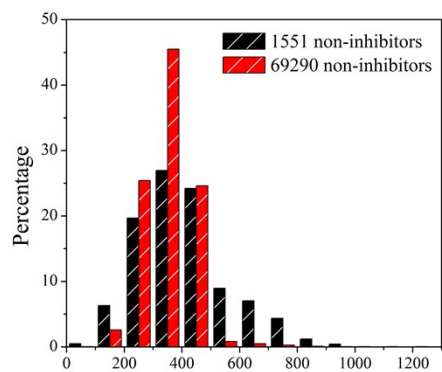


Supporting Information

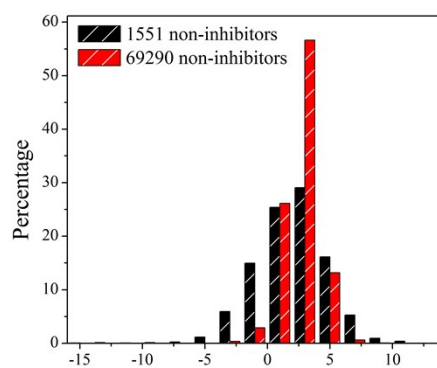
Table S1. Averaged energetic contributions of the most important 10 residues with the highest Times values.

MIEC matrix	Energy term	Inhibitors	Non-inhibitors	Times*	MIEC matrix	Energy term	Inhibitors	Non-inhibitors	Times*
(I)	PRO318	-0.29	-1.13	3.90	(II)	PHE247-vdW	-3.33	-1.67	2.00
	THR251	-0.86	-0.36	2.36		ALA348-vdW	-1.54	-0.73	2.10
	HIS245	-0.62	-0.67	1.08		HIS245-SA	-0.11	-0.18	1.56
	ARG437	-0.26	-1.31	4.98		GLY316-SA	-0.12	-0.24	1.94
	PHE247	-3.30	-1.75	1.89		ARG437-SA	-0.04	-0.19	4.39
	THR343	-0.82	-1.02	1.24		THR343-SA	-0.04	-0.05	1.20
	VAL362	-0.11	-0.23	2.08		PRO318-vdW	-0.32	-1.12	3.53
	ASP422	0.38	0.94	2.46		GLY315-SA	-0.03	-0.03	1.18
	GLY246	-0.56	-0.37	1.50		PRO318-ele	0.07	0.14	1.89
	GLY316	-0.64	-0.94	1.48		LEU342-SA	-0.11	-0.18	1.72
(III)	ILE434	-0.18	-0.58	3.19	(IV)	PHE247-vdW	-3.35	-1.70	1.97
	PRO318	-0.31	-1.15	3.75		ARG437-vdW	-0.25	-1.23	4.99
	THR251	-0.85	-0.36	2.37		GLY316-SA	-0.12	-0.24	1.95
	HIS245	-0.62	-0.64	1.03		ARG437-SA	-0.04	-0.19	4.59
	SER198	-0.01	-0.27	25.69		SER420-vdW	-0.04	-0.16	3.61
	ARG437	-0.29	-1.33	4.60		ALA348-vdW	-1.55	-0.75	2.06
	SER420	-0.03	-0.11	3.70		HIS245-SA	-0.12	-0.18	1.55
	THR343	-0.83	-1.09	1.32		LEU342-SA	-0.10	-0.18	1.73
	ARG218	-0.29	-0.32	1.11		GLY246-vdW	-0.74	-0.45	1.65
	ALA348	-1.55	-0.76	2.04		ILE351-GB	-0.11	-0.06	1.77
(V)	ILE423	-0.01	-0.03	6.48	(VI)	GLY421-vdW	-0.01	-0.06	3.75
	THR343	-0.82	-1.06	1.29		ASP436-vdW	-0.03	-0.15	4.94
	LEU438	0.02	0.06	3.95		PHE247-vdW	-3.32	-1.68	1.98
	SER198	0.003	-0.29	-76.5		ALA348-vdW	-1.53	-0.74	2.07
	VAL288	-0.03	-0.09	3.42		GLY316-SA	-0.12	-0.24	1.94
	ASN197	0.03	0.01	4.69		HIS245-SA	-0.11	-0.18	1.57
	ALA348	-1.55	-0.76	2.04		ILE349-vdW	-0.12	-0.09	1.35
	PRO289	-0.02	-0.06	4.08		LEU342-SA	-0.11	-0.18	1.70
	ASP436	0.004	-0.02	-5.23		SER198-SA	-0.02	-0.08	3.37
	PRO318	-0.28	-1.13	3.97		THR345-vdW	-0.15	-0.13	1.17

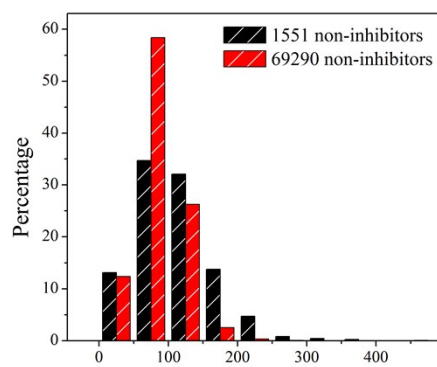
* Times = the maximum value of Inhibitors/Non-inhibitors and Non-inhibitors/Inhibitors



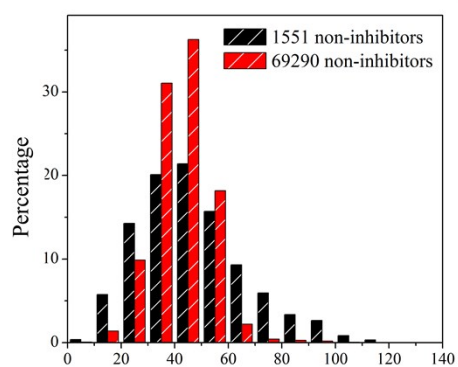
(a) MW



(b) AlogP



(c) PSA



(d) Polar

Figure S1. Distributions of (a) molecular weight (MW), (b) AlogP, (c) polar surface area (PSA) and (d) molecular polarizability (Polar) for the selected non-inhibitors and non-inhibitors in the whole dataset.

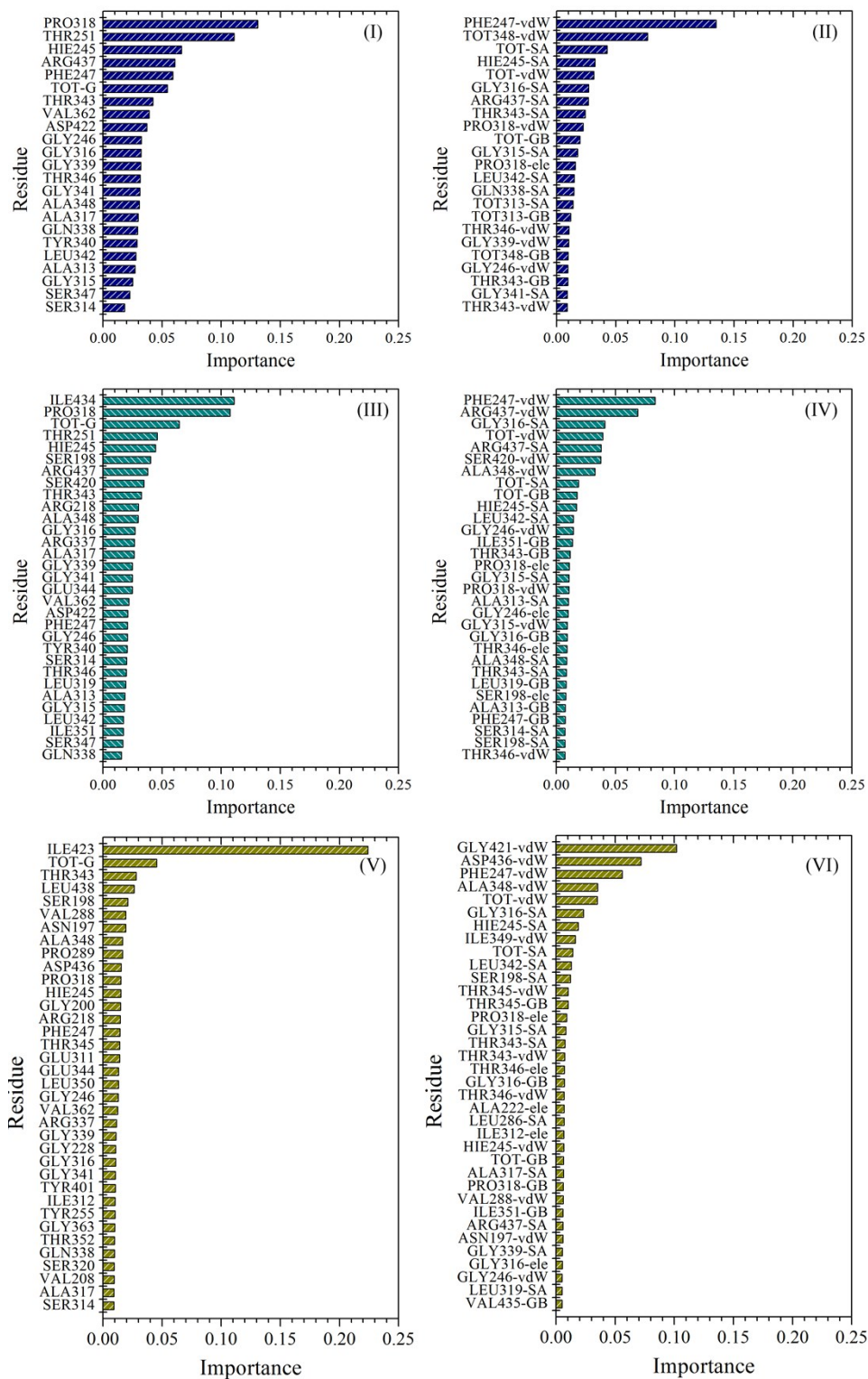


Figure S2. The most important components for each MIEC matrix given by the GBDT algorithm.

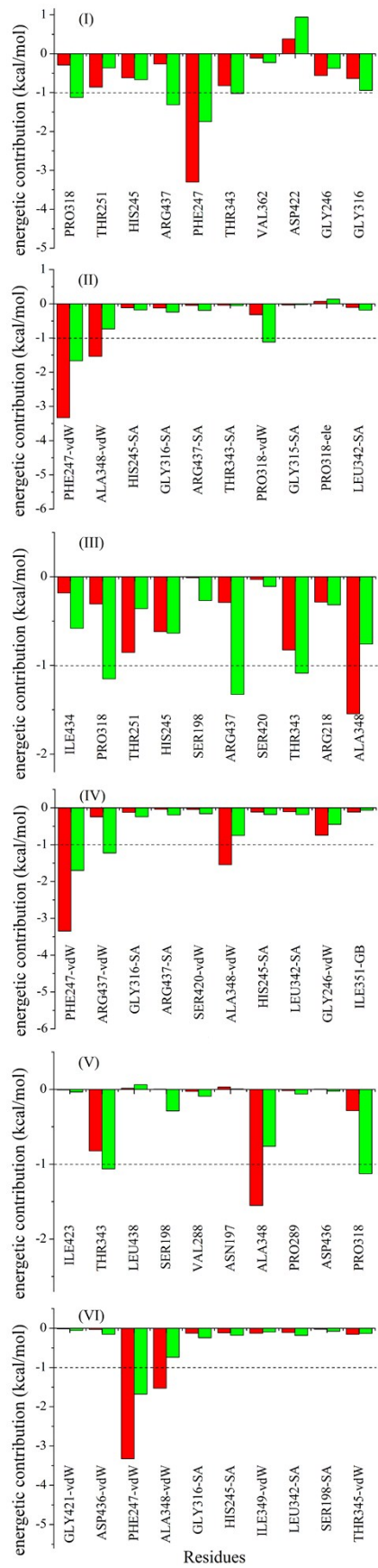


Figure S3. The difference of the energetic contributions of the inhibitors (red) and those of the non-inhibitors (green) for the important residues.