

**Table S2.** Comparison of  $K_i$  values for reference protein interactions with  $K_i$  and  $K_d$  values from the literature.

Competitor	Species	Family	$K_i$ ( $\mu\text{M}$ ) <sup>a,b</sup>					
			PDZ1		PDZ2		PDZ3	
			Literature	Result	Literature	Result	Literature	Result
CRIPT	Human	CRIPT	$97 \pm 18^{c,d}$	$76 \pm 6.7$	$25 \pm 1.6^{c,d}$	$25 \pm 2.5$	$2.1 \pm 0.15^{c,d}$	$2.9 \pm 0.01^c$
GluN2B	Human	Glutamate gated ion channel	$18 \pm 0.92^{c,d}$	$29 \pm 2.5^c$	$4.1 \pm 0.17^{c,d}$	$5.5 \pm 0.89^c$	NA <sup>d</sup>	NA
KIF1B $\alpha$	Human	Kinesin-like	$2.4^{e,f}$	$7 \pm 0.2$	$2.1^{e,f}$	$3.8 \pm 0.42$	$2.7^{e,f}$	$14 \pm 2.2$

<sup>a</sup>The shown data are  $K_i \pm$  fitting error, unless otherwise noted.

<sup>b</sup>NA, no affinity, defined as a  $K_i$  value above 1000  $\mu\text{M}$ .

<sup>c</sup>Shown data are mean  $K_i \pm$  standard error of the mean from two or more independent experiments.

<sup>d</sup>Bach A, Chi CN, Olsen TB, Pedersen SW, Røder MU, et al. (2008) Modified peptides as potent inhibitors of the postsynaptic density-95/*N*-methyl-D-aspartate receptor interaction. *J Med Chem* 51: 6450-6459.

<sup>e</sup> $K_d$  value.

<sup>f</sup>Stiffler MA, Chen JR, Grantcharova VP, Lei Y, Fuchs D, et al. (2007) PDZ binding selectivity is optimized across the mouse proteome. *Science* 317: 364-369.