0.17	0.36	-28.18	1.75	-26.43	25.54	-1.71	23.83	-0.2	-2.44
N8	-1.32	-0.69	-2.01	-2.87	0.97	-1.9	4.11	-1.2	2.9	-0.14	-1.14
V9	-0.7	-0.64	-1.34	1.13	-3.17	-2.04	-1.15	3.58	2.43	-0.07	-1.02
Y112	-2.81	-0.12	-2.92	-0.28	-2.05	-2.33	1.16	2.14	3.3	-0.36	-2.32
L140	-1.74	-0.17	-1.91	1.49	-2.57	-1.08	-1.35	2.95	1.6	-0.28	-1.68
N143	-2.55	-0.62	-3.18	-10	2.48	-7.52	10.05	-1.28	8.78	-0.46	-2.38
P144	-1.46	-0.2	-1.66	16.83	-26.55	-9.72	-16.42	24.66	8.24	-0.24	-3.38
V146	-2.19	-0.36	-2.55	1.45	-3.39	-1.94	-1.38	3.64	2.26	-0.3	-2.52
R148	-0.4	-0.05	-0.44	25.74	12.36	38.09	-30.11	-12.05	-42.16	-0.38	-4.88
H1610A											
K1415	0.03	-0.09	-0.06	-67.52	-10.71	-78.23	64.85	10.89	75.74	-0.18	-2.73
K1419	-1.69	-0.88	-2.57	-39.32	-9.53	-48.85	39.43	10.52	49.95	-0.41	-1.89
I1420	-2.66	-0.73	-3.39	-1.41	-2.05	-3.45	1.31	2.27	3.59	-0.43	-3.68
W1526	-2.57	-0.13	-2.7	-2.82	1.4	-1.41	3.64	-1.05	2.59	-0.42	-1.94
V1532	-1.38	-0.47	-1.85	-0.42	-1.24	-1.65	0.5	1.43	1.93	-0.19	-1.76
N1533	-1.4	-0.49	-1.89	-4.31	-1.75	-6.06	4.33	1.42	5.75	-0.2	-2.39
F1536	-7.38	-1.3	-8.69	-1.68	-3.6	-5.28	2.83	4.75	7.59	-0.89	-7.27
V1537	-1.86	-0.49	-2.36	-0.71	2.42	1.71	0.71	-1.64	-0.94	-0.21	-1.79
D1539	0.59	-0.15	0.44	-21.48	2.71	-18.78	18.65	-2.52	16.13	-0.15	-2.35
Y1589	-0.56	-0.02	-0.58	-5.28	0.22	-5.06	4.48	-0.2	4.28	-0.24	-1.59
N7	-1.73	-1.74	-3.47	1.25	-5.56	-4.31	0.15	6.82	6.98	-0.36	-1.16
N8	-1.76	-0.92	-2.68	-4.07	1.1	-2.97	4.91	-1.33	3.57	-0.23	-2.31
V9	-0.67	-0.64	-1.31	1.05	-3.12	-2.07	-1.07	3.54	2.46	-0.06	-0.97
Y112	-2.94	-0.13	-3.07	0.86	-1.93	-1.07	0.37	2.01	2.39	-0.32	-2.07
L140	-1.77	-0.18	-1.95	1.44	-2.37	-0.93	-1.27	2.74	1.47	-0.28	-1.69
N143	-1.7	-0.44	-2.14	-8.08	2.07	-6.01	7.87	-1.36	6.51	-0.34	-1.97
P144	-1.42	-0.48	-1.9	16.65	-20.74	-4.09	-16.21	20.43	4.22	-0.24	-2.01

V146	-2.25	-0.28	-2.53	1.26	-2.53	-1.26	-1.22	2.75	1.53	-0.27	-2.54
R148	-1.05	-0.06	-1.11	20.17	11.33	31.5	-24.49	-11.02	-35.51	-0.42	-5.53
F1509A											
K1419	-3	-1.52	-4.52	-46.8	-9.88	-56.69	47.29	12.05	59.34	-0.63	-2.49
I1420	-2.22	-0.93	-3.15	-1.54	1.09	-0.45	1.51	0.03	1.55	-0.38	-2.43
T1422	-0.93	-0.41	-1.34	-3.42	0.13	-3.29	3.15	0.27	3.42	-0.34	-1.55
P1462	-0.67	-0.22	-0.9	-10.06	8.93	-1.13	10.14	-9.04	1.1	-0.11	-1.03
K1463	-0.64	-0.48	-1.11	-45.37	-13.25	-58.62	45.15	13.66	58.81	-0.17	-1.09
H1464	-1.66	-0.33	-1.99	-4.61	-4.48	-9.09	4.44	4.7	9.14	-0.31	-2.26
W1526	-2.76	-0.17	-2.93	-2.27	1.82	-0.45	3.07	-1.46	1.61	-0.47	-2.24
V1532	-1.41	-0.48	-1.89	-0.44	-1.21	-1.64	0.52	1.4	1.92	-0.19	-1.8
N1533	-1.42	-0.52	-1.94	-4.35	-1.87	-6.22	4.32	1.48	5.8	-0.19	-2.55
F1536	-6.77	-1.14	-7.91	-1.74	-3.43	-5.17	2.77	4.51	7.29	-0.86	-6.65
V1537	-1.91	-0.44	-2.36	-0.74	2.5	1.76	0.74	-1.83	-1.09	-0.22	-1.9
D1539	0.78	-0.13	0.66	-20.02	3.04	-16.98	17.34	-2.88	14.46	-0.15	-2
Y1589	-0.48	-0.02	-0.5	-5.79	0.11	-5.67	4.84	-0.09	4.75	-0.23	-1.66
N7	-1.78	-1.79	-3.57	0.81	-5.61	-4.8	0.59	6.79	7.38	-0.36	-1.36
N8	-1.87	-0.95	-2.82	-4.49	1.19	-3.29	5.36	-1.41	3.96	-0.24	-2.39
V9	-0.71	-0.75	-1.46	1.02	-3.37	-2.35	-1.05	3.85	2.8	-0.07	-1.08
L140	-3.01	-0.23	-3.24	1.46	-2.78	-1.32	-1.33	3.04	1.71	-0.38	-3.23
S142	-0.21	-0.25	-0.46	0.85	-7.52	-6.67	-1.18	7.53	6.35	-0.21	-0.98
P144	-1.16	-0.3	-1.47	15.92	-20.97	-5.06	-15.54	20.39	4.85	-0.2	-1.87
V146	-1.81	-0.23	-2.04	1.21	-2.51	-1.3	-1.18	2.71	1.54	-0.26	-2.07
R148	-0.57	-0.05	-0.62	19.54	10.77	30.31	-23.65	-10.49	-34.15	-0.39	-4.84
Y1607A											
K1415	0.01	-0.06	-0.04	-42.34	-8.71	-51.06	41.36	8.79	50.14	-0.04	-1
K1419	-1.41	-0.75	-2.16	-38.36	-9.53	-47.89	38.29	10.25	48.53	-0.39	-1.91
I1420	-2.56	-0.72	-3.28	-1.35	-2.23	-3.58	1.28	2.33	3.61	-0.43	-3.69
T1422	-1.38	-0.63	-2	-1.68	-0.62	-2.3	2.17	0.96	3.12	-0.22	-1.4
F1536	-6.87	-1.09	-7.96	-1.75	-2.62	-4.37	2.68	3.71	6.39	-0.87	-6.8
V1537	-2.08	-0.4	-2.48	-0.39	1.55	1.16	0.43	-0.95	-0.53	-0.25	-2.1
D1539	0.38	-0.18	0.2	-29.41	0.73	-28.68	27.35	-0.52	26.82	-0.23	-1.88
Y1582	-1.69	-0.09	-1.79	-2.01	-5.19	-7.19	2.44	4.76	7.21	-0.27	-2.05
Y1589	-2.83	-0.08	-2.91	-4.19	0.67	-3.51	4.28	-0.62	3.66	-0.46	-3.22
N8	-1.25	-0.69	-1.94	-2.65	0.81	-1.84	3.73	-1.1	2.63	-0.14	-1.3
I31	-1.44	-0.31	-1.75	1.09	-1.57	-0.48	-1.06	1.81	0.74	-0.24	-1.73
R69	-4.7	-0.66	-5.37	39.47	9.52	48.99	-36.43	-8.59	-45.02	-0.59	-1.99
Y112	-2.9	-0.12	-3.03	0.79	-1.76	-0.97	0.35	1.84	2.19	-0.29	-2.09
L140	-1.8	-0.25	-2.05	1.29	-2.43	-1.14	-1.15	2.87	1.72	-0.28	-1.74
N143	-2.38	-0.62	-3.01	-11.92	2.33	-9.6	10.78	-1.46	9.31	-0.36	-3.65
P144	-1.49	-0.47	-1.96	15.95	-22.14	-6.19	-15.56	21.44	5.89	-0.25	-2.52
V146	-1.93	-0.29	-2.23	1.28	-2.99	-1.71	-1.24	3.28	2.04	-0.27	-2.17
R148	-0.28	-0.04	-0.32	19.9	11.36	31.26	-24.67	-11.06	-35.73	-0.36	-5.15
V94A											
K1419	-2.65	-1.09	-3.74	-57.46	-10.91	-68.37	57.79	12.44	70.23	-0.62	-2.5
I1420	-2.72	-0.76	-3.48	-1.43	0.12	-1.3	1.4	1.09	2.49	-0.42	-2.7
T1422	-1.17	-0.23	-1.4	-1.88	0.16	-1.72	2.35	0.21	2.55	-0.34	-0.91
P1462	-0.8	-0.25	-1.05	-10.19	8.9	-1.29	10.36	-9.08	1.28	-0.11	-1.18
K1463	-0.84	-0.45	-1.29	-47.79	-12.86	-60.65	47.65	13.5	61.15	-0.24	-1.03

H1464	-2.17	-0.23	-2.4	-0.83	-8.04	-8.87	1.8	6.66	8.46	-0.26	-3.07
S1465	0.34	-0.2	0.14	-9.2	-3.54	-12.74	6.37	2.48	8.85	-0.09	-3.84
K1535	-2.03	-0.79	-2.82	-32.59	-7.12	-39.71	33.08	8.73	41.81	-0.49	-1.22
F1536	-6.7	-1.12	-7.82	-1.72	-1.83	-3.55	2.77	3.04	5.81	-0.87	-6.43
V1537	-1.28	-0.33	-1.6	-0.5	1.58	1.08	0.49	-1.04	-0.55	-0.19	-1.27
P1538	-0.86	-0.19	-1.05	0.31	2.3	2.61	-0.06	-2.24	-2.3	-0.13	-0.87
D1539	0.53	-0.15	0.38	-25.07	1.67	-23.4	23.06	-1.63	21.44	-0.16	-1.74
Y1589	-1.37	-0.03	-1.4	-5.51	0.68	-4.82	4.98	-0.66	4.33	-0.3	-2.2
N8	-1.33	-0.69	-2.02	-2.84	1.05	-1.79	3.99	-1.24	2.75	-0.15	-1.21
V9	-0.72	-0.67	-1.39	1.1	-3.02	-1.92	-1.12	3.45	2.33	-0.07	-1.05
V92	-1.86	-0.26	-2.11	1.44	-0.92	0.53	-1.36	1.2	-0.16	-0.32	-2.07
Y112	-2.43	-0.14	-2.57	1.19	-1.61	-0.42	-0.52	1.77	1.24	-0.22	-1.97
L140	-2.09	-0.19	-2.29	1.34	-2.66	-1.32	-1.34	2.98	1.64	-0.29	-2.25
P144	-1.45	-0.22	-1.67	16.63	-24.64	-8.01	-16.25	23.65	7.4	-0.27	-2.55
V146	-1.96	-0.3	-2.27	1.32	-2.84	-1.52	-1.26	3.08	1.82	-0.28	-2.24
R148	-0.66	-0.05	-0.71	21.76	11.33	33.08	-25.22	-11.03	-36.25	-0.4	-4.28
V10A											
K1415	-0.21	-0.12	-0.34	-46.07	-10.43	-56.5	45.33	10.65	55.98	-0.06	-0.91
Y1418	-0.46	-0.14	-0.6	-0.95	-3.83	-4.78	1.09	3.14	4.23	-0.13	-1.27
K1419	-3.12	-1.69	-4.81	-65.86	-8.99	-74.85	65.01	11.34	76.35	-0.75	-4.06
I1420	-2.24	-0.91	-3.15	-1.41	-0.51	-1.92	1.4	1.35	2.75	-0.39	-2.72
W1526	-1.96	-0.07	-2.03	-1.67	0.37	-1.3	2.75	-0.17	2.58	-0.37	-1.12
V1532	-1.44	-0.52	-1.97	-0.08	-0.98	-1.05	0.1	1.07	1.17	-0.17	-2.02
N1533	-1.72	-0.46	-2.18	-2.23	-2.67	-4.89	3.68	2.39	6.07	-0.2	-1.22
F1536	-6.81	-1.13	-7.94	-1.37	-3.63	-5	2.7	4.61	7.3	-0.88	-6.51
V1537	-2.01	-0.41	-2.41	-0.48	1.74	1.26	0.49	-1.18	-0.69	-0.23	-2.07
Y1589	-1.93	-0.03	-1.96	-2.16	0.91	-1.25	3.27	-0.87	2.4	-0.33	-1.13
N8	-2.04	-0.67	-2.71	-1.56	1.71	0.15	2.73	-1.13	1.6	-0.32	-1.28
A48	-0.37	-0.04	-0.41	2.55	-7.73	-5.17	-2.52	7.2	4.68	-0.07	-0.97
E49	-0.09	-0.12	-0.22	-84.14	-12.78	-96.93	83.54	12.44	95.97	-0.17	-1.34
V92	-1.27	-0.13	-1.4	1.46	-0.77	0.69	-1.39	0.96	-0.43	-0.2	-1.33
V109	-1.24	-0.22	-1.46	1.05	0.81	1.86	-1.08	-0.92	-2	-0.1	-1.7
Y112	-2.56	-0.13	-2.69	1.47	-1.62	-0.15	-0.72	1.69	0.97	-0.17	-2.04
L140	-1.75	-0.17	-1.92	1.2	-2	-0.81	-1.15	2.39	1.24	-0.23	-1.72
S142	-1.87	-0.94	-2.81	-0.27	-6.08	-6.35	0.51	6.75	7.25	-0.45	-2.36
N143	-1.1	-0.61	-1.71	-7.72	1.15	-6.56	7.11	-0.19	6.92	-0.23	-1.58
P144	-1.8	-0.55	-2.34	16.94	-24.19	-7.25	-16.46	23.03	6.57	-0.31	-3.33
V146	-1.74	-0.27	-2	1.38	-3.6	-2.22	-1.31	3.76	2.45	-0.26	-2.04
R148	-0.65	-0.03	-0.68	26.39	11.13	37.52	-27.94	-10.88	-38.81	-0.25	-2.22
V92A											
I1420	-1.04	-0.07	-1.1	-0.87	0.53	-0.35	0.85	-0.38	0.47	-0.1	-1.08
F1536	-5.98	-1.12	-7.1	-1.4	-3.26	-4.66	2.24	4.81	7.05	-0.8	-5.52
V1537	-1.77	-0.46	-2.23	-0.36	2.6	2.24	0.34	-1.74	-1.4	-0.23	-1.62
D1539	1.13	-0.12	1	-29.41	2.37	-27.04	25.51	-2.17	23.34	-0.13	-2.82
V6	-1.18	-0.97	-2.15	1.15	-2.78	-1.62	-1.12	4.08	2.96	-0.2	-1.01
N7	-1.17	-0.83	-2	2.88	-6.84	-3.96	-1.84	7.05	5.21	-0.25	-1
I31	-1.2	-0.4	-1.6	1.34	-1.36	-0.02	-1.25	1.78	0.53	-0.23	-1.32
N143	-2.85	-0.44	-3.29	-9.37	1.68	-7.7	10.57	-0.77	9.8	-0.59	-1.78
V146	-1.45	-0.16	-1.61	1.26	-2.52	-1.26	-1.22	2.82	1.59	-0.22	-1.49

R148	-0.76	-0.05	-0.8	26.38	12.01	38.39	-30.67	-11.7	-42.36	-0.46	-5.24
Y112A											
I1420	-1.74	-0.22	-1.96	-0.9	0.89	-0.01	0.88	-0.67	0.2	-0.19	-1.96
W1526	-1.8	-0.09	-1.89	-0.72	-0.48	-1.2	1.57	0.62	2.19	-0.29	-1.19
F1536	-6.55	-1.05	-7.6	-2.02	-2.01	-4.03	2.64	3.25	5.89	-0.83	-6.56
V1537	-1.58	-0.36	-1.94	-0.45	1.66	1.21	0.43	-1.12	-0.69	-0.21	-1.63
D1539	0.86	-0.13	0.73	-28.24	1.93	-26.3	25.29	-1.81	23.47	-0.2	-2.3
Y1589	-0.87	-0.03	-0.9	-7.21	0.37	-6.84	5.37	-0.35	5.02	-0.29	-3.01
N8	-1.48	-0.72	-2.2	-3.46	1	-2.46	4.8	-1.35	3.45	-0.18	-1.39
V9	-0.78	-0.79	-1.56	1.08	-3.96	-2.88	-1.12	4.48	3.37	-0.08	-1.15
S142	-1.59	-1.19	-2.77	1.35	-7.93	-6.58	-0.16	8.98	8.81	-0.42	-0.96
N143	-2.1	-0.7	-2.8	-7.87	1.47	-6.39	8.12	-0.88	7.23	-0.34	-2.29
P144	-2.2	-0.63	-2.82	16.51	-20.6	-4.09	-16	20.28	4.28	-0.31	-2.95
V146	-1.3	-0.21	-1.51	1.23	-3.54	-2.31	-1.17	3.84	2.67	-0.24	-1.4
R148	0.33	-0.03	0.3	22.8	11.86	34.66	-28.18	-11.58	-39.77	-0.31	-5.12

Table S3. Hydrogen bonds between CIA/ASF1 and DBD for all systems at the binding site 1 in the last 20 ns. For every system, the cut-off used for hydrogen bond distance and angle is 3.5 Å and 120°, respectively. The percent hydrogen bond occupancy that hydrogen bonds formed during the MD simulations is produced by the CPPTRAJ module of AMBER14. In addition, each hydrogen bond distance is measured between the heavy atom of donor and the heavy atom of acceptor.

#Acceptor	DonorH	Donor	Occupancy	Distance (Å)
WT				
ASP_1539@OD1	ARG_148@HH12	ARG_148@NH1	0.3797	2.9068
ASP_1539@OD2	ARG_148@HH22	ARG_148@NH2	0.3651	2.8988
ASP_1539@OD2	ARG_148@HH12	ARG_148@NH1	0.3404	2.9145
GLU_29@OE2	TYR_1589@HH	TYR_1589@OH	0.3376	2.7138
ASP_1539@OD1	ARG_148@HH22	ARG_148@NH2	0.3374	2.9175
PHE_1536@HZ	VAL_9@HB	VAL_9@CB	0.3223	3.3096
GLU_29@OE1	TYR_1589@HH	TYR_1589@OH	0.2596	2.7162
ASP_1539@CG	ARG_148@HH12	ARG_148@NH1	0.257	3.3652
GLU_29@CD	TYR_1589@HH	TYR_1589@OH	0.2254	3.2955
ILE_1420@O	ASN_143@HD21	ASN_143@ND2	0.221	2.9546
ASP_1539@CG	ARG_148@HH22	ARG_148@NH2	0.2047	3.384
F1536A				
ASP_1416@OD2	SER_47@HG	SER_47@OG	0.7855	2.6271
ASP_1416@OD1	ASH_88@HD2	ASH_88@OD2	0.7204	2.6179
ASP_1416@OD2	ALA_48@H	ALA_48@N	0.6173	3.0352
ASP_1416@CG	ASH_88@HD2	ASH_88@OD2	0.5943	3.1942
TYR_1459@O	ASN_114@HD22	ASN_114@ND2	0.5896	2.9069
GLU_116@OE2	HIE_1464@HE2	HIE_1464@NE2	0.4979	2.9558
GLU_116@OE1	HIE_1464@HE2	HIE_1464@NE2	0.4879	2.9605
GLU_49@H	LYS_1419@HD3	LYS_1419@CD	0.3823	3.2495
GLU_116@CD	HIE_1464@HE2	HIE_1464@NE2	0.3039	3.3548
ASP_1416@HB2	VAL_92@H	VAL_92@N	0.2273	3.1527
ASN_114@HD22	ASN_1458@HA	ASN_1458@CA	0.2152	3.3152
Y1589A				
LYS_1535@O	ARG_148@HH22	ARG_148@NH2	0.4833	2.8629
ILE_1420@O	ASN_143@HD21	ASN_143@ND2	0.3635	2.9587
PHE_1536@HZ	VAL_9@HB	VAL_9@CB	0.3304	3.3111
ASP_1539@OD1	ARG_148@HH22	ARG_148@NH2	0.2138	2.911
ASP_1539@OD2	ARG_148@HH12	ARG_148@NH1	0.2085	2.8811
ASP_1539@OD2	ARG_148@HH22	ARG_148@NH2	0.1881	2.9168
ASP_1539@OD1	ARG_148@HH12	ARG_148@NH1	0.1821	2.9134
H1610A				
ASN_7@O	ASN_1533@H	ASN_1533@N	0.5701	3.0806
ASP_1539@OD2	ARG_148@HH12	ARG_148@NH1	0.5279	2.8989
ASP_1539@OD2	ARG_148@HH22	ARG_148@NH2	0.5199	2.9152
ASP_1539@OD1	ARG_148@HH22	ARG_148@NH2	0.5166	2.894
ASP_1539@OD1	ARG_148@HH12	ARG_148@NH1	0.5074	2.899
PHE_1536@HZ	VAL_9@HB	VAL_9@CB	0.4396	3.2814
ILE_1420@O	ASN_143@HD21	ASN_143@ND2	0.3966	2.9578
ASN_8@OD1	ASN_1533@HD21	ASN_1533@ND2	0.3916	2.9372
ASP_1539@CG	ARG_148@HH12	ARG_148@NH1	0.3428	3.38
ASP_1539@CG	ARG_148@HH22	ARG_148@NH2	0.3253	3.387

F1509A				
ASN_7@O	ASN_1533@H	ASN_1533@N	0.6995	3.0705
ASN_8@OD1	ASN_1533@HD21	ASN_1533@ND2	0.4933	2.9258
ASP_1539@OD2	ARG_148@HH22	ARG_148@NH2	0.4547	2.8855
ASP_1539@OD1	ARG_148@HH12	ARG_148@NH1	0.4492	2.9022
ASP_1539@OD2	ARG_148@HH12	ARG_148@NH1	0.446	2.9018
ASP_1539@OD1	ARG_148@HH22	ARG_148@NH2	0.4405	2.8953
THR_1422@OG1	SER_142@HG	SER_142@OG	0.4368	2.7813
PHE_1536@HZ	VAL_9@HB	VAL_9@CB	0.4002	3.2966
ASN_114@HB2	ILE_1420@HG12	ILE_1420@CG1	0.3028	3.299
ASP_1539@CG	ARG_148@HH12	ARG_148@NH1	0.2965	3.3794
THR_1422@HG1	SER_142@HG	SER_142@OG	0.2883	3.3008
ASP_1539@CG	ARG_148@HH22	ARG_148@NH2	0.2567	3.388
ILE_1420@HG12	ASN_114@HB2	ASN_114@CB	0.2097	3.2636
GLU_29@OE2	TYR_1589@HH	TYR_1589@OH	0.2077	2.7471
GLU_29@CD	TYR_1589@HH	TYR_1589@OH	0.205	3.2722
Y1607A				
ASP_1539@OD1	ARG_148@HH12	ARG_148@NH1	0.5185	2.8836
ASP_1539@OD2	ARG_148@HH22	ARG_148@NH2	0.5095	2.8983
ASP_1539@OD1	ARG_148@HH22	ARG_148@NH2	0.5072	2.9039
ASP_1539@OD2	ARG_148@HH12	ARG_148@NH1	0.484	2.8955
ILE_1420@O	ASN_143@HD21	ASN_143@ND2	0.4522	2.9127
ASP_1539@CG	ARG_148@HH12	ARG_148@NH1	0.3857	3.3607
ASP_1539@CG	ARG_148@HH22	ARG_148@NH2	0.3553	3.3772
GLU_29@OE2	TYR_1589@HH	TYR_1589@OH	0.3445	2.7111
PHE_1536@HZ	VAL_9@HB	VAL_9@CB	0.3407	3.3045
GLU_29@OE1	TYR_1589@HH	TYR_1589@OH	0.2742	2.708
TYR_1582@OH	GLN_5@HE22	GLN_5@NE2	0.267	3.1446
GLU_29@CD	TYR_1589@HH	TYR_1589@OH	0.2482	3.3292
Y112A				
ASN_7@O	ASN_1533@H	ASN_1533@N	0.9067	3.0208
PRO_1531@O	ASN_8@HD21	ASN_8@ND2	0.8063	2.9184
VAL_9@H	PHE_1536@HE1	PHE_1536@CE1	0.246	3.2893
TYR_1418@O	SER_142@HG	SER_142@OG	0.2172	2.7232
V10A				
ASN_7@O	ASN_1533@H	ASN_1533@N	0.9067	3.0208
PRO_1531@O	ASN_8@HD21	ASN_8@ND2	0.8063	2.9184
VAL_9@H	PHE_1536@HE1	PHE_1536@CE1	0.246	3.2893
TYR_1418@O	SER_142@HG	SER_142@OG	0.2172	2.7232
LEU_140@HD13	ILE_1420@HA	ILE_1420@CA	0.1915	3.2379
LEU_140@HD12	ILE_1420@HA	ILE_1420@CA	0.1905	3.2397
V92A				
ASP_1539@OD1	ARG_148@HH22	ARG_148@NH2	0.5697	2.8826
ASP_1539@OD2	ARG_148@HH12	ARG_148@NH1	0.5685	2.8838
ASP_1539@OD1	ARG_148@HH12	ARG_148@NH1	0.5282	2.8937
ASP_1539@OD2	ARG_148@HH22	ARG_148@NH2	0.5157	2.8908
ASN_7@O	ASN_1533@HD21	ASN_1533@ND2	0.511	2.899
ASP_1539@CG	ARG_148@HH12	ARG_148@NH1	0.447	3.361
ASP_1539@CG	ARG_148@HH22	ARG_148@NH2	0.3832	3.3746

ILE_31@O	TYR_1589@HH	TYR_1589@OH	0.2774	2.8145
PHE_1536@HB3	VAL_6@HB	VAL_6@CB	0.2237	3.3259
V94A				
ASP_1539@OD2	ARG_148@HH12	ARG_148@NH1	0.4406	2.8998
ASP_1539@OD1	ARG_148@HH22	ARG_148@NH2	0.4358	2.9061
ASP_1539@OD2	ARG_148@HH22	ARG_148@NH2	0.4173	2.9093
ASP_1539@OD1	ARG_148@HH12	ARG_148@NH1	0.4104	2.9008
PHE_1536@HZ	VAL_9@HB	VAL_9@CB	0.3787	3.3133
ASP_1539@CG	ARG_148@HH12	ARG_148@NH1	0.3133	3.3763
ASP_1539@CG	ARG_148@HH22	ARG_148@NH2	0.2708	3.3817
ILE_1420@O	ASN_143@HD21	ASN_143@ND2	0.246	2.9383