Supporting Materials

Table S1. Binding free energy contributions of key binding site residues calculated by the MM/GBSA binding energy decomposition analysis for four representative compounds (kcal/mol)

	Inhibitor 3					Inhibitor 5				
	ΔE_{VDW}	ΔE_{ELE}	ΔG_{GB}	ΔG_{SA}	ΔG_{total}	ΔE_{VDW}	ΔE_{ELE}	ΔG_{GB}	ΔG_{SA}	ΔG_{total}
Pro1	-2.14	-3.80	5.02	-0.32	-1.26	-2.02	-3.40	4.60	-0.26	-1.06
Met2	-1.98	0.28	0.20	-0.18	-1.70	-2.60	-0.38	0.52	-0.16	-2.64
Lys32	-0.14	1.24	-1.04	-0.04	0.04	-0.50	-1.08	1.32	-0.20	-0.46
Tyr36	-0.22	0.18	-0.26	0.00	-0.30	-2.54	0.28	0.10	-0.50	-2.66
Hie62	-1.58	0.26	-0.06	-0.04	-1.42	-1.80	-0.06	0.04	-0.06	-1.86
Ser63	-1.18	-1.84	0.44	-0.06	-2.64	-1.36	0.18	0.32	-0.04	-0.90
Ile64	-2.10	-1.30	1.38	-0.24	-2.26	-3.22	-0.04	0.50	-0.52	-3.26
Val106	-2.62	0.30	-0.46	-0.22	-3.00	-2.26	0.08	-0.30	-0.20	-2.68
Phe113	-1.06	-0.10	0.28	-0.18	-1.06	-3.82	0.20	0.52	-0.50	-3.60
Tyr209	-2.70	0.74	-0.42	-0.24	-2.62	-2.80	0.04	0.32	-0.24	-2.68
Ile210	-0.42	-3.00	1.28	-0.04	-2.18	-0.20	0.04	0.02	0.00	-0.14
Asn211	-0.94	-0.64	0.32	-0.04	-1.32	-0.36	-2.62	1.72	-0.04	-1.30

	Inhibitor 11					Inhibitor 13				
	ΔE_{VDW}	ΔE_{ELE}	ΔG_{GB}	ΔG_{SA}	ΔG_{total}	ΔE_{VDW}	ΔE_{ELE}	ΔG_{GB}	ΔG_{SA}	ΔG_{total}
Pro1	-1.18	-14.34	13.92	-0.34	-1.94	-1.38	-7.30	7.86	-0.30	-1.14
Met2	-3.18	-0.12	0.28	-0.18	-3.22	-1.14	0.20	0.08	-0.12	-0.98
Lys32	-1.24	-0.46	0.94	-0.24	-1.02	-1.74	0.18	0.88	-0.46	-1.14
Tyr36	-3.22	0.18	0.28	-0.30	-3.04	-3.34	0.42	-0.16	-0.44	-3.52
Hie62	-2.08	0.62	-0.32	-0.06	-1.84	-0.32	0.20	-0.16	-0.02	-0.30
Ser63	-1.28	-0.10	0.50	-0.02	-0.90	-0.60	-0.14	0.34	-0.04	-0.46
Ile64	-2.78	0.02	0.22	-0.32	-2.82	-3.40	-0.52	0.70	-0.50	-3.70
Val106	-1.90	0.00	-0.10	-0.16	-2.16	-2.60	0.18	-0.46	-0.30	-3.16
Phe113	-1.98	-0.12	0.30	-0.24	-2.02	-4.44	-0.86	0.68	-0.62	-5.22
Tyr209	-2.40	-0.08	0.30	-0.16	-2.36	-4.22	0.86	-0.06	-0.36	-3.78
Ile210	-0.14	-0.04	0.06	0.00	-0.12	-0.70	-2.28	1.06	-0.02	-1.94
Asn211	-0.46	-2.50	1.78	-0.06	-1.24	-0.90	-0.78	0.56	-0.02	-1.16

Table S2. The docking scores and the contributions of the individual energy components for inhibitor 1 and three designed molecules.

Compounds	Score	E_{vdw}	E_{coul}	E_{HBond}	$E_{internal}$	$E_{Sitemap}$
1	-9.28	-29.79	-8.81	-0.19	6.51	-0.06
P1	-9.66	-28.91	-10.27	-0.32	1.00	-0.13
P2	-8.87	-29.78	-7.36	-0.32	3.76	0.00
P3	-8.72	-28.00	-13.97	-0.46	2.76	-0.17

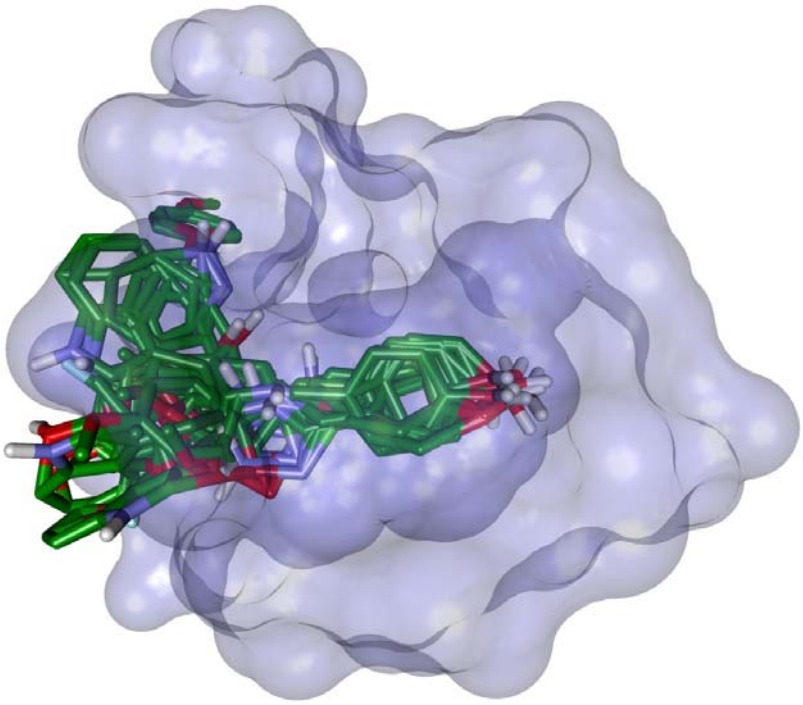

Figure S1. Superposition of the docked binding structure of the 15 inhibitors in the binding pocket of MIF predicted by Glide XP docking calculations.

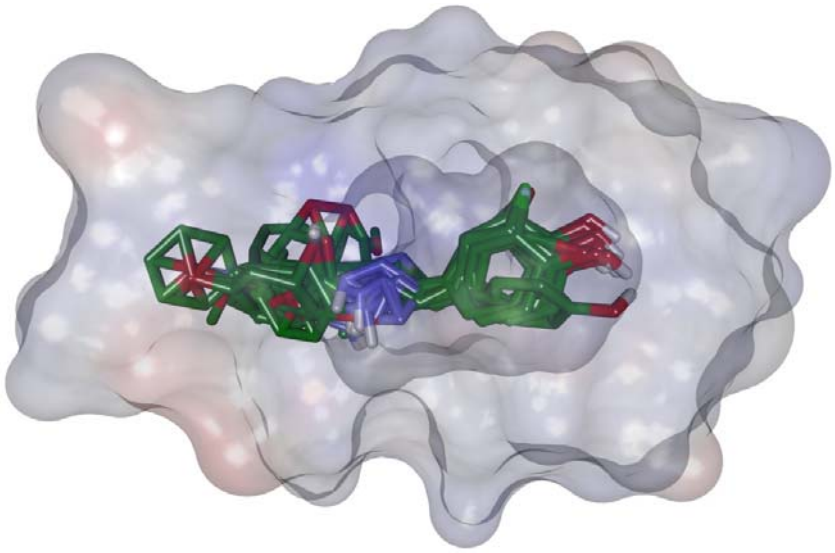

Figure S2. Superposition of the docked binding structures for the 15 inhibitors in the binding pocket of MIF predicted by the IFD protocol.