

mouse	1	MATTTTPEKSAAWWNYFFLYDGSVKVKEGDPTRAGICYFYPPQTLLDQQEELLCGQLAGV	60
human	1	MATSTSTEAKSASWWNYFFLYDGSVKVKEGDPTRAGICYFYPSQTLLDQQEELLCGQIAGV	60
<i>X. laevis</i> (+/+)	1	MASSIPTEHRPASWLNYYFFLYDGSKVRGEGDPTSVGINIFYPTQTILDQQEELLCGQIAGV	60
<i>X. laevis</i> (<i>a^p/a^p</i>)	1	MASSIPTEHRPASWLNYYFFLYDGSKVRGEGDPTSVGINIFYPTQTILDQQEELLCGQIAGV	60
mouse	61	VRCLWDLSGTTPMLIRMRNLKFAIRADGDYLWALGCGVEISDASCRQFLDQLIGFFHFYM	120
human	61	VRCVSDISDSPPTLVRLRKLKFAIKVDGDLWVLCAGVELPDVSCKRFLDQLVGFNFYFN	120
<i>X. laevis</i> (+/+)	61	VRCMTEITNSSPNLIRLRKLKFAIVVDGDLWALGCSVDVADVSCKHFLQELIGLFLFYN	120
<i>X. laevis</i> (<i>a^p/a^p</i>)	61	VRCMTEITNSSPNLIRLRKLKFAIVVDGDLWALGCSVDVADVSCKHFLQELIGLFLFYN	120
mouse	121	GPVSLAYKSHPQEELSLOWDTSITQVLRSTSESHRIFNALWNLDRTKVEPLLLLKAALIL	180
human	121	GPVSLAYENCSEQEELSTEWDTFIEQILKNTSDLHKIFNSLWNLDRTKVEPLLLLKAARIL	180
<i>X. laevis</i> (+/+)	121	GPLRDAYEVRSAEELSNEWNLYIEFIQNTSTDHLRIFNSLSHLDKTKVDPLLLLKAALIL	180
<i>X. laevis</i> (<i>a^p/a^p</i>)	121	GPLRDAYEVRSAEELSNEWNLYIEFIQNTSTDHLRIFNSLSHLDKTKVDPLLLLKAALIL	180
mouse	181	QTCQRSPhVLagCilyKGLIVNSQLLPSLTAKVLLHQTVPA-DQRlPGAGAAPQETGAAL	239
human	181	QTCQRSPhILagCilyKGLIVSTQLPPSLTAKVLLHRTAPQ-EQRlPTGEDAPQEHGAAL	239
<i>X. laevis</i> (+/+)	181	QTCQRFPYILagCilyKHNIVSTQLPPSITSKILLIQRVGLVQSPSSVNNQDAELPQDV--	238
<i>X. laevis</i> (<i>a^p/a^p</i>)	181	QTCQRFPYILagCilyKNCrVTPGCLYDPCICN	214
mouse	240	PPDVQITSVFLSEEEVASLHEFFVEHETRL-----QGSS-VQYPP-WDQS----SP	284
human	240	PPNVQIIPVfvtKEEAIslHEFFVEQmTRSLASPA--GLQDGS-AQHHP-KGGSTsALKE	295
<i>X. laevis</i> (+/+)	239	--CMIPVfVIENEITslRHYP--AEWmTRmPTPSrTLSTLgKKPAGNqFPVSEdGTQEGi	294
mouse	285	TQaedAWASAAIPEPTPH-DGA--CPSGSGA-----DERLPRLEQECAGPTGLCTTACGQ	336
human	296	N-ATGHVESMAWTTPDPT-SPDEACPDGRKE-----NGCLSGHDLESIRPAGLHNSARGE	348
<i>X. laevis</i> (+/+)	295	TGGGESFPVHLpTEETPIQgAGAGLLVDKsVELPFLsLMTDSPMQCSSPLNqERTRQsKE	354
mouse	337	GsGLSSRLQkELCLsREELDSSE-----MHVSEAQEAfPPLpALGDLETLH-S-	383
human	349	VlGLSSSLGkELVfLQEEldLSEIHipeAQEVEMASGHfAFLhVPVP-DGRAPyCKA-sL	406
<i>X. laevis</i> (+/+)	355	PKSSGGNPVK-----AHSDIN--SSLYNLVLIVPKQKAISE	388
mouse	384	---SHSAPTLpEDTAIC-SCLHPCPLERlpESGRlGQLADLpLTNGQTVPGTDpLPSSM	439
human	407	SASSSLEPTPPEDTAIS-SLRPPSAPeMLTQhGAQEQLEDHPGHSSQAPIPRADpLPRRT	465
<i>X. laevis</i> (+/+)	389	ETEDNNDIN---RERLSTGSfATCDsVMEfETKEDGLE--TFEDYVPVSLKDNtSTEDQT	443
mouse	440	PVALPPQHPVgVEPSVep-----YNGAQE-SHSALPR--SSRSPDSPGpSPS---	484
human	466	RrPLLLPRLDPGQRGNKlPTGEOGLDEDVDGvCE-SHAAPGLECSSGSANCQgAGPS---	521
<i>X. laevis</i> (+/+)	444	DSCEQSILLGkPESVS-----DRKDNTEfNTND--STLDKSSPSSQTTDIGfSP	490
mouse	485	----ADRTG--FKPSPSGRHAGlVPMNLYTHSVNGLVLSLLAEETLLSDTAAIEEVYHSS	538
human	522	----ADGIS--SRLTPAESCMGLVRMNLyTHcVKGLVLSLLAEePLLGDSAAIEEVYHSS	575
<i>X. laevis</i> (+/+)	491	KVfGVTdWSSLlVSSTQSSDStQLVQmMLyVhNvKGLVLALLAECPfQHDKASIQDvYDSt	550
mouse	539	LASLNGLEVHLkETLpRDEASLTsSTYNfLHYDRiQSVL-----SANLpLVtAPQDRRfL	593
human	576	LASLNGLEVHLkETLpRDEAAASTsSTYNfTHYDRiQSLL-----MANLpQvATPQDRRfL	630
<i>X. laevis</i> (+/+)	551	LASLNGLEVHLkETLpVNNNLTkSSYSfTHYDPIQHILtANLpSVSSThDRHfLRAATL	610
mouse	594	QAVNLMHSDfALLPMLyEMTIrNASTAVYACSSPAQETyFQQLAPtARSSGFNPQDCAF	653
human	631	QAVSLMHSEfAQLpALyEMTVrNASTAVYACCNPIQETyFQQLAPAArSSGFNPQDGAf	690
<i>X. laevis</i> (+/+)	611	IHSDFsQHq-----SFQEMTVrNAASAVYGCQSAVhETyFQQLAPPIrNSGVpDPQDNAf	665
mouse	654	SLAGKAKQKLLKHGVNLL	671
human	691	SLSGKAKQKLLKHGVNLL	708
<i>X. laevis</i> (+/+)	666	FLSSKAKQKLLKHGLNLL	683

Fig. S3. Amino acid sequence alignment of HPS4 from mouse, human, wild-type and mutant *X. laevis*.

The Hps4 protein of mutant *X. laevis* lacks amino acid residues 215–683, when compared with that of wild-type *X. laevis*. Identical residues are shaded. Asterisks (*) show critical residues reported to be responsible for Rab9 binding in HPS4 in mice (Ohishi et al., 2019).

Reference sequences: mouse HPS4, NP_001346782.1; human HPS4, NP_001336825.1

Accession numbers: +/+ *X. laevis* *hps4.L*, LC577762 (DDBJ); *a^p/a^p* *X. laevis* *hps4.L*,

LC577763 (DDBJ)