

Table S4: Phosphorylation specificity switch for proteins containing domains of the PDZ family

A

1		HtrA1 (1/1)	Magi-2 (6/6)
	NLKAGRET TV (Kif1b)	24634	-1
	CLDTSRET DL (Kcna5)	-1	22260
2		SAP97 (3/3)	Scrb1 (2/4)
	SPLHSLET SL (Atp2b1)	43518	-1
	SNKAVET DV (Kcna4)	-1	28774
3		Gm1582 (2/3)	SAP97 (1/3)
	PLATCDET SI (Sema4f)	97014	-1
	CLDTSRET DL (Kcna5)	-1	65366
4		Gm1582 (2/3)	Semcap3 (1/2)
	PLATCDET SI (Sema4f)	97014	-1
	PRPLRRE SEI (Kcnj2)	-1	45847
5		Gm1582 (2/3)	PTP-BL (2/5)
	PLATCDET SI (Sema4f)	97014	-1
	SNKAVET DV (Kcna4)	-1	38848
6		Lin7c (1/1)	Semcap3 (1/2)
	PDSNP EESV (Sema4c)	41233	-1
	PRPLRRE SEI (Kcnj2)	-1	45847
7		Lin7c (1/1)	PTP-BL (2/5)
	VDFFPK ESSL (Acvr2a)	11852	-1
	KKMP SI ESDV (Grin2a)	-1	52174
8		HtrA1 (1/1)	g1-syntrophin (1/1)
	GNDPDRGT SI (Grid2)	26129	-1
	CLDTSRET DL (Kcna5)	-1	21074
9		Semcap3 (1/2)	Chapsyn-110 (3/3)
	VDFFPK ESSL (Acvr2a)	18329	-1
	AHFSS LESEV (Grin2c)	-1	14263
10		Chapsyn-110 (3/3)	PSD95 (1/3)
	ELDEF PETSV (Trpv3)	4948	-1
	EKLSS IESDV (Grin2b)	-1	17859
11		MUPP1 (13/13)	Magi-2 (6/6)
	TNSKQGET TV (Fzd1)	46387	-1
	ANLVK EDSDV (Megalin)	-1	15895
12		Lin7c (1/1)	Chapsyn-110 (3/3)
	VDFFPK ESSL (Acvr2a)	11852	-1
	PRPLRRE SEI (Kcnj2)	-1	5439
13		HtrA1 (1/1)	Gm1582 (2/3)
	NLKAGRET TV (Kif1b)	24634	-1
	EKLSS IESDV (Grin2b)	-1	92597
14		Semcap3 (1/2)	Gm1582 (2/3)
	NLKAGRET TV (Kif1b)	12485	-1
	AHFSS LESEV (Grin2c)	-1	27870
15		g1-syntrophin (1/1)	Magi-2 (6/6)
	SPLHSLET SL (Atp2b1)	78075	-1
	VNIKK IFTDV (Kcna3)	-1	59433
16		Gm1582 (2/3)	TIP-1 (1/1)
	NVVSE RISV (Htr2c)	97451	-1
	PRPLRRE SEI (Kcnj2)	-1	49074
17		Lin7c (1/1)	Gm1582 (2/3)
	DTKNY KQTSV (CRIPT)	41217	-1
	EKLSS IESDV (Grin2b)	-1	92597
18		Gm1582 (2/3)	PTP-BL (2/5)
	TNSKQGET TV (Fzd1)	39246	-1
	KKMP SI ESDV (Grin2a)	-1	52174
19		HtrA1 (1/1)	TIP-1 (1/1)
	GNDPDRGT SI (Grid2)	26129	-1
	PRPLRRE SEI (Kcnj2)	-1	49074
20		Gm1582 (2/3)	PTP-BL (2/5)
	TNSKQGET TV (Fzd1)	39246	-1
	RRIS SESEV (Grin2c)	-1	27872
21		PTP-BL (2/5)	TIP-1 (1/1)
	NVVSE RISV (Htr2c)	26003	-1
	VRPYRRE SEI (Kcnj12)	-1	36503
22		Lin7c (1/1)	PTP-BL (2/5)
	NLKAGRET TV (Kif1b)	7258	-1
	KKMP SI ESDV (Grin2a)	-1	52174
23		HtrA1 (1/1)	PTP-BL (2/5)
	TNSKQGET TV (Fzd1)	20699	-1
	EKLSS IESDV (Grin2b)	-1	26446
24		Lin7c (1/1)	PTP-BL (2/5)
	VDFFPK ESSL (Acvr2a)	11852	-1
	EKLSS IESDV (Grin2b)	-1	26446
25		Gm1582 (2/3)	PSD95 (1/3)
	ELDEF PETSV (Trpv3)	3133	-1
	KKMP SI ESDV (Grin2a)	-1	8176
26		Magi-3 (5/5)	Magi-2 (6/6)
	NVVSE RISV (Htr2c)	37603	-1
	PAGKH MVTEV (Kcna7)	-1	79666
27		HtrA1 (1/1)	Magi-3 (5/5)
	NLKAGRET TV (Kif1b)	24634	-1
	ANLVK EDSDV (Megalin)	-1	91467
28		Lin7c (1/1)	PTP-BL (2/5)
	DTKNY KQTSV (CRIPT)	41217	-1
	KKMP SI ESDV (Grin2a)	-1	52174

B

1		Scrb1 (3/4)	HtrA3 (1/1)
	GNDPDRGT SI (Grid2)	37966	-1
	NNNLI KVDSV (Mella/b)	-1	34912

C

1		Shank1 (1/1)	Lin7c (1/1)
	RDYKQSSSTL (Grm1)	13595	-1
	TNSKQGETTV (Fzd1)	-1	14635
2		Shank1 (1/1)	Lin7c (1/1)
	RDYKQSSSTL (Grm1)	13595	-1
	VDFPPKESL (Acvr2a)	-1	11852
3		Shank1 (1/1)	Lin7c (1/1)
	RDYKQSSSTL (Grm1)	13595	-1
	NLKAGKETTV (Kif1b)	-1	7258
4		Shank3 (1/1)	Lrrc7 (1/1)
	EVLDSTSSL (Grm3)	15260	-1
	GARVPKETAL (Mapk12)	-1	41794
5		Shank3 (1/1)	Lin7c (1/1)
	RDYKQSSSTL (Grm1)	8203	-1
	GARVPKETAL (Mapk12)	-1	11878
6		OMP25 (1/1)	Magi-2 (6/6)
	NTANRRTPV (Stargazin)	7198	-1
	CLDTSRETDL (Kcna5)	-1	22260
7		Shank1 (1/1)	Scrb1 (3/4)
	AHEDYVTRL (Trpc4)	379	-1
	SNKAVETDV (Kcna4)	-1	7414
8		Pdzk1 (1/4)	Scrb1 (3/4)
	GQEEQVTRL (Trpc5)	14911	-1
	TNSKQGETTV (Fzd1)	-1	33133

The table is divided into sub-tables, each including the following data: (1) Pair-wise alignment of peptide sequences, where the S/T/Y and the D/E residues are colored in red. Protein names are given in parentheses. The interaction-relevant C-terminal residues are in black. (2) Names of proteins (Uniprot or gene names) that include the PDZ domains. Numbers in parentheses indicate the domain identifier (e.g. 2/4 means the second out of four PDZ domains in the relevant protein). (3) Affinity values for each domain-peptide interaction. Values represent the equilibrium dissociation constant (nM), as measured using fluorescence polarization. A value of (-1) stands for array negatives (*i.e.* no interaction was detected). All values were taken from [1,2]. The table is split into three sections (A, B and C), representing different positions of the Asp/Glu residue in the pseudo-phosphorylated motifs. **(A)**: Asp/Glu residues are positioned one residue upstream to the C-terminal residue. **(B)**: Asp/Glu residues are positioned two residues upstream to the C-terminal residue. **(C)**: Asp/Glu residues are positioned three residues upstream to the C-terminal residue. Note that 11 different proteins that are involved in nine of the 37 putative double switches (Acvr2a, Atp2b1, Chapsyn-110, Grm1, Grm3, Lin7c, SAP97, Scrb1, SEMCAP3, Shank1 and Trpc5) were experimentally verified as associated with the post-synaptic density [3-12]. Note that this table reports 37 PDZ double-switch cases out of the 82 identified: in cases where several PDZ pairs displayed double-switch binding pattern with a specific peptide-pair, we list in the table the one with the highest affinity values for the 'non-phosphorylated or 'pseudo-phosphorylated' peptide pair. Accordingly, we present 28 out of 60 examples for the 'position (-1)' cases, one case of 'position -2' and 8 out of 20 examples of the 'position (-3)' cases. All peptide pairs are sorted according to sequence similarity, taking into account higher weight for the C-terminal positions. When sequence similarities had almost identical scores, we added the affinity values into the sorting criteria (higher affinities were ranked higher).

Table S4 references

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