Appendix

Human ALPI deficiency causes inflammatory bowel disease and highlights a key mechanism of gut homeostasis

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Table of Content

Appendix Fig S1: BLAST sequence alignment and coordinates of ALPP (entry code 1EW2)[1].

Sequence alignment Query= ALPP; Sbjct= ALPI

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sp|P05187|PPB1_HUMAN Alkaline phosphatase, placental type OS=Homo sapiens
GN=ALPP PE=1 SV=2
Sequence ID: Query_182371Length: 535Number of Matches: 1
Related Information
Range 1: 23 to 516 Graphics Next Match Previous Match

Query  20   VIPAEEENPAFWNRQAAEALDAAKKLQPIQKVAKNLILFLGDGLGVPTVTATRILKGQKN  79
            +IP EENP FWNR+AAEAL AAKKLQP Q  AKNLI+FLGDG+GV TVTA RILKGQK
Sbjct  23   IIPVEEENPDFWNREAAEALGAAKKLQPAQTAAKNLIIFLGDGMGVSTVTAARILKGQKK  82

Query  80   GKLGPETPLAMDRFPYLALSKTYNVDRQVPDSAATATAYLCGVKANFQTIGLSAAARFNQ  139
             KLGPE PLAMDRFPY+ALSKTYNVD+ VPDS ATATAYLCGVK NFQTIGLSAAARFNQ
Sbjct  83   DKLGPEIPLAMDRFPYVALSKTYNVDKHVPDSGATATAYLCGVKGNFQTIGLSAAARFNQ  142

Query  140  CNTTRGNEVISVMNRAKQAGKSVGVVTTTRVQHASPAGTYAHTVNRNWYSDADMPASARQ  199
            CNTTRGNEVISVMNRAK+AGKSVGVVTTTRVQHASPAGTYAHTVNRNWYSDAD+PASARQ
Sbjct  143  CNTTRGNEVISVMNRAKKAGKSVGVVTTTRVQHASPAGTYAHTVNRNWYSDADVPASARQ  202

Query  200  EGCQDIATQLISNMDIDVILGGGRKYMFPMGTPDPEYPADASQNGIRLDGKNLVQEWLAK  259
            EGCQDIATQLISNMDIDVILGGGRKYMF MGTPDPEYP D SQ G RLDGKNLVQEWLAK
Sbjct  203  EGCQDIATQLISNMDIDVILGGGRKYMFRMGTPDPEYPDDYSQGGTRLDGKNLVQEWLAK  262

Query  260  HQGAWYVWNRTELMQASLDQSVTHLMGLFEPGDTKYEIHRDPTLDPSLMEMTEAALRLLS  319
             QGA YVWNRTELMQASLD SVTHLMGLFEPGD KYEIHRD TLDPSLMEMTEAALRLLS
Sbjct  263  RQGARYVWNRTELMQASLDPSVTHLMGLFEPGDMKYEIHRDSTLDPSLMEMTEAALRLLS  322

Query  320  RNPRGFYLFVEGGRIDHGHHEGVAYQALTEAVMFDDAIERAGQLTSEEDTLTLVTADHSH  379
            RNPRGF+LFVEGGRIDHGHHE  AY+ALTE +MFDDAIERAGQLTSEEDTL+LVTADHSH
Sbjct  323  RNPRGFFLFVEGGRIDHGHHESRAYRALTETIMFDDAIERAGQLTSEEDTLSLVTADHSH  382

Query  380  VFSFGGYTLRGSSIFGLAPSKAQDSKAYTSILYGNGPGYVFNSGVRPDVNESESGSPDYQ  439
            VFSFGGY LRGSSIFGLAP KA+D KAYT +LYGNGPGYV   G RPDV ESESGSP+Y+
Sbjct  383  VFSFGGYPLRGSSIFGLAPGKARDRKAYTVLLYGNGPGYVLKDGARPDVTESESGSPEYR  442

Query  440  QQAAVPLSSETHGGEDVAVFARGPQAHLVHGVQEQSFVAHVMAFAACLEPYTACDLAPPA  499
            QQ+AVPL  ETH GEDVAVFARGPQAHLVHGVQEQ+F+AHVMAFAACLEPYTACDLAPPA
Sbjct  443  QQSAVPLDEETHAGEDVAVFARGPQAHLVHGVQEQTFIAHVMAFAACLEPYTACDLAPPA  502

Query  500  CTTDAAHPVAASLP  513
             TTDAAHP  + +P
Sbjct  503  GTTDAAHPGRSVVP  516
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[1] Le Du MH, Stigbrand T, Taussig MJ, Menez A, Stura EA. Crystal structure of alkaline phosphatase from human placenta at 1.8 A resolution. Implication for a substrate specificity. J Biol Chem. 2001 Mar 23;276(12):9158-65.

Appendix Table S1: Autosomal recessive and *de novo* variants identified by WES in Patient1

Gene	Variant	Protein	SIFT	MUTATION TASTER	POLYPHEN
de novo: SETD1A	16 :30991333 C/A	p.Pro1409Gln	Tolerated	Polymorphism	Benign
de novo: ADAMTS14	rs758220536	p.Arg451His	Deleterious	Disease causing	Probably damaging
AR[1]: *ALPI*	2:233321394 G/A	p.Ala97Thr	Deleterious	Disease causing	Probably damaging
	2:233322984 C/T	p.Ala350Val	Tolerated	Disease causing	Possibly damaging
AR: *NWD1*	19:16918475 C/T	p.Thr1272Met	Tolerated	Polymorphism	Probably damaging
	rs191976059	p.His843Gln	Tolerated	Polymorphism	Benign
AR: *KRTAP5-4*	rs200027081	p.Val152Gly	not scored	not scored	not scored
	11:1643184_TGAG CCACAGCCCCCA	frameshift	not scored	not scored	not scored
AR: *TLN1*	rs141770878	p.Lys2115Glu	Deleterious	Disease causing	Probably damaging
	rs200664793	p.Thr585Met	Tolerated	Disease causing	Possibly damaging
	rs144809355	p.Ala2013Thr	Tolerated	Disease causing	Possibly damaging
AR*: HGFAC*	rs149401735	p.Pro84Arg	Tolerated	Polymorphism	Benign
AR: *TBX22*	X:79277859 G/C	p.Glu31Gln	Tolerated	Polymorphism	Benign
AR: *ARSF*	rs764160465	p.Thr299Met	Deleterious	Disease causing	Possibly damaging
AR: *KIAA1875*	rs540903279	p.Glu1207Lys	not scored	not scored	Possibly damaging

Appendix Table S2: Autosomal Recessive and *de novo* variants identified by WES in Patient2

Gene	Variant	Protein	SIFT	MUTATION TASTER	POLYPHEN
de novo: ADRA1D	rs55915202	p.Ala460Val	Tolerated	Disease causing	Benign
de novo: FKBP10	17:39973373	frameshift	not scored	not scored	not scored
de novo: FOXP2	7:114271580	3 nt deletion in splice_acceptor	not scored	not scored	not scored
AR: *ALPI*	rs146257849	p.Ala360Val	Tolerated	Disease causing	Probably damaging
	2:233323584 C/T	p.Gln439X	not scored	not scored	not scored
AR: *FLG*	rs12750571	p.Arg1437Cys	Tolerated	Polymorphism	Possibly damaging
	rs143382793	p.Gly929Val	Tolerated	Polymorphism	Possibly damaging
AR: *FRMPD1*	rs200027081	p.Val152Gly	Deleterious	Disease causing	Possibly damaging
	rs140778637	p.Glu1519Ala	Deleterious	Disease causing	Possibly damaging
AR: *MUC17*	7:100678206 C/T	p.Thr1170Met	Deleterious	Disease causing	Possibly damaging
	rs145956810	p.Ser1788Leu	Deleterious	Disease causing	Possibly damaging
AR: *NT5C3B*	rs139142062	p.Arg263His	Deleterious	Disease causing	Probably damaging
	7:39992191 C/A	p.Ala11Ser	Tolerated	Disease causing	Benign
AR*: PCDH9*	rs149158184	p.Ser1209Arg	Tolerated	Disease causing	Benign
	rs149470963	p.Ser1017Arg	Tolerated	Disease causing	Benign
	rs139732295	p.Val885Leu	Deleterious	Disease causing	Probably damaging
AR: *FAT2*	rs61743253	p.Arg368Lys	Tolerated	Polymorphism	Possibly damaging
AR: *RIOK1*	rs55698032	p.Arg114Gln	Tolerated	Disease causing	Benign
AR: *STX8*	rs55698032	p.Arg141Gln	Tolerated	Disease causing	Benign