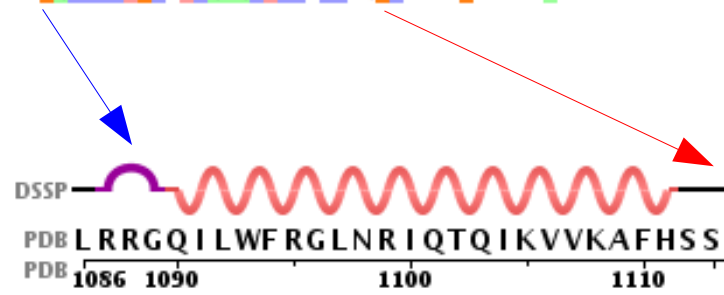


A Seed sequence alignment for PF12424

Q6UUX1_9CNID/1078-1143	ARLLWIRGLTRLQHQIRVVNAFRSVID.GRSQRAIASPAV.FNSLLAPVRTA.MVYDSDSQYPSALDSTE
B4H868_DROPE/1067-1132	GQILWIRGLTRLQTQLRVIRAFRSTLEDLNERMSHSLHS.LRSPTGVPV.GGGHPLYNFNLLSPNY
Q7PRK3_ANOGA/1041-1108	GQILWIRGLTRLQTQLRVVAFRSTLEDLEERRSIHSLHS.LRSSRSHPGGMSTSVTRRLADQIPSSWQ
Q9TYP9_CAEEL/1073-1128	GQSLWLLGLTRLQTQIRVVKAFQSVNDDSHPNSLTTSTAD.....RLRASYRRLRIARELE
A8PFU1_BRUMA/670-725	GQMLWLLGLTRLQTQMRVIRAFQTNACTHTPTSLTTSTAE.....RLRASYRRLQLARERE
B7CED8_CAEEL/1099-1165	GQILWVRGLTRLQTQIRVVKAFQAGLDRREPSLTGQSAAR.LREISRQLRLQ.VDSENRSRSTSRGNIK
Q4TA79_TETNG/1127-1187	GQILWFRGLNRIQTQ.....MRGGASAVCGGRLSASSPS.LEEAVELLWMW.SIPRAARRSLGALR
Q9N1A0_CANFA/8-74	GQILWFRGLNRIQTQIDVINTFQTGASFKGVLRKQT.MGQHLDVKHPSSSYVTVAPVTSPPTTSPVA
Q4JQ03_STRPU/1077-1141	AQILWMRGLTRLQQQIRVVHAFQSGL.QHRIERKSLSNS.VHEFMSPDNTY.DIETTKQDQDAAPMVS
B2CZC1_DANRE/1096-1160	GQILWFRGLNRIQTQIKVVNAFRSSL.YEGLEKPESSRS.IHNFMSHPEFV.PISEEESRISTIDEGC
Q3L582_HUMAN/119-182	GQILWFRGLNRIQTQIRVVNAFRSSL.YEGLEKPESSRS.IHNFMTHEFV.RIEDSEPHIPLIDDTD
B055H3_DANRE/1100-1163	GQILWFRGLNRIQTQIRVVKAFRSSL.YDGIERPESRNS.IHDFQAHPEF.IITDSVHNIPLIDETD
AT2B3_RAT/1147-1201	LST.....PTHIRVVKAFRSSL.YEGLEKPESSRS.IHNFMTHEFV.LINDYTHNIPLIDDTD
AT2B4_RAT/1089-1150	GQILWVRGLNRIQTQIRVVVFHFS.RDVIHKSKNQVS.IHSFMTQPEY.AADEMSQ.SFLNQUEE
Q6Q477_MOUSE/1090-1151	GQILWVRGLNRIQTQIRVVKLFHNN.HEVAHKPKNRSS.IHTFMTQPEY.PADELSQ.SFLDIQE
Q3YB86_PIG/134-197	GQILWFRGLNRIQTQIKVVKAFHSSL.HESIQKPKNQNS.IHNFMTHEFV.AIDEEGPRTPLEEQE
AT2B4_HUMAN/1126-1188	GQHLVK.LVPSSSYIKVVKAFHSSL.HESIQKPKNQNS.IHNFMTHEFV.AIEEELPRTPLLEEE
B7Q9C2_IXOSC/971-1038	GQILWIRGLTRLQTQIRVVNAFRSNLDARNNPAYQTALLR.KASAASPSGTGGFARPOLHSQPSQPOSS
B3N0M2_DROAN/1054-1109	GQILWIRGLTRLQTQIRVVNAFRQGLDARYGDHNTSLAE.....VLRKQNSMSKRLSETS

B



C

ENST00000357681	LRRGQILWFRGLNRIQTQIKVVKAFHSSL--HESIQK
ENST00000341360	LRRGQILWFRGLNRIQTQIDVINTFQTGASFKGVLRR
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Figure S17. The Pfam domain broken in the splice variants of *ATP2B1* and *ATP2B4*

A. Seed alignment for Pfam domain PF12424 (Plasma membrane calcium transporter ATPase C terminal). B. Structure resolved for this domain, from PDB structure 2KNE, chain B, which is a single helix, bound to calmodulin. C. The alignment between the two homologous isoforms of *ATP2B1* identified in the experiments. The blue and red arrows show where the Pfam seed alignment begins (blue) and where the conserved section of the Pfam domain ends (red). The Pfam domain is highly conserved over the first part of the alignment (the part of the alignment that coincides with the crystallised helix structure), but has little conservation at the C-terminal end. The (distant) homology detected for the *ATP2B1* isoforms (and all other members of this family) is clear up to the residue indicated with the red arrow, but it not conserved after and therefore the splice event would break the domain. However, the evidence from the PDB structure (and the lack of conservation in the Pfam seed alignment itself) suggests that the Pfam alignment should not be extended beyond the red arrow. In fact the residues before the first N-terminal residue of PF12424 are just as conserved as the residues between the ed and blue arrows, suggesting that perhaps the plasma membrane calcium transporter ATPase C terminal domain should also be extended towards the N-terminal end.