Figure 1: Superposition of all 20 poses of Tyrosine residue docked in the P1 binding site. The overall conformation of poses is highly similar with only subtle variations in the orientation of the benzyl and p-hydroxyl moiety (OH group) of the sidechain. These results are typical of docking runs for the most of the amino acids.

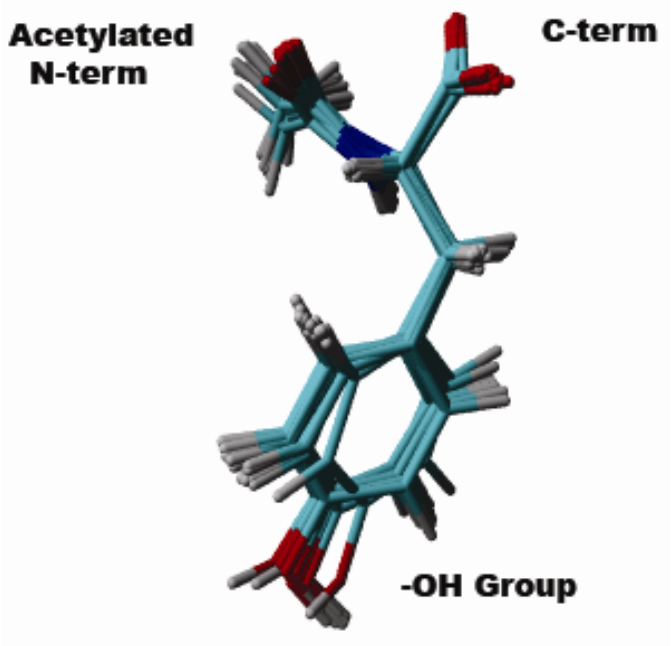

Table 1: The GOLD score and the individual energy terms for all 20 poses resulting from the docking of Tyrosine residue at the P1 binding site (Figure 1). The GOLD score for each pose is a sum of energy terms corresponding to the interaction between the substrate and the protease (inter-hydrogen bonds between peptide and protease, i.e. HB_ext; and Van der Waals energy between peptide and protease, i.e. VDW_ext) and the internal energy components within the peptide substrate (intra hydrogen bonds within the peptide, i.e. HB_int; and strain within the peptide molecules, i.e. S_int). The S_cov denote the constraint energy related to the covalent bond between the peptide and the protease. The zero values for HB_int and S_cov means the absence of internal hydrogen bonds and formation of an ideal covalent bond respectively. The final ranking of the 20 poses based on their GOLD score: pose # 12, 5, 4, 20, 17, 16, 1, 7, 13, 19, 11, 9, 2, 10, 18, 3, 8, 6, 14, 15

	GScore	HB_ext	VDW_ext	HB_int	S_int	S_cov
1	43.7	6.35	29.42	0	-3.1	0
2	43.32	6.09	29.57	0	-3.42	0
3	42.6	4.42	29.95	0	-3	0
4	43.83	6.57	29.31	0	-3.05	0
5	43.86	6.58	29.32	0	-3.03	0
6	42.33	5.3	28.9	0	-2.7	0
7	43.65	6.11	29.7	0	-3.3	0
8	42.51	5.91	30	0	-4.64	0
9	43.33	6.06	29.56	0	-3.38	0
10	42.8	6.28	28.92	0	-3.24	0
11	43.38	5.92	29.37	0	-2.93	0
12	43.95	6.55	29.42	0	-3.05	0
13	43.49	6.66	29.03	0	-3.08	0
14	42.13	5.2	28.78	0	-2.64	0
15	41.97	5.64	28.78	0	-3.24	0
16	43.73	6.27	29.57	0	-3.19	0
17	43.79	6.53	29.3	0	-3.02	0
18	42.69	6.89	28.39	0	-3.23	0
19	43.42	6.14	29.66	0	-3.51	0
20	43.79	6.4	29.56	0	-3.26	0

Table 2: The GOLD score and the individual energy terms for all 20 amino acids docked at the P1 binding site of PSA. The GOLD score for each pose is sum of energy terms resulting from the interaction between peptide substrate and the protease (inter-hydrogen bonds between peptide and protease, i.e. HB_ext; and Van der Waals energy between peptide and protease, i.e. VDW_ext) and the internal energetics within the peptide substrate (intra hydrogen bonds within the peptide, i.e. HB_int; and strain within the peptide molecules, i.e. S_int). The S_cov denote the constraint energy due to the specification of a covalent bond between the peptide and the protease. The zero values for HB_int and S_cov means the absence of internal hydrogen bonds and formation of an ideal covalent bond respectively.

	Amino Acid	GScore	HB_ext	VDW_ext	HB_int	S_int	S_cov
1	ALA	19.08	4.23	12.71	0	-2.63	0
2	ARG	44.4	9.32	30.69	0	-7.12	0
3	ASN	27.14	4.44	18.25	0	-2.39	0
4	ASP	28.42	10.35	15.91	0	-3.81	0
5	CYS	25.46	4.42	16.72	0	-1.95	0
6	GLN	33.89	6.23	22.81	0	-3.71	0
7	GLU	37.09	12.25	21.02	0	-4.06	0
8	GLY	15.49	4.43	9.29	0	-1.71	0
9	HIS	37.22	5.85	23.5	0	-0.94	0
10	ILE	23.98	4.57	17.53	0	-4.69	0
11	LEU	29.11	4.24	20.79	0	-3.71	0
12	LYS	37.58	10.75	25.7	0	-8.5	0
13	MET	35.67	4.56	24.23	0	-2.2	0
14	PHE	41.46	4.2	28.7	0	-2.21	0
15	PRO	16.04	17.54	18.43	0	-26.84	0
16	SER	19.96	4.33	13.51	0	-3.94	0
17	THR	23.06	4.21	16.83	0	-4.29	0
18	TRP	45.78	4.46	32.67	0	-3.6	0
19	TYR	43.95	6.55	29.42	0	-3.05	0
20	VAL	19.57	2.8	15.73	0	-4.85	0

Figure 2: A representative figure depicting the quality of the experimental data obtained from the Inhibitory potency Assays as described in the 'Materials and Methods' section of the manuscript. The specific inhibitor used to generate this data was: cbz-SSKLL-CHO.