

**Supplementary figure 4. Structure based sequence alignment of PtdInsPs interacting PDZ domains.**

Indicated in red are residues of the conserved positive charge cluster. Residues in blue indicate the alternative positive charge cluster of PICK1 (Pan et al., 2007). Basic residues in orange have been shown by mutagenic analysis to be of importance for SDCBPs PDZ-PtdInsPs interactions (Meerschaert et al., 2007; Mortier et al., 2005; Zimmermann et al., 2002). In magenta are residues defining a basic cluster in SLC9A3R2\_1 potentially involved in PtdInsPs binding. Sequences of the predicted PtdInsPs binders APBA3-1, INADL\_7, LIN7A and MPDZ\_8 are included for comparison.

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SLC9A2_1      PRLCRLVRGEQ--GYGFHLHGEKGR-----R-GQFIRRVEP-GSPAEAAALRA
SNTX27       PRVVRIVKSES--GYGFNVRGQVSEGGQLRSINGELYAPLQHVSAVLPGGAADRAG-VRK
PDZD11      PRITTLKKPPGA-QLGFNIRGGKASQ-----LGIFISKVIPDSDAHRAG-LQE
DFNB31_1    VRLVSLRRAKAHEGLGFSIRGGSEHG-----VGIYVSLVEP-GSLAEKEGLRV
LIN7A       PRVVELPKTTD-EGLGFNVMGGKEQN-----SPIYISRIIPGVAERHGGLKR
SNTG1       ERTVTIRRQTVG-GFGLSIKGAEHN-----IPVVVSKISKEQRAELSGLLFI
SNTA1       RRRVTVRKADAG-GLGISIKGRENK-----MPILISKIFKGLAADQTEALFV
LNx1_4      CKDIVLRRNTAG-SLGFCIVGGYEEYNG-----NKPFFIKSIVEGTPAYNDGRIRC
SDCBP2_2    QRTVTMHKDSMG-HVGFVIK--KG-----KIVSLVKGSSAARNG-LLT
SDCBP1_2    FETITMHKDSTG-HVGFIFK--NG-----KITSIVKDSSAARNG-LLT
IL16_1     ISNIVLMKGQAK-GLGFSIVGGKDSIYG-----PIGIYVKTIFAGGAAAADGRLQE
PDZD2_3    ISIIGLYKEKGK-GLGFSIAGGRDCIRG-----QMGIFVKTIFPNGSAEDGRLKE
IL16_3     IHVTILHKEEGA-GLGFSLAGGADLEN-----KVITVHRVFPNGLSAQEGTIQK
MPDZ_8     LHMIELEKGHS--GLGLSLAGNKDRS-----RMSVFIVGIDPNGAGKDGRLQI
INADL_7    LHIIELEKDKN--GLGLSLAGNKDRS-----RMSIFVVGINPEGPAAADGRMRI
SDCBP2_1    VREIHLCKDERG-KTGLRLRKVDQ-----GLFVQLVQANTPASLVG-LRF
SDCBP1_1    IREVILCKDQDG-KIGLRLKSIDN-----GIFVQLVQANSPASLVG-LRF
CASK       SRLVQFQKNTDE-PMGITLKMN---EL-----NHCIVARIMHGGMIHRQGTLHV
MAGI1_6    FYTVELERGAK--GFGFSLRGGREYN-----MDLYVLRLAEDGPAERCGKMRI
PARD3_2    RLNIQLKKGTE--GLGFSITSRDVTIGG-----SAPIYVKNILPRGAAIQDGRLKA
PICK1      PGKVTLQKDAQN-LIGSIGGGAQYC-----PCLYIVQVFDNTPAALDGTVAA
DFNB31_3   STLVRVKSAA--TLGIAEGGANTR-----QPLPRIVTIFRGSAHNCGQLKV
MAGI3_3    LVTIPLIKGPK--GFGFAIADSP-----TGQKVKMIL-D-S-QWCQGLQK
ZO1_2     PTKVTLVKSRKNEEYGLRLA-----SHIFVKEISQDSLAARDGNIQE
APBA3_1    CREVHLEKRRG-EGLGVALVESGWGSLLP-----TAAVIANLLHGGPAERSGALSI
PARD3_1    VKLVEVPNDGG--PLGIHVVPFSARGR-----TLGLLVKRLEKGKAEHENLFRE

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SLC9A2_1      GDRLVEVNGVNVEGETHHQVVQRIKAV--EG---QTRLLVVD
SNTX27       GDRILEVNVHVNVEGATHKQVVDLIRAG--EK---ELILTVLS
PDZD11      GDQVLAVNDVDFQDIEHSKAVEILKTA---R---EISMRVRF
DFNB31_1    GDQILRVNDKSLARVTHAEAVKALKGS---K---KLVLSVYS
LIN7A       GDQLLSVNGVSVEGEHHEKAVELLKAA---KD--SVKLVVRY
SNTG1       GDAILQINGINVRKCRHEEVQVLRNA--GE---EVTLTVSF
SNTA1       GDAILSVNGEDLSSATHDEAVQVLKKT--GK---EVLVEVKY
LNx1_4      GDILLAVNGRSTSGMIHACLARLLKEL---KG--RITLTIVS
SDCBP2_2    NHYVCEVDGQNVIGLKDKKIMEILATA---GN-VVTLTIP
SDCBP1_2    EHNICEINGQNVIGLKDSQIADILSTS---GT-VVTITIMP
IL16_1     GDEILENGESMAGLTHQDALQKFKQA---KKG--LLTLTVRT
PDZD2_3    GDEILDVNGIPIKGLTFQEAIHTFKQI---RSG-LFVLTVRT
IL16_3     GNEVLSINGKSLKGTTHHDALAILRQAREPR---QAVIVTRK
MPDZ_8     ADELLEINGQILYGRSHQNASSIKCA---PS--KVKIIFIR
INADL_7    GDELLEINNQILYGRSHQNASAIIKTA---PS--KVKLVFIR
SDCBP2_1    GDQLLQIDGRDCAGWSSHKAHQVVKKA---SGD-KIVVVVRD
SDCBP1_1    GDQVLRINGENCAGWSSDKAHKVLKQA---FGE-KITMTIRD
CASK       GDEIREINGISVANQTVEQLQKMLREEM--RG--SITFKIVP
MAGI1_6    GDEILEINGETTKNMKHSRAELIKNG--GR---RVRLFLKR
PARD3_2    GDRLIEVNGVDLVGKSQEEVVSLLRST---KMEGTVSLLVFR
PICK1      GDEITGVNGRSIKGKTKVEVAKMIQEV--KG--EVTIHYNK
DFNB31_3   GHVILEVNGLTLRGKEHREAARIIAEAFKTKDRDYIDFLVTE
MAGI3_3    GDIKEIYHQNVQNLTHLQVVEVLKQF--PVG-ADVPLLILR
ZO1_2     GDVVLKINGTVTENMSLTDAKTLIERS---KG--KLKMVVQR
APBA3_1    GDRLTAINGTSLVGLPLAACQAAVRETKS-QT--SVTLSIVH
PARD3_1    NDCIVRINDGLRNRRFEQAQHMFRQAM--RTP-IIWFHVVP

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