

Table S1 The square of the correlation coefficient (R^2) of the models in the stepwise regression.[#]

Model	Number	Descriptors	R^2
1	1	RDF:PiEN:Cor3D:ori1_82	0.061
2	2	RDF:PiEN:Cor3D:ori1_82, 2DACorr:Polariz_4	0.111
3	3	RDF:PiEN:Cor3D:ori1_82, 2DACorr:Polariz_4, RDF:TotChg:Cor3D:ori1_28	0.146
4	4	RDF:PiEN:Cor3D:ori1_82, 2DACorr:Polariz_4, RDF:TotChg:Cor3D:ori1_28, SurfACorr:HBP:Cor3D:ori1_1,	0.173
5	5	RDF:PiEN:Cor3D:ori1_82,2DACorr:Polariz_4,RDF:TotChg:Cor3D:ori1_28,SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7	0.196
6	6	RDF:PiEN:Cor3D:ori1_82,2DACorr:Polariz_4,RDF:TotChg:Cor3D:ori1_28,SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7, RDF:PiChg:Cor3D:ori1_23	0.226
.....			
13	13	Stereo,SurfACorr:HBP:Cor3D:ori1_2,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10,SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3D:ori1_23,3DACorr:PiEN:Cor3D:ori1_9,RDF:PiEN:Cor3D:ori1_82, 2DACorr:Polariz_4, 3DACorr:Polariz:Cor3D:ori1_2	0.585
14	14	Stereo,SurfACorr:HBP:Cor3D:ori1_2,RDF:SigChg:Cor3D:ori1_33,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10, SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3D:ori1_23,3DACorr:PiEN:Cor3D:ori1_9,RDF:PiEN:Cor3D:ori1_82, 2DACorr:Polariz_4, 3DACorr:Polariz:Cor3D:ori1_2	0.592
15	15	Stereo,SurfACorr:HBP:Cor3D:ori1_2,RDF:SigChg:Cor3D:ori1_33,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10, SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor3D:ori1_81,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3D:ori1_23, 3DACorr:PiEN:Cor3D:ori1_9, RDF:PiEN:Cor3D:ori1_82, 2DACorr:Polariz_4, 3DACorr:Polariz:Cor3D:ori1_2	0.599
16	16	Stereo,SurfACorr:HBP:Cor3D:ori1_2,RDF:SigChg:Cor3D:ori1_33,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10, SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor3D:ori1_81,3DACorr:SigEN:Cor3D:ori1_4,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3D:ori1_23,3DACorr:PiEN:Cor3D:ori1_9,RDF:PiEN:Cor3D:ori1_82,2DACorr:Polariz_4, 3DACorr:Polariz:Cor3D:ori1_2	0.603
17	17	Stereo,SurfACorr:HBP:Cor3D:ori1_2,RDF:SigChg:Cor3D:ori1_33,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10, SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor3D:ori1_81,3DACorr:SigEN:Cor3D:ori1_4,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3D:ori1_23,3DACorr:SigChg:Cor3D:ori1_1,3DACorr:PiEN:Cor3D:ori1_9,RDF:PiEN:Cor3D:ori1_82,2DACorr:Polariz_4, 3DACorr:Polariz:Cor3D:ori1_2	0.607

		i1_82, 2DACorr:Polariz_4, 3DACorr:Polariz:Cor3D:ori1_2	
18	18	Stereo,SurfACorr:HBP:Cor3D:ori1_2,SurfACorr:HBP:Cor3D:ori1_6,RDF:SigChg:Cor3D:ori1_33,RDF:TotChg:Cor3D:ori1_28,3 DACorr:PiEN:Cor3D:ori1_10,SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor3D:ori1_81,3DACorr:SigEN:Co r3D:ori1_4,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3D:ori1_23,3DACorr:SigChg:Cor3D:ori1_1,3DACorr:PiEN:Cor3 D:ori1_9,RDF:PiEN:Cor3D:ori1_82,2DACorr:Polariz_4,3DACorr:Polariz:Cor3D:ori1_2	0.611
19	19	SurfACorr:HBP:Cor3D:ori1_8,Stereo,SurfACorr:HBP:Cor3D:ori1_2,SurfACorr:HBP:Cor3D:ori1_6,RDF:SigChg:Cor3D:ori1_3 3,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10,SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor 3D:ori1_81,3DACorr:SigEN:Cor3D:ori1_4,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3D:ori1_23,3DACorr:SigChg:Co r3D:ori1_1,3DACorr:PiEN:Cor3D:ori1_9, RDF:PiEN:Cor3D:ori1_82, 2DACorr:Polariz_4, 3DACorr:Polariz:Cor3D:ori1_2	0.616
20	20	SurfACorr:HBP:Cor3D:ori1_8,Stereo,SurfACorr:HBP:Cor3D:ori1_2,SurfACorr:HBP:Cor3D:ori1_6,RDF:SigChg:Cor3D:ori1_3 3,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10,SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor 3D:ori1_81,3DACorr:SigEN:Cor3D:ori1_4,SurfACorr:HBP:Cor3D:ori1_3,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3 D:ori1_23,3DACorr:SigChg:Cor3D:ori1_1,3DACorr:PiEN:Cor3D:ori1_9,RDF:PiEN:Cor3D:ori1_82,2DACorr:Polariz_4,3DACo rr:Polariz:Cor3D:ori1_2	0.620
21	21	SurfACorr:HBP:Cor3D:ori1_8,Stereo,SurfACorr:HBP:Cor3D:ori1_2,SurfACorr:HBP:Cor3D:ori1_6,RDF:SigChg:Cor3D:ori1_3 3,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10,SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor 3D:ori1_81,3DACorr:SigEN:Cor3D:ori1_4,SurfACorr:HBP:Cor3D:ori1_3,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3 D:ori1_23,3DACorr:SigChg:Cor3D:ori1_1,2DACorr:PiEN_10,3DACorr:PiEN:Cor3D:ori1_9,RDF:PiEN:Cor3D:ori1_82,2DACo rr:Polariz_4,3DACorr:Polariz:Cor3D:ori1_2	0.621
22	22	SurfACorr:HBP:Cor3D:ori1_8,Stereo,SurfACorr:HBP:Cor3D:ori1_2,SurfACorr:HBP:Cor3D:ori1_6,RDF:SigChg:Cor3D:ori1_3 3,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10,SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor 3D:ori1_81,3DACorr:SigEN:Cor3D:ori1_4,SurfACorr:HBP:Cor3D:ori1_3,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3 Dori1_23,3DACorrSigChgCor3Dori1_1,RDFPolarizCor3Dori1_25,2DACorrPiEN_10,3DACorrPiENCor3Dori1_9,RDFPiENCor 3D:ori1_82,2DACorr:Polariz_4, 3DACorr:Polariz:Cor3D:ori1_2	0.623
23	23	SurfACorr:HBP:Cor3D:ori1_8,Stereo,SurfACorr:HBP:Cor3D:ori1_2,SurfACorr:HBP:Cor3D:ori1_6,RDF:SigChg:Cor3D:ori1_3 3,RDF:TotChg:Cor3D:ori1_28,3DACorr:PiEN:Cor3D:ori1_10,SurfACorr:HBP:Cor3D:ori1_1,2DACorr:PiChg_7,RDF:PiEN:Cor	0.623

3D:ori1_81,3DACorr:SigEN:Cor3:Dori1_4,SurfACorr:HBP:Cor3D:ori1_3,RDF:PiEN:Cor3D:ori1_96,HDonO,RDF:PiChg:Cor3D:ori1_23,3DACorr:SigChg:Cor3D:ori1_1,RDF:Polariz:Cor3D:ori1_25,2DACorr:PiEN_10,2DACorr:LpEN_3,3DACorr:PiEN:Cor3D:ori1_9,RDF:PiEN:Cor3D:ori1_82, 2DACorr:Polariz_4, 3DACorr:Polariz:Cor3D:ori1_2

#HDonO: Number of hydrogen bonding donors derived from the sum of oxygen atoms in the molecule;

Stereo: Total number of tetrahedral chiral centers in the molecule;

2DACorr:PiChg_7: 2D autocorrelation weighted by π atom charges, where $d=6$;

2DACorr:Polariz_4: 2D autocorrelation weighted by effective atom polarizabilities, where $d=3$;

2DACorr:LpEN_3: 2D autocorrelation weighted by lone pair electronegativities, where $d=2$;

2DACorr:PiEN_10: 2D autocorrelation weighted by π atom electronegativities, where $d=9$;

3DACorr:SigChg:Cor3D:ori1_1: 3D autocorrelation weighted by σ atom charges, where d is in the range of 1–2Å;

3DACorr:PiEN:Cor3D:ori1_9: 3D autocorrelation weighted by π atom electronegativities, where d is in the range of 9–10Å;

3DACorr:PiEN:Cor3D:ori1_10: 3D autocorrelation weighted by π atom electronegativities, where d is in the range of 9–10Å;

3DACorr:SigEN:Cor3D:Dori1_4: 3D autocorrelation weighted by σ atom electronegativities, where d is in the range of 3–4Å;

3DACorr:Polariz:Cor3D:ori1_2: 3D autocorrelation weighted by effective atom polarizabilities, where d is in the range of 2–3Å;

RDF:PiChg:Cor3D:ori1_23: Radial distribution function weighted by π atom charges, where $d=2.3$ Å;

RDF:SigChg:Cor3D:ori1_33: Radial distribution function weighted by σ atom charges, where $d=3.3$ Å;

RDF:PiEN:Cor3D:ori1_81: Radial distribution function weighted by π atom electronegativities, where $d=8.1$ Å;

RDF:PiEN:Cor3D:ori1_82: Radial distribution function weighted by π atom electronegativities, where $d=8.2$ Å;

RDF:PiEN:Cor3D:ori1_96: Radial distribution function weighted by π atom electronegativities, where $d=9.6$ Å;

RDF:TotChg:Cor3D:ori1_28: Radial distribution function weighted by total atom charges (sum of σ and π charges), where $d=2.8$ Å;

RDF:Polariz:Cor3D:ori1_25: Radial distribution function weighted by effective atom polarizabilities, where $d=2.5$ Å;

SurfACorr:HBP:Cor3D:ori1_1: Autocorrelation functions weighted by the hydrogen bonding potential, where d is in the range of 1–2Å;

SurfACorr:HBP:Cor3D:ori1_2: Autocorrelation functions weighted by the hydrogen bonding potential, where d is in the range of 2–3Å;

SurfACorr:HBP:Cor3D:ori1_3: Autocorrelation functions weighted by the hydrogen bonding potential, where d is in the range of 3–4Å;

SurfACorr:HBP:Cor3D:ori1_6: Autocorrelation functions weighted by the hydrogen bonding potential, where d is in the range of 6–7Å;

SurfACorr:HBP:Cor3D:ori1_8: Autocorrelation functions weighted by the hydrogen bonding potential, where d is in the range of 8–9Å;

The CORINA Symphony molecular descriptors (www.molecular-networks.com) were used in this work.

Table S2 The brief results for SVM models based on the parameters obtain by cross-validation[#].

Model	Descriptors	c	γ	Cross-validation	Accuracy		
					Cross-validation	Training set	Test set
Model1A_1	MACCS fingerprints	8.0	0.00098	5	64.0%	85%	82.4324%
Model1A_2	MACCS fingerprints	8.0	0.00098	10	65.0%	85%	82.4324%
Model1A_3	MACCS fingerprints	0.5	0.03125	20	66.5%	74%	71.62%
Model1A_4	MACCS fingerprints	0.5	0.03125	LOO	66.5%	74%	71.62%
Model1B_1	CORINA Symphony	128.0	0.03125	5	75.5%	77.5%	79.72297%
Model1B_2	CORINA Symphony	128.0	0.00625	10	75.5%	75.5%	82.4324%
Model1B_3	CORINA Symphony	194.0	0.02915	10	74.5%	77%	78.3784%
Model1B_4	CORINA Symphony	3.249	1.0	10	75.5%	81.0%	78.3784%
Model1B_5	CORINA Symphony	1024.0	0.03125	LOO	75.0%	79.0%	79.7297%

[#]c: the optimum loss parameter C; γ :

the kernel function parameters;

Model 1A_4 was the best model based on MACCS fingerprints; Model 1B_4 was the best model based on CORINA Symphony molecular descriptors.

Table S3 The brief results for DT models with different parameters.#

Model	Descriptors	C	M	Cross-validation	Accuracy		
					Cross-validation	Training set	Test set
Model2A_1	MACCS fingerprints	0.35	2	5	64.0%	92.0%	83.4324%
Model2A_2	MACCS fingerprints	0.2	2	5	63.0%	88.0%	83.4324%
Model2A_3	MACCS fingerprints	0.25	2	5	63.5%	90.0%	83.4324%
Model2A_4	MACCS fingerprints	0.2	3	5	63.5%	85.5%	83.7838%
Model2A_5	MACCS fingerprints	0.1	3	5	62.0%	79.0%	79.7297%
Model2A_6	MACCS fingerprints	0.08	3	5	62.0%	79.0%	79.7297%
Model2A_7	MACCS fingerprints	0.06	3	5	61.5%	76.0%	74.3243%
Model2A_8	MACCS fingerprints	0.06	4	5	60.0%	76.5%	77.027%
Model2A_9	MACCS fingerprints	0.06	5	5	59.0%	79.5%	79.7297%
Model2A_10	MACCS fingerprints	0.06	2	5	61.0%	77.5%	74.3243%
Model2A_11	MACCS fingerprints	0.06	1	5	57.5%	79.0%	77.027%
Model2A_12	MACCS fingerprints	0.05	3	5	62.0%	75.0%	74.3243%
Model2B_1	CORINA Symphony	0.10	2	5	63.0%	79.0%	77.027%
Model2B_2	CORINA Symphony	0.20	2	5	63.0%	80.5%	79.7297%
Model2B_3	CORINA Symphony	0.25	2	5	64.0%	80.5%	79.7297%
Model2B_4	CORINA Symphony	0.30	2	5	64.0%	80.5%	79.7297%
Model2B_5	CORINA Symphony	0.10	3	5	63.0%	78.0%	75.6757%
Model2B_6	CORINA Symphony	0.10	1	5	63.0%	79.0%	77.027%
Model2B_7	CORINA Symphony	0.05	2	5	63.0%	79.0%	77.027%
Model2B_8	CORINA Symphony	0.05	3	5	63.0%	76.0%	75.6757%

C: the confidence factor; M: the minimum number of instances per leaf;

Model 2A_7 was the best model based on MACCS fingerprints; Model 2B_5 was the best model based on CORINA Symphony molecular descriptors.

Table S4 The brief results for FT models with different parameters.[#]

Model	Descriptors	I	M	W	Cross-validation	Accuracy		
						Cross-validation	Training set	Test set
Model3A_1	MACCS fingerprints	15	15	0	5	60.0%	92.5%	79.7297
Model3A_2	MACCS fingerprints	15	10	0	5	62.0%	92.5%	79.7297
Model3A_3	MACCS fingerprints	15	20	0	5	60.0%	86.0%	77.027%
Model3A_4	MACCS fingerprints	10	20	0	5	59.5%	86.5%	74.3243%
Model3A_5	MACCS fingerprints	5	20	0	5	58.0%	86.0%	83.7838%
Model3A_6	MACCS fingerprints	5	20	0.1	5	55.5%	85.5%	75.6757%
Model3A_7	MACCS fingerprints	5	20	0.2	5	61.5%	74.5%	79.7297%
Model3A_8	MACCS fingerprints	5	20	0.3	5	61.5%	71.0%	79.7297%
Model3A_9	MACCS fingerprints	5	20	0.4	5	60.0%	72.0%	74.3243%
Model3B_1	CORINA Symphony	15	15	0	5	66.5%	83.5%	81.0811%
Model3B_2	CORINA Symphony	15	12	0	5	68.0%	88.0%	77.027%
Model3B_3	CORINA Symphony	15	18	0	5	68.5%	83.5%	81.0811%
Model3B_4	CORINA Symphony	12	18	0	5	69.0%	79.5%	78.7834%
Model3B_5	CORINA Symphony	18	18	0	5	66.5%	81.5%	79.7297%

[#] I: the fixed number of iterations; M: the minimum number of instances; W: the beta value used for weight trimming;

Model 3A_7 was the best model based on MACCS fingerprints; Model 3B_3 was the best model based on CORINA Symphony molecular descriptors.

Table S5 The brief results for RF models with different parameters.#

Model	Descriptors	T	K	S	depth	Cross-validation	Accuracy		
							Cross-validation	Training set	Test set
Model4A_1	MACCS fingerprints	10	0	1	0	5	56%	99.5%	89.1892%
Model 4A_2	MACCS fingerprints	12	2	1	0	5	55.5%	100%	81.0811%
Model 4A_3	MACCS fingerprints	12	2	1	1	5	56.5%	56%	52.7027%
Model 4A_4	MACCS fingerprints	14	5	1	1	5	56.5%	56.5%	52.7027%
Model 4A_5	MACCS fingerprints	14	10	1	1	5	55.5%	57.5%	52.7027%
Model 4A_6	MACCS fingerprints	14	10	1	3	5	60.5%	72.0%	75.6757%
Model 4A_7	MACCS fingerprints	14	13	1	3	5	62.5%	76.0%	75.6757%
Model 4A_8	MACCS fingerprints	14	15	1	5	5	61.0%	75.0%	74.3243%
Model 4A_9	MACCS fingerprints	10	0	1	0	5	64.0%	99.0%	77.027%
Model4B_1	CORINA Symphony	10	0	1	3	5	62.5%	76.0%	78.3784%
Model4B_2	CORINA Symphony	11	0	1	3	5	63.0%	80.0%	77.027%
Model4B_3	CORINA Symphony	9	0	1	3	5	65.0%	79.5%	77.027%
Model4B_4	CORINA Symphony	11	4	1	3	5	63.0%	80.5%	77.027%
Model4B_5	CORINA Symphony	13	4	1	3	5	65.0%	80.5%	78.3784%
Model4B_6	CORINA Symphony	11	12	1	3	5	63.0%	79.0%	79.7297%

#T: the number of trees to be generated; K: the number of attributes used in random selection; S: the random number seed; depth: the maximum depth of the trees;
Model 4A_7 was the best model based on MACCS fingerprints; Model 4B_5 was the best model based on CORINA Symphony molecular descriptors.

Table S6 The predicted results of the 11 compounds by eight models in this work. The inhibitors which were predicted the active inhibitors were labeled by “1”, and the inhibitors which were predicted the weakly active inhibitors were labeled by “0”.

Compounds No. [#]	Model 1A	Model 2A	Model 3A	Model 4A	Model 1B	Model 2B	Model 3B	Model 4B
1	1	0	1	1	1	1	0	1
2	1	1	1	0	1	1	1	0
3	1	1	0	1	1	1	0	1
4	1	0	1	1	1	1	1	0
5	0	1	0	1	0	1	1	1
6	1	1	0	1	1	1	1	0
7	1	1	1	1	1	0	1	1
8	1	1	1	1	1	1	1	1
9	1	1	1	1	1	0	1	1
10	1	1	1	1	0	1	1	1
11	1	0	1	1	1	0	1	0

[#]The structures of the compounds were shown in Table 4.