

Table-S1: PDB codes, resolution and affinities of protein-ligand complexes examined in this work. The stars at the rear of K_i 's values indicate they are apparent K_i , meaning the related experiments are performed in biological medium, e.g. living organisms, blood assay. The last column lists the original publications that report K_i 's involved in our study. Double blank lines are used to separate protein families and single lines for segregation of sub-families according to 90% homology.

Protein Family	PDB code	Resolution	Affinity	Ref
trypsn β	1c1r	1.37	$K_i=0.0235\mu\text{M}$	1
	1c5p	1.43	$K_i=21\mu\text{M}$	2
	1c5q	1.43	$K_i=0.44\mu\text{M}$	2
	1c5s	1.36	$K_i=1.0\mu\text{M}$	2
	1c5t	1.37	$K_i=80\mu\text{M}$	2
	1ce5	1.9	$K_i=18.4\mu\text{M}$	3
	1f0t	1.8	$K_i=1000\text{nM}$ *	4,5
	1g3b	1.8	$K_i=1.8\mu\text{M}$	6-9
				10
	1ghz	1.39	$K_i=16\mu\text{M}$	
	1gi1	1.42	$K_i=3.4\mu\text{M}$	10
	1gi4	1.37	$K_i=0.065\mu\text{M}$	10
	1gj6	1.5	$K_i=0.10\mu\text{M}$	10
	1k1i	2.2	$K_d=264\text{nM}$	
	1k1j	2.2	$K_d=28\text{nM}$	
	1k1l	2.5	$K_d=125\text{nM}$	
	1k1m	2.2	$K_d=40\text{nM}$	
	1o2h	1.77	$K_i=0.068\mu\text{M}$	11
	1o2j	1.65	$K_i=0.12\mu\text{M}$	11
	1o2n	1.5	$K_i=0.81\mu\text{M}$	11
	1o2o	1.63	$K_i=0.44\mu\text{M}$	11
	1o2q	1.5	$K_i=0.021\mu\text{M}$	11
	1o2s	1.65	$K_i=3.4\mu\text{M}$	11
	1o2w	1.38	$K_i=1.4\mu\text{M}$	11
	1o2x	1.46	$K_i=1.4\mu\text{M}$	11
	1o2z	1.65	$K_i=0.78\mu\text{M}$	11
	1o30	1.55	$K_i=0.17\mu\text{M}$	11
	1o33	1.46	$K_i=1.8\mu\text{M}$	11
	1o36	1.7	$K_i=1.1\mu\text{M}$	11
	1o38	1.38	$K_i=0.15\mu\text{M}$	11
	1o3d	1.33	$K_i=0.074\mu\text{M}$	11
	1o3f	1.55	$K_i=0.011\mu\text{M}$	11
	1o3h	1.53	$K_i=0.05\mu\text{M}$	11
	1o3i	1.51	$K_i=0.05\mu\text{M}$	11
	1o3j	1.4	$K_i=0.17\mu\text{M}$	11

1o3k	1.43	Ki=0.17uM	11
1pph	1.9	Ki=1.2uM	12
1qb6	1.8	Ki=870nM	13
1qb9	1.8	Ki=36nM	13
1qbn	1.8	Ki=1400nM	13
1qbo	1.8	Ki=18nM	13
1tng	1.8	Ki=1.17mM	14
1tnh	1.8	Ki=0.43mM	14
1tni	1.9	Ki=0.10mM	14
1tnj	1.8	Ki=11.0mM	14
1tnk	1.8	Ki=32.5mM	14
1tnl	1.9	Ki=13.3mM	14
1v2j	1.9	Ki=566uM	15
1v2k	2	Ki=0.65uM	15
1v2l	1.6	Ki=51uM	15
1v2n	1.8	Ki=1.25uM	15
1v2s	1.72	Ki=68uM	15
1v2u	1.8	Ki=427uM	15
2bza	1.9	Ki=1.58mM	3
1j14	2.4	Ki=32.2uM	16, 17
1j16	1.6	Ki=143uM	16, 17
1j17	2	Ki=6.05uM	16, 17
1h4w	1.7	Ki=22uM	18
1bcu	2	Kd=0.53mM	
1c1u	1.75	Ki=0.0056uM	1
1c1v	1.98	Ki=0.023uM	1
1c5n	1.5	Ki=20uM	2
1c5o	1.9	Ki=320uM	2
1d3d	2.04	Kd=0.81nM	
1d4p	2.07	Kd=0.5uM	
1ghv	1.85	Ki=45uM	10
1ghw	1.75	Ki=63uM	10
1ghy	1.85	Ki=0.008uM	10
1mu6	1.99	Ki=4.2nM	19
1mu8	2	Ki=1.0nM	19
1mue	2	Ki=2.3nM	20
1oyt	1.67	Ki=0.057uM	21
1qbv	1.8	Ki=4100nM	22
1tom	1.8	Ki=5nM	23, 24

thrombin α

	1vzq	1.54	Ki=36nM	25
	1d6w	2	Ki=1100nM	26
	1d9i	2.3	Ki=0.78nM	26
	1nm6	1.8	Ki=0.09nM	27
	1nt1	2	Ki=1.3nM	27
	1s13	1.81	Ki=1.4pM	28
	1ta2	2.3	Ki=3nM	29
	1z71	1.8	Ki=0.66nM	30
	1zgi	2.2	Ki=4.6uM	31
	1c4u	2.1	Ki=0.043nM	26
	1c4v	2.1	Ki=0.016nM	26
	1uvt	2.5	Ki=0.023uM	32
CDK+PKA	1b38	2	Kd=0.254uM	
	1b39	2.1	Kd=0.120uM	
	1e1v	1.95	Ki=12uM	23
	1e1x	1.85	Ki=1.3uM	23
	1pxn	2.5	Ki=0.07uM	33
	1pxo	1.96	Ki=2.0nM	33
	1pxp	2.3	Ki=0.22uM	33
	2fvd	1.85	Ki=3nM	34
	1h1p	2.1	Ki=12uM	35
	1h1s	2	Ki=6nM	35
	1rej	2.2	Ki=5nM	36
	1q8t	2	Kd=17.5uM	
	1q8u	1.9	Kd=1.1uM	
	1q8w	2.2	Kd=5.7uM	
	1stc	2.3	Ki=8nM	37
	1ydr	2.2	Ki=3.0uM	38
	1yds	2.2	Ki=1.2uM	38
1ydt	2.3	Ki=48nM	38	
2erz	2.2	Ki=2.2uM	39	

urokinase-type plasminogen activator	1c5x	1.75	Ki=0.21uM	2	
	1c5y	1.65	Ki=63uM	2	
	1c5z	1.85	Ki=97uM	2	
	1gi7	1.79	Ki=31uM	10	
	1gj7	1.5	Ki=0.013uM	40	
	1gj8	1.64	Ki=0.11uM	40	
	1gja	1.56	Ki=3.8uM	40	
	1gjb	1.9	Ki=0.45uM	40	
	1gjc	1.73	Ki=0.45uM	40	
	1gjd	1.75	Ki=6.0uM	40	
	1o3p	1.81	Ki=0.22uM	11	
	1ejn	1.8	Ki=2.4uM	41	
	1f5k	1.8	Ki=180uM	42	
	1f5l	2.1	Ki=5.3uM	42	
	1owe	1.6	Ki=631nM	43	
	1owh	1.61	Ki=40nM	43	
	1sqa	2	Ki=0.62nM	44	
	1sqa	2	Ki=0.62nM	44	
	1sqo	1.84	Ki=0.035uM	44	
	1sqt	1.9	Ki=0.63uM	44	
β -glucosidase A	1oif	2.12	Kd=19nM	45	
	1uz1	2	Ki=130nM		
	1w3j	2	Kd=484nM		
	2cbu	1.85	Kd=2.1uM		
	2cbv	1.95	Kd=3.3uM		
	2ces	2.15	Kd=56nM		
	2cet	1.97	Kd=9.6nM		
	2j75	1.85	Kd=225nM		
	2j77	2.1	Kd=12.9uM		
	2j78	1.65	Kd=384nM		
	2j79	1.94	Kd=1.1uM		
	2j7b	1.87	Kd=240nM		
	2j7d	2.24	Kd=74nM		
	2j7e	2.19	Kd=48nM		
	2j7f	2.28	Kd=445nM		
	2j7g	1.91	Kd=100nM		
	2j7h	1.95	Kd=65nM		
	2cer	2.29	Ki<=0.6nM		46

coagulation factor Xa	1f0r	2.1	Ki=22nM *	5
	1f0s	2.1	Ki=18nM *	5
	1ksn	2.1	Ki=0.4nM	47
	1lpk	2.2	Ki=28nM *	48
	1lpz	2.4	Ki=25nM *	48
	1nfw	2.1	Ki=1.1nM *	49
	1nfx	2.15	Ki=3.0nM *	49
	1nfy	2.1	Ki=1.3nM *	49
	2boh	2.2	Ki=3nM *	50
	1fjs	1.92	Ki=0.11nM	51
	1mq5	2.1	Ki=1nM *	52
	1mq6	2.1	Ki=7pM *	52
	2bok	1.64	Ki=0.28uM	53
	1nfu	2.05	Ki=18nM *	49
	1xka	2.3	Ki=131nM *	54

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