Supporting Materials

Table S1. The structures of 41 inhibitors



No.	Х	Y	R	R ₁	R_2	R_3	R_4	R_5	R_6	pIC ₅₀
1	CH	0	Н	Н	Н	Н	Me	Н	Н	6.1
5a*	CH	0	2-Me	Н	Н	Н	Me	Н	Н	4.94
5b*	CH	0	3-Me	Н	Н	Н	Me	Н	Н	6.19
5c*	CH	0	4-Me	Н	Н	Н	Me	Н	Н	5.89
5d*	CH	0	3-OMe	Н	Н	Н	Me	Н	Н	6.28
5e*	CH	0	4-OMe	Н	Н	Н	Me	Н	Н	5.82
5f	CH	0	3-OPh	Н	Н	Н	Me	Н	Н	7.19
5g*	CH	0	3-Br	Н	Н	Н	Me	Н	Н	6.52
11a*	Ν	0	3-Me	Н	Н	Н	Me	Н	Н	7.04
11b*	Ν	0	3-OMe	Н	Н	Н	Me	Н	Н	6.85
11c*	Ν	0	3-Br	Н	Н	Н	Me	Н	Н	7.42
12*	Ν	NCN	3-Br	Н	Н	Н	Me	Н	Н	7.96
13*	Ν	0	3-Br	(S)-Me	Н	Н	Me	Н	Н	8.41
14*	Ν	NCN	3-Br	(S)-Me	Н	Н	Me	Н	Н	9.05
15*	Ν	0	3-Br	(S)-Me	Н	Н	Me	Н	Н	7.43
16*	Ν	NCN	3-Br	(S)-i-Pr	Н	Н	Me	Н	Н	8.38
17	Ν	NCN	3-Br	Me(trans)	Н	Me	Me	Н	Н	8.41
18	Ν	0	3-Br	Me(cis)	Me	Н	Me	Н	Н	6.88
19	Ν	0	3-Br	-CH ₂ CH ₂ -	-CH ₂ CH ₂ -	Н	Me	Н	Н	7.80
20	Ν	NCN	3-Br	-CH ₂ -	Н	-CH ₂ -	Me	Н	Н	7.12
21a	Ν	NCN	3-Br	(S)-Me	Н	Н	Н	Н	Н	8.09
21b*	Ν	NCN	3-Br	(S)-Me	Н	Н	Cl	Н	Н	8.92
21c	Ν	NCN	3-Br	(S)-Me	Н	Н	Н	Me	Н	8.38
22a*	Ν	NSO ₂ Me	3-Br	(S)-Me	Н	Н	Me	Н	Н	8.17
22b	Ν	NCN	3-Cl	(S)-Me	Н	Н	Me	Н	Н	8.8
22c	Ν	0	3-Cl	(S)-Me	Н	Н	Me	Н	Н	8.64
22d	Ν	NCN	3-F	(S)-Me	Н	Н	Me	Н	Н	8.74
22e	Ν	NCN	3-Br,4-F	(S)-Me	Н	Н	Me	Н	Н	8.82
22f	Ν	0	3-Br,4-F	(S)-Me	Н	Н	Me	Н	Н	8.49
22g	Ν	NCN	3-CF ₃	(S)-Me	Н	Н	Me	Н	Н	8.72
22h	Ν	NCN	3-CN	(S)-Me	Н	Н	Me	Н	Н	8.92

22i	Ν	NCN	3-t-Bu	(S)-Me	Н	Н	Me	Н	Н	8.96
22j	Ν	Ο	3-OCONMe ₂	(S)-Me	Н	Н	Me	Н	Н	8.92
22k	Ν	NCN	3-CONH-i-Pr	(S)-Me	Н	Н	Me	Н	Н	8.46
221	Ν	0	3-CONH-i-Pr	(S)-Me	Н	Н	Me	Н	Н	8.26
22m*	Ν	NCN	3-CONH(CH2) ₂ OH	(S)-Me	Н	Н	Me	Н	Н	9.10
22n	Ν	0	3-CONH(CH2) ₂ OH	(S)-Me	Н	Н	Me	Н	Н	8.52
220	Ν	0	3-CONHCH(CH ₂ OH) ₂	(S)-Me	Н	Н	Me	Н	Н	8.52
22p	Ν	NCN	3-CONH(CH ₂) ₂ NMe ₂	(S)-Me	Н	Н	Me	Н	Н	8.47
22q	Ν	NCN	SO ₂ NH-i-Pr	(S)-Me	Н	Н	Me	Н	Н	8.77
22r	Ν	NCN	SO ₂ NH(CH ₂) ₂ OH	(S)-Me	Н	Н	Me	Н	Н	8.54

*Molecules selected for the MD simulations and free energy calculations

101 111	e studied mon	ceutes oused of	the solute and	ciecule constal	it of 1 (Real/III)	51)
No.	$\Delta E_{ m vdw}$	$\Delta E_{ m ele}$	$\Delta G_{ m SA}$	$\Delta G_{ m GB}$	$\Delta G_{ m pred}$	pIC ₅₀
22m	-53.71±3.50	-52.02±5.13	-7.59±0.36	64.24±3.42	-49.09±3.31	9.10
14	-50.95±2.94	-26.53±6.28	-6.53±0.13	42.45±4.78	-41.56±2.92	9.05
21b	-52.61±3.63	-22.02±5.82	-6.42±0.21	37.81±4.17	-43.23±3.92	8.92
13	-48.68±3.14	-7.99±6.35	-6.27±0.12	25.54±5.48	-37.39±2.59	8.41
16	-56.03±3.57	-34.29±2.93	-6.79±0.08	49.42±3.42	-47.85±2.38	8.38
22a	-50.10±2.78	-24.04±7.17	-6.96±0.18	46.34±6.67	-34.76±2.89	8.17
12	-50.49±2.72	-31.37±5.01	-6.47±0.21	48.64±4.15	-39.68±2.74	7.96
15	-45.35±3.11	-17.94±5.24	-6.47±0.17	33.25±4.30	-36.51±3.11	7.43
11c	-52.50±3.76	-7.78±6.40	-6.07±0.13	27.03±5.89	-39.31±3.29	7.42
11a	-40.42±3.21	-6.56±4.71	-6.08 ± 0.17	20.66±3.56	-32.41±2.81	7.04
11b	-47.08±2.96	-7.95±3.21	-6.44 ± 0.28	25.52±2.69	-35.96±2.82	6.85
5g	-44.55±3.28	-27.62±10.43	-6.16±0.19	42.25±9.06	-36.08±3.99	6.52
5d	-46.88 ± 4.42	4.12±11.50	-6.75±0.30	15.31±11.87	-34.20±3.58	6.28
5b	-47.94±3.49	-13.31±4.71	-5.90±0.17	31.73±4.12	-35.42±3.26	6.19
5c	-43.49±3.68	-13.17±5.72	-6.54±0.20	30.75±5.77	-32.45±3.47	5.89
5e	-46.76±2.83	-22.15±3.86	-6.41±0.12	40.31±2.76	-35.01±2.78	5.82
5a	-41.79±4.74	-14.52±6.39	-5.75±0.28	31.01 ±6.18	-31.06±4.68	4.94

Table S2. The predicted binding free energies and the individual energy components for the studied molecules based on the solute dielectric constant of 1 (kcal/mol)

1	10	20	30 40	50	60	70	80	90 100	
1 *		*	1*	*	. * *		* <mark></mark>	1*	*
~~SQQIFF	RPCDLIHGEVL	GKGFFGQAIK	THKATGKVMVMK	ELIRCDEETQKT	FLTEVKVMRSLI	DHPNVLKFIGVLY	KDKKLNLLTEYI	EGGTLKDFLRSMD~I	PFPW
SMPHRIFF	RPSDLIHGEVL	GKGCFGQAIK	THRETGEVMVMK	ELIRFDEETORT	FLKEVKVMRCLE	HPNVLKFIGVLY	KDKRLNFITEYI	KGGTLRGIIKSMDS	YPW
\rightarrow				> - •			\rightarrow	0	
110	120	190	140	150 14	.0 170	190	190	200 21	0
				*		*	*		<u></u>
QQKVRFAP	GIASGMAYLH	SMCIIHRDLNS	HNCLIKLDKTVV	VADFGLSRLIVE	ERKRAPMEKAT	TKKRTLRKNDRKK	RYTVVGNPYWMA	PEMLNGKSYDETVD	FSF
0	<u>→ </u>								1
SQRVSFAR	KDIASGMAYLH	SMNIIHRDLNS	SHNCLVRENKNVV	VADFGLARLMV~	~~~~~~~~~	~~~~~~~~~	~ YTVVGNPYWMA	PEMINGRSYDEKVD	/FSF
2								2	
220	230	240	250	260	270	280 290	300	310	320
*	*	*	.*	<mark> </mark> *	*	· • • • • • • • • • • •	*	. * *	
GIVLCEII	IGQVYADPDCL	PRTLDFGLNVF	LFWEKFVPTDCP	PAFFPLAAICCR	LEPESRPAFSKI	LEDSFEALSLYLG	ELGIPLPAELEE	LDHTVSMQYGLTRD	*
CTULCETT	COUNTODOVT	DDEMORCT NUT	CELDBYCDDNCD	DOPEDIMUNCOD	TDDEKBBCEUKI	FUNTE	-0		
GIVECTI	GRANADEDID	FRITTDE GTUAL	GEDDRICEPNCE	ESTEFIIVRCCD	IDEERRESEVRI	DELINITE			*

Figure S1. The sequence alignment between LIMK1 and LIMK2.



Figure S2. The docked pose of staurosporine predicted by *IFD* in the active site of LIMK2 overlapped with its original structure in the homology model (carbon atoms in the homology model are colored in dark green, and those in the docked structure in yellow).



Figure S3. The Profile-3D scores for the LIMK2 structure generated by homology modeling



Figure S4. The alignments of 41 docked structures in the binding site of LIMK2.