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**Table 1**. Relative ion intensities for the dissociated ions of ligands in the L-289 library. The ion intensity of each ligand was normalized to that of Gly-Gly compound. The uncertainty is 10-20% (precision of the three measurements, not accuracy).

| L-AA | Phe | Tyr | Leu | Ile | Val | Ala | His | Thr | Gly | Gln | Asn | Ser | Pro | Lys | Arg | Glu | Asp |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Phe | 3.13 | 3.09 | 4.07 | 4.07 | 2.52 | 1.53 | 1.24 | 1.41 | 1.80 | 1.54 | 1.04 | 1.15 | 2.48 | 1.74 | 1.46 | 1.09 | 1.11 |
| Tyr | | 3.37 | 4.35 | 4.35 | 2.98 | 1.15 | 1.17 | 1.52 | 1.54 | 1.26 | 0.87 | 1.00 | 1.70 | 1.33 | 1.15 | 0.87 | 1.00 |
| Leu | | | 3.80 | 3.80 | 2.39 | 2.48 | 2.07 | 2.13 | 2.37 | 2.22 | 1.70 | 1.93 | 2.50 | 2.28 | 1.96 | 1.04 | 0.75 |
| Ile | | | | 3.80 | 2.39 | 2.48 | 2.07 | 2.13 | 2.37 | 2.22 | 1.70 | 1.93 | 2.50 | 2.28 | 1.96 | 1.04 | 0.75 |
| Val | | | | | 1.76 | 2.37 | 1.35 | 1.93 | 1.74 | 1.70 | 1.13 | 1.50 | 1.43 | 1.33 | 1.20 | 0.85 | 0.72 |
| Ala | | | | | | 0.63 | 0.52 | 0.70 | 0.65 | 0.85 | 0.50 | 0.50 | 0.65 | 0.72 | 1.13 | 0.67 | 0.30 |
| His | | | | | | | 0.46 | 0.72 | 0.57 | 0.54 | 0.46 | 0.50 | 0.76 | 0.72 | 0.63 | 0.39 | 0.43 |
| Thr | | | | | | | | 1.02 | 0.50 | 0.63 | 0.54 | 0.59 | 0.63 | 0.98 | 0.48 | 0.67 | 0.28 |
| Gly | | | | | | | | | 1.00 | 0.50 | 0.26 | 0.46 | 0.85 | 0.48 | 0.74 | 0.30 | 0.37 |
| Gln | | | | | | | | | | 0.70 | 0.65 | 0.54 | 0.93 | 0.48 | 0.52 | 0.43 | 0.30 |
| Asn | | | | | | | | | | | 0.70 | 0.30 | 0.83 | 0.63 | 0.46 | 0.30 | 0.39 |
| Ser | | | | | | | | | | | | 0.54 | 0.59 | 0.35 | 0.33 | 0.28 | 0.35 |
| Pro | | | | | | | | | | | | | 0.26 | 0.63 | 0.65 | 0.48 | 0.67 |
| Lys | | | | | | | | | | | | | | 0.70 | 0.46 | 0.48 | 0.33 |
| Arg | | | | | | | | | | | | | | | 0.43 | 0.41 | 0.37 |
| Glu | | | | | | | | | | | | | | | | 0.52 | 0.74 |
| Asp | | | | | | | | | | | | | | | | | 0.46 |

**Table 2.** Relative ion intensities for the dissociated ions of ligands in the D-256 library. The ion intensity of each ligand was normalized to that of Gly-Gly compound. The uncertainty is 10-20% (precision of the three measurements, not accuracy).

| D-AA | Phe | Tyr | Leu | Val | Ala | His | Thr | Gly | Gln | Asn | Ser | Pro | Lys | Arg | Glu | Asp |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Phe | 1.49 | 1.43 | 2.13 | 1.57 | 0.97 | 0.93 | 1.16 | 1.15 | 0.92 | 0.76 | 0.86 | 0.71 | 0.66 | 0.54 | 0.47 | 0.47 |
| Tyr | | 1.42 | 2.09 | 1.77 | 0.86 | 0.75 | 1.01 | 0.93 | 0.68 | 0.62 | 0.98 | 0.66 | 0.59 | 0.47 | 0.54 | 0.33 |
| Leu | | | 2.47 | 2.01 | 1.25 | 1.33 | 1.71 | 1.53 | 1.47 | 1.22 | 1.53 | 0.61 | 0.85 | 0.89 | 0.67 | 0.88 |
| Val | | | | 1.72 | 1.53 | 1.25 | 1.53 | 1.42 | 1.22 | 0.87 | 1.38 | 0.49 | 1.08 | 0.84 | 0.88 | 0.85 |
| Ala | | | | | 0.84 | 0.51 | 0.63 | 0.76 | 0.62 | 0.55 | 0.76 | 0.61 | 0.45 | 0.82 | 0.38 | 0.42 |
| His | | | | | | 0.48 | 0.55 | 0.58 | 0.39 | 0.37 | 0.61 | 0.58 | 0.39 | 0.28 | 0.24 | 0.15 |
| Thr | | | | | | | 0.54 | 0.76 | 0.41 | 0.52 | 0.99 | 0.58 | 0.36 | 0.29 | 0.59 | 0.34 |
| Gly | | | | | | | | 1.00 | 0.55 | 0.52 | 0.78 | 0.92 | 0.50 | 0.58 | 0.42 | 0.30 |
| Gln | | | | | | | | | 0.51 | 0.38 | 0.52 | 0.53 | 0.17 | 0.34 | 0.45 | 0.25 |
| Asn | | | | | | | | | | 0.59 | 0.53 | 0.60 | 0.40 | 0.21 | 0.25 | 0.30 |
| Ser | | | | | | | | | | | 1.10 | 0.77 | 0.48 | 0.29 | 0.34 | 0.34 |
| Pro | | | | | | | | | | | | 0.29 | 0.38 | 0.40 | 0.70 | 0.64 |
| Lys | | | | | | | | | | | | | 0.29 | 0.28 | 0.29 | 0.29 |
| Arg | | | | | | | | | | | | | | 0.24 | 0.26 | 0.20 |
| Glu | | | | | | | | | | | | | | | 0.36 | 0.23 |
| Asp | | | | | | | | | | | | | | | | 0.26 |



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**Table 3**. The amino acid analysis shows that each amino acid in the two libraries has a similar molar ratio.[a] The analyses were provided by the Harvard Microchemistry Facility.

| Amino acids | Asx[b] | Glx[b] | Ser | Gly | His | Arg | Thr+β-Ala[c] | Ala | Pro | Tyr | Val | Ile | Leu | Phe | Lys |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| D-form | 1.86 | 1.97 | 0.80 | 1.00 | 1.10 | 1.04 | 8.93 | 1.07 | 0.98 | 0.87 | 0.82 | 0.63 | 1.03 | 1.10 | 1.07 |
| L-form | 2.00 | 1.93 | 0.82 | 1.00 | 0.96 | 1.02 | 8.37 | 0.92 | 0.97 | 0.69 | 0.88 | d | 0.91 | 1.01 | 0.77 |

[a]The molar ratio of each amino acid was normalized based on Gly. [b]Amino acid analysis can not distinguish between Asp and Asn (Asx), and between Glu and Gln (Glx). [c]Thr and β-Ala coelute in the HPLC analysis and can not be distinguished. [d] D-Ile is excluded in the D-library.



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**Table 4**. Correlation of binding constants in solution with relative ion intensities for the seven individual peptide inhibitors.

| $AA_1$, $AA_2$ | Ion Intensity[a] | $K_b$(x10$^6$, $M^{-1}$)[b] | $\Delta G_b$(kcal/mol)[b] |
|---|---|---|---|
| L-Leu | 3.8 | 140 | -11.2 |
| D-Leu | 2.4 | 41 | -10.5 |
| L-Thr | 1.0 | 8.8 | -9.5 |
| D-Thr | 0.5 | 5.8 | -9.3 |
| L-Ser | 0.5 | 7.5 | -9.4 |
| D-Ser | 1.1 | 16 | -9.9 |
| Gly | 1.0 | 4.9 | -9.2 |

[a]The ion intensity of each ligand in both libraries is normalized to that of Gly-Gly. The uncertainty determined from three experiments is 20%. [b]The binding affinity of these ligands were measured in 20 mM phosphate buffer (pH = 7.5) at 37 °C. The uncertainty of $K_b$ is 10%.