Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Materials

Table S1. Binding free energy contributions of the key binding-site residues calculated from the binding energy decomposition for CXCR2 (kcal/mol)

	CXCR2				
	ΔE_{vdw}	ΔE_{ele}	ΔG_{GB}	ΔG_{SA}	ΔG_{bind}
Leu20	-3.62	0.22	-0.04	-0.8	-4.26
Thr28	-8.52	-1.68	2.78	-1.46	-8.88
Leu29	-3.86	1.02	-0.42	-0.38	-3.66
Phe32	-0.92	-0.20	0.36	-0.08	-0.82
Leu33	-3.70	-1.56	1.76	-0.76	-4.26
Pro38	-9.02	-0.60	0.82	-1.24	-10.02
Cys39	-5.46	-1.32	1.58	-0.90	-6.10
Glu40	-2.68	-14.88	15.08	-0.76	-3.26
Val187	-3.66	-1.64	1.66	-0.86	-4.50
Tyr188	-4.91	-0.62	1.48	-1.20	-10.14
Ser189	-5.38	-1.54	2.10	-0.76	-5.58
Asn191	-4.12	-2.38	2.34	-0.80	-4.96
Asn203	-1.84	0.26	0.54	-0.48	-1.50
Gln280	-2.22	-1.15	2.38	-0.60	-2.71
Gln283	-5.50	-2.94	2.82	-0.86	-6.48
Glu284	-4.12	-3.66	3.04	-0.44	-5.16

Table S2. Binding free energy contributions of the key binding-site residues calculated from the binding energy decomposition for MIF monomer (kcal/mol)

	MIF				
	ΔE_{vdw}	ΔE_{ele}	ΔG_{GB}	ΔG_{SA}	ΔG_{bind}
Arg11	-1.20	3.80	-3.24	-0.34	-0.96
Asp44	-2.14	-4.38	4.56	-0.66	-2.60
Gln45	-9.02	-0.92	2.58	-1.02	-8.38
Leu46	-7.46	-0.96	1.14	-1.28	-8.58
Phe49	-6.20	-0.92	1.22	-0.52	-6.42
Ser60	4.36	-5.70	1.48	0.02	-16.56
His62	-7.42	-0.16	1.16	0.36	35.52
Ile64	5.42	13.46	0.02	0.34	31.92
Gly68	2.42	94.40	2.60	-1.54	43.68
Asn72	-4.82	-37.00	-1.78	-0.40	-51.16
Arg86	-2.96	-104.88	5.74	0.94	-61.16
Arg93	-3.10	-102.74	16.72	-0.08	-72.34
Asp100	1.08	-1.44	-28.42	0.60	-50.30
Trp108	-16.98	0.10	2.22	-0.44	19.98
Asn110	-0.56	-39.58	-0.84	0.50	-16.40

Table S3. Binding free energy contributions of the key binding-site residues calculated from the binding energy decomposition for CXCR2 of mutant (kcal/mol)

	CXCR2				
	ΔE_{vdw}	ΔE_{ele}	ΔG_{GB}	ΔG_{SA}	ΔG_{bind}
Leu20	0.00	0.10	-0.10	0.00	0.00
Thr28	-5.88	-1.04	1.52	-0.70	-6.08
Leu29	-8.14	-4.00	3.20	-1.84	-10.78
Phe32	-6.46	-0.84	1.56	-1.36	-7.12
Leu33	-0.60	0.00	0.10	-0.02	-0.50
Pro38	-8.81	0.06	0.44	-1.52	-9.86
Cys39	-1.18	-0.26	0.54	-0.08	-1.00
Glu40	-1.16	-6.30	6.96	-0.20	-0.70
Val187	-0.70	-0.06	0.20	-0.18	-0.74
Tyr188	-0.94	0.16	0.08	-0.14	-0.82
Ser189	-0.90	-0.46	0.66	-0.22	-0.92
Asn191	-0.66	0.04	0.22	-0.10	-0.50
Asn203	-0.18	-0.06	0.26	0.00	0.02
Gln280	-2.58	0.16	0.72	-0.76	-2.46
Gln283	-7.14	-2.62	2.96	-1.48	-8.28
Glu284	-3.76	-1.66	2.60	-0.36	-3.18

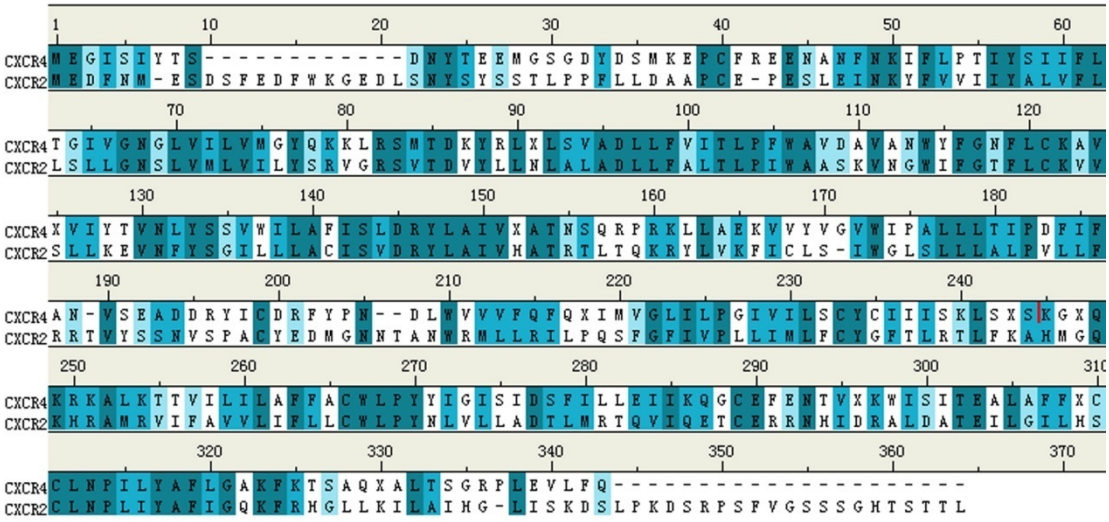


Figure S1. Sequence alignment of CXCR2 (residues 1-339) against that of CXCR4 (PDB ID: 3ODU) used for homology modeling.

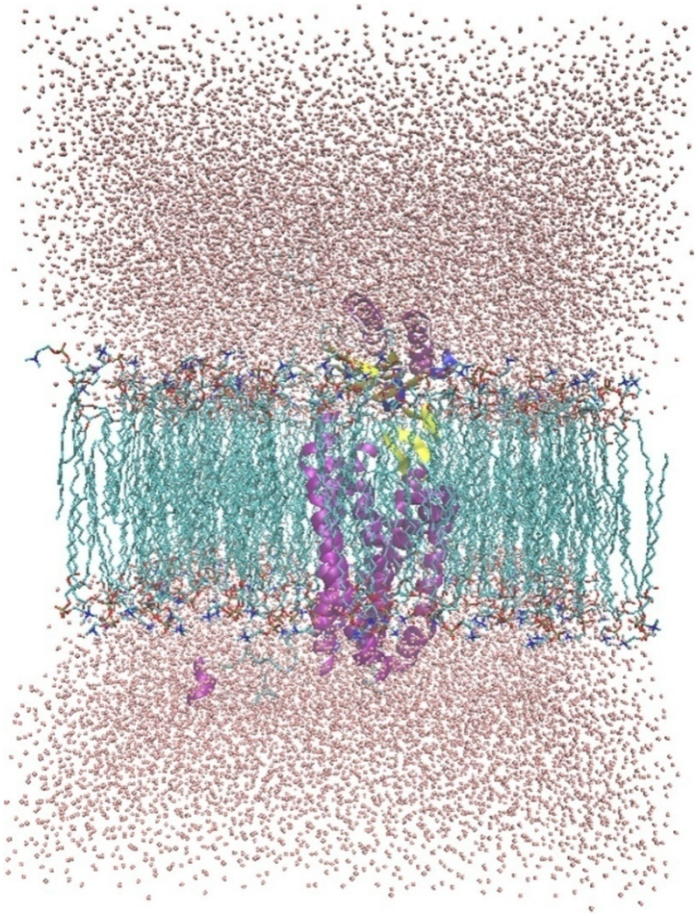


Figure S2. MD simulation box of the MIF-CXCR2 complex, the lipid and water molecules. There are 125121 atoms in the simulation box (Model I was chosen to represent).

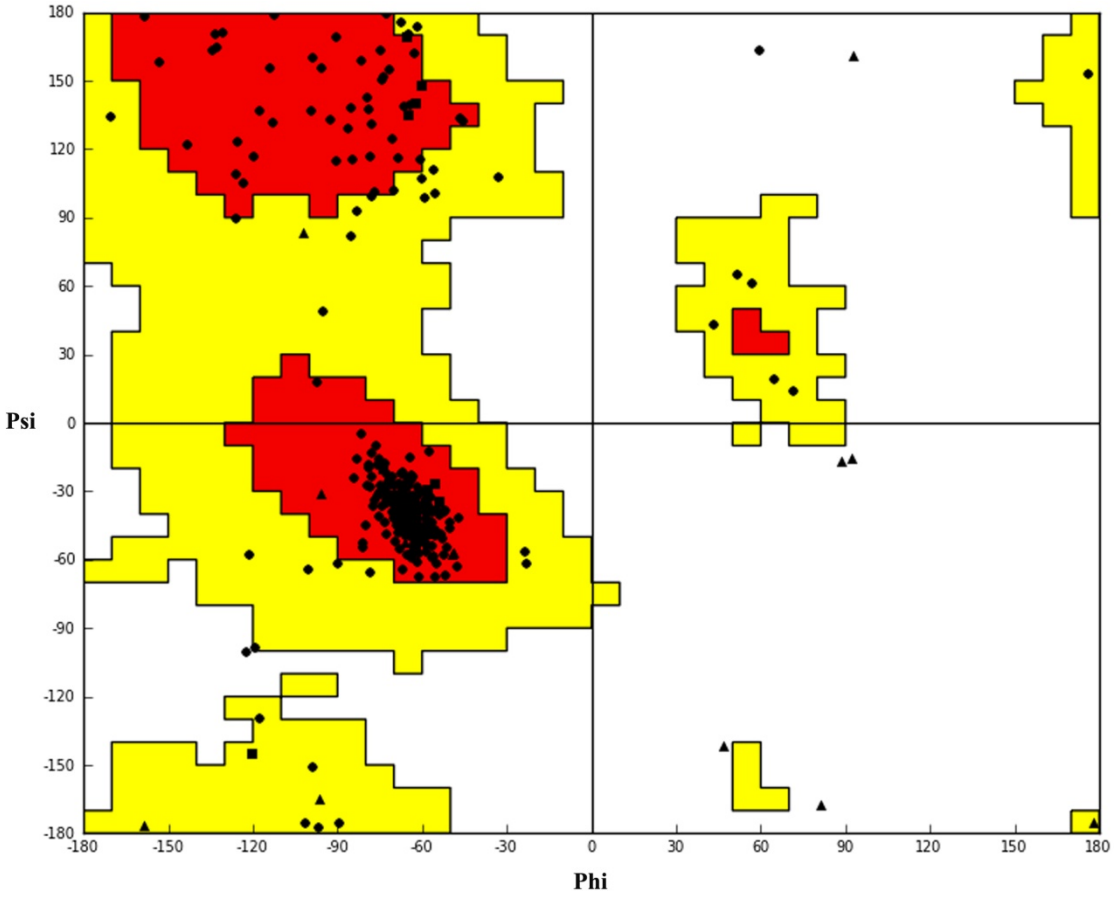


Figure S3. Ramachandran plot of CXCR2 constructed by homology modeling.

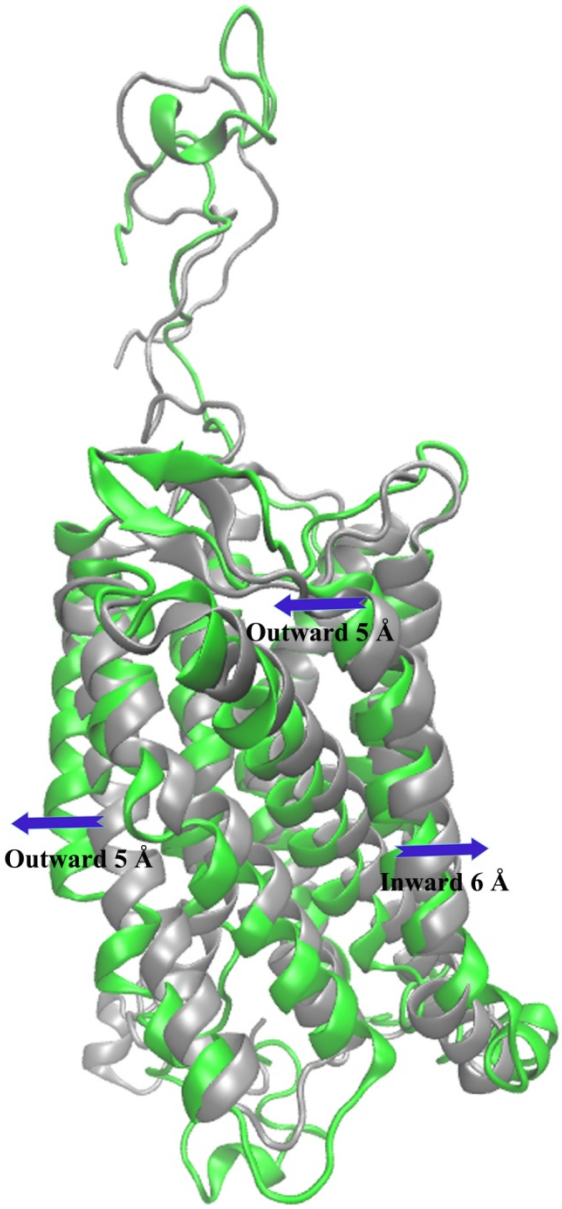
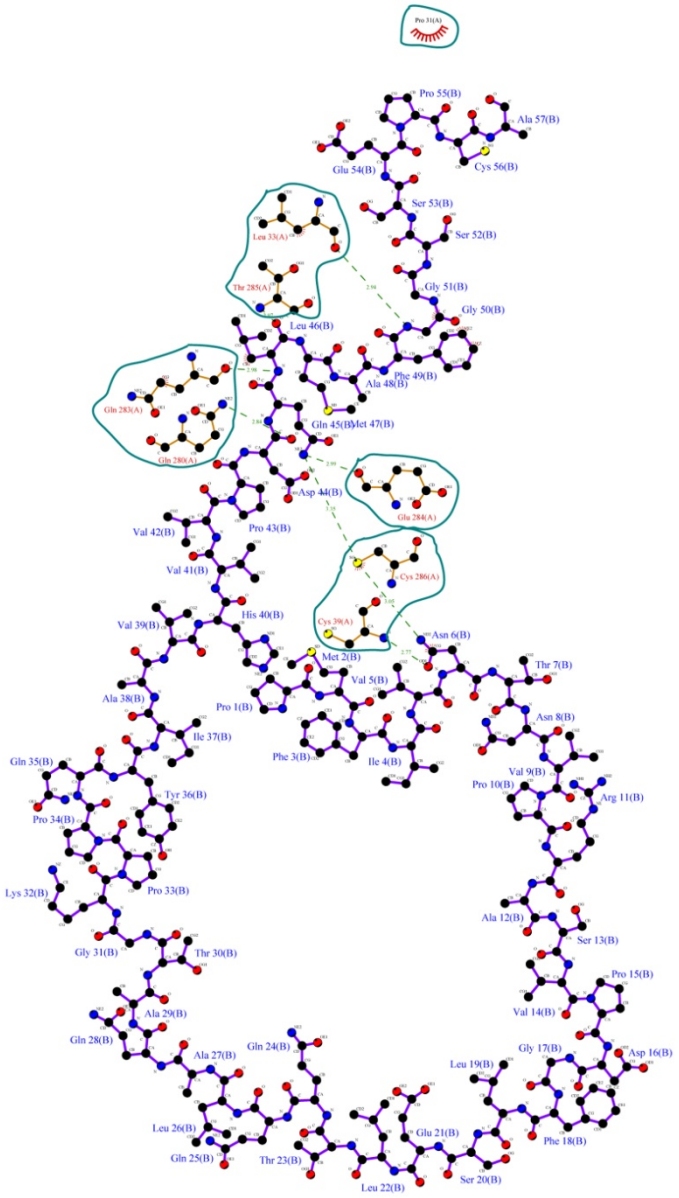


Figure S4. Comparison of the complex structure predicted by protein-protein docking (ribbon colored in gray) and the conformation after last 20 ns MD trajectory (ribbon colored in green). The arrow indicates the movement of TM1, TM4 and TM5.



Key

Ligand bond

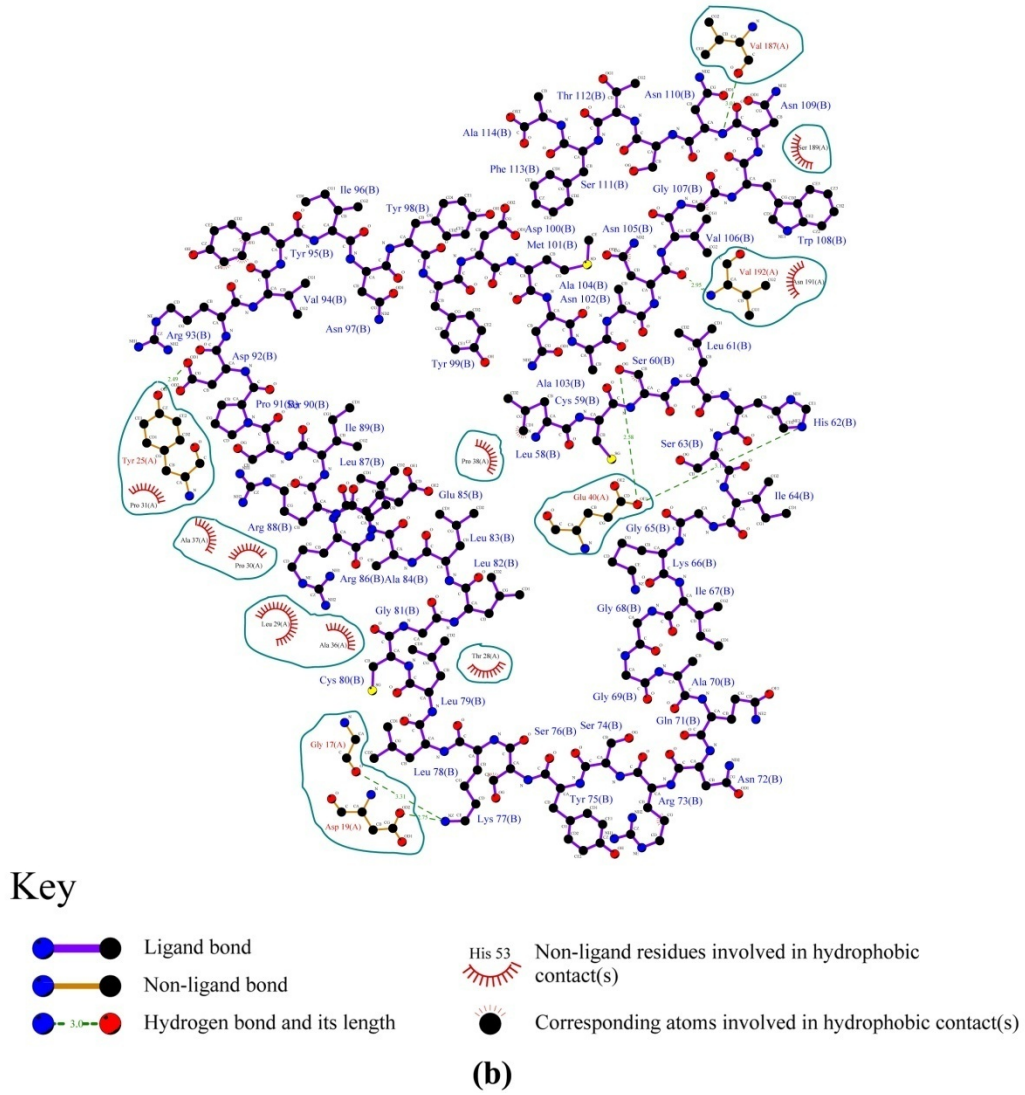
Non-ligand bond

Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

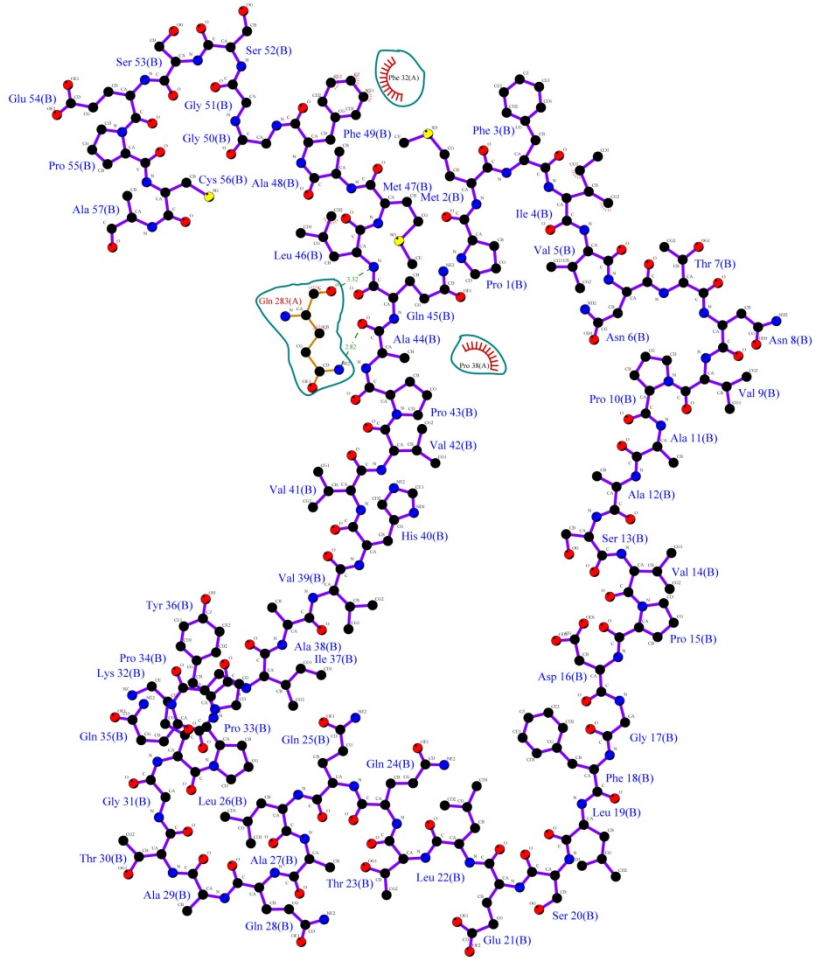
Corresponding atoms involved in hydrophobic contact(s)

(a)



(b)

Figure S5. Schematic depiction of the major interactions of the MIF-CXCR2 averaged structure over the last 10 ns MD trajectory (generated by the LIGPLOT program[1]). (a) and (b) represent residues 1 to 57 and 58 to 114 of MIF respectively.



Key

Ligand bond

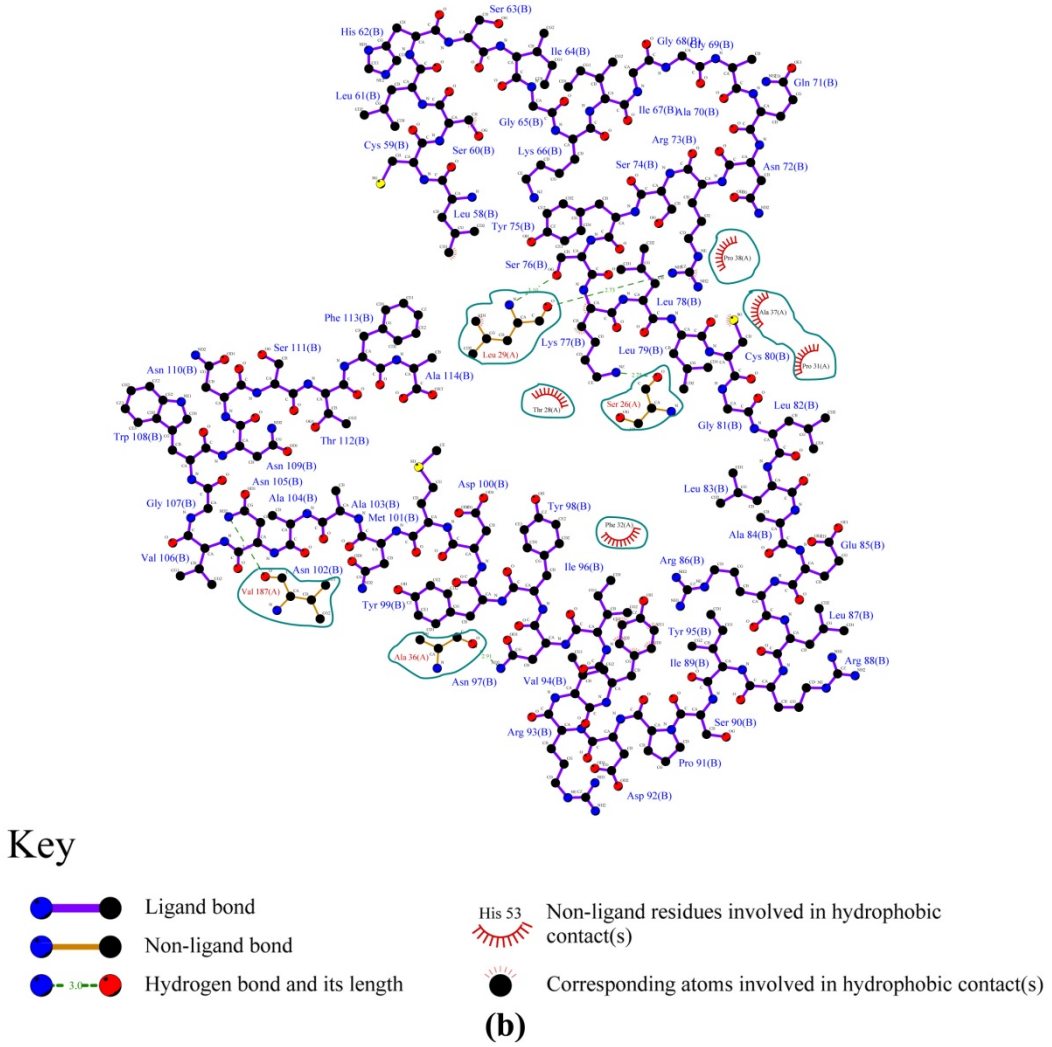
Non-ligand bond

3.0 Hydrogen bond and its length

His 53 Non-ligand residues involved in hydrophobic contact(s)

Corresponding atoms involved in hydrophobic contact(s)

(a)



(b)

Figure S6. Schematic depiction of the major interactions of averaged structure of R11A/D44A-double mutant of MIF with CXCR2 over the last 10 ns MD trajectory (generated by the LIGPLOT program[1]). (a) and (b) represent residues 1 to 57 and 58 to 114 of MIF respectively.

References

1. Wallace, A. C.; Laskowski, R. A.; Thornton, J. M. LIGPLOT: a program to generate schematic diagrams of protein-ligand interactions. *Protein Eng.* **1995,** 8, 127-134.