

Supplementary information for

Regulation of VEGFR2 trafficking and signaling by Rab

GTPase-activating proteins

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Supplementary Figure 1: Alignment RabGAP domains. The RabGAP domain was identified based on the crystal structure of TBC1D15 (Chen et al., 2017). It starts at position 47 (LKI...) and ends at position 488 (...GSE). Conserved amino acids based on this publication are marked in green.

	5	15	25	35	45	55	65	75	85	95	105	115
TBC1D15	-----SL	RGSDP-STHQ	RPPSEMADFL	SDAIPG----	-----LKIN	QQEEPGFVEI	TRID-LGERP	VVDRREP--V	SLEEWTKNID	SEGRILNVDN	MKQMIFRGGGL	SHALFKQANK
TBC1D17	-----VVS	FLQDPYSTTF	SSFSRVTNFF	RGALQPQPEG	AASDLPPPPD	DEPEPGFEVI	SCVE-LGPRP	TVEKGGP--V	TEEEWARHVG	PEGRLQQVPE	LKNRIFSGGL	SPSLRREANK
TBC1D16	-----	SRESQYKVFH	FHHGGDLKLS	DVFQQWKYCT	EMQLKDQVVA	PDKTCMQFSI	RRPKLPSSST	HPPEESMYKRL	GVSAWLNHLN	ELGQVEEYK	LRKAIFFGGI	DVSTIGVEVP
RUTBC1	-----	RLIHRDSTIS	NDVFLSVDDL	EPPEPQDPED	SRPKP----E	QEAGPGTPTG	AVVE-QQHSV	EFDSPDSGLP	SSRNYSVASG	IQSSLDEGQS	VGFEEDGGG	EEGSSGPGPA
RUTBC2	-----	NFSSGLSEHS	EPSLSTEDSV	LDAQRNTPTV	LRPRDGSVDD	RQSEFATTSQ	DEAP-REELA	VQDSLESDDL	ANESMDEFMS	ITGSLD----	MALPEKDDVV	MEGWRSETTE
TBC1D5	--MYHSLSET	RHPLQPEEQE	VGIDPLSSYS	NKSGGDSNKN	GRTTSSPLDS	EGTFNSYRKE	WEELFVNMY	LATIRQKGIN	GQLRSSRFRS	ICWKLFLCVL	PQDKSQWISR	IEELRAWYSN
TBC1D10A	-----	-----	-----S	LKSDSE--A	NG-FAERRID	KFGFIVGSQG	AEGALEEVP-	LEVLIRQR---	ESKWDLMLNN	WDKWMMAKHKH	KIRLRQCKGI	PPSLRGRAMQ
TBC1D10B	-----	-----	-----S	MGSDSE--I	NG-LALRKT	KYGFLGGSQY	SGSLESSIP-	VDVARQR---	ELKWLDMFSN	WDKWLSRRFQ	KVKLRCRKG	PSSLRAKAWQ
TBC1D10C	-----	-----	-----S	LKSDSE--L	SGPGPYQAD	RYGFIGGSS-	AEPGPGHPP-	ADLIRQR---	EMKWVEMTSH	WEKTMSTRYK	KVKMQCRKGI	PSALRARCWP
TBC1D3C	---MDVVEVA	GSWWAQERED	IIMKYEKGHR	AGLPEDKGP	PFRSYNNNVD	HLGIVHETEL	PPLTAREAKQ	IRREISR---	KSKWVDMGLD	WEKYKSS--R	KLIDRAYKGM	PMNIRGPMWS
TBC1D3B	---MDVVEVA	GSWWAQERED	IIMKYEKGHR	AGLPEDKGP	PFRSYNNNVD	HLGIVHETEL	PPLTAREAKQ	IRREISR---	KSKWVDMGLD	WEKYKSS--R	KLIDRAYKGM	PMNIRGPMWS
USP6	---MDMVENA	DSLQAQERKD	ILMKYDKGHR	AGLPEDKGP	PVG-INSSID	RFGLHETEL	PPVTAREAKK	IRREMTR---	TSKWMEMLGE	WETYKHS--S	KLIDRVYKGI	PMNIRGPMWS
RN-TRE	---MNSDQDV	ALKLAQERAE	IVAKYDRG-R	EGAEIEPWED	ADYLVYKVT	RFGFLHEEEL	PDHNAVERQ	KHLEIER---	TTKWLKMLKG	WEKYKNT--E	KFHRRYKGI	PLQLRGEVWA
TBC1D1	-----	--GPPPEEKK	RTSRELRELW	QKAILQQILL	LRMEKENQKL	QASENDLLNK	RLKLDYEEIT	PCLKEVT---	TVWEKMLSTP	GRSKIKFDME	KMHSAVGQV	PRHHRGEIWK
TBC1D4	-EPLVVFLSG	EDDPEKIEER	KKSKELRSLW	RKAIHQQILL	LRMEKENQKL	EASRDELQSR	KVKLDYEEVG	ACEKLEVL---	ITWDKLLLN-	CRAKIRCDME	DIHTLLKEGV	PKSRGEIWK
RabGAP-1	-----VCL	ESESERERRK	TTASPSVRLP	QSGSQSSVIP	-----SPP	EDDEEDNDE	PLLSGSGDVS	KECAEKI---	LETWGELLSK	WHLNLRVPRK	QLSSLVRNGV	PEALRGEVWQ
TBC1D18	-----S	EGKGHTNAGD	AIYEVVSLQR	ESDKEEPVT	TSGGGPMSPQ	DDEAEESDN	ELSSGTGDVS	KDCPEKI---	LYSWGELGK	WHSNLGARPK	GLSTLVKSGV	PEALRAEVWQ
EVI5	-----T	PALSPSSPSQ	LSPDLELLA	KLEEQRNLE	TDSKSLRSVN	GSRNRSGLL	VSSSSASSNL	SHLEEDS---	WILWGRIVNE	WEDVRKKKEK	QVKELVHKGI	PHHFRAIVWQ
EVI5L	-----	---TSDSEN	LSPDELELLA	KLEEQRNLE	ADSKSMRSMN	GSRNRSGLL	VSSSSASSNL	SHLEEDT---	WILWGRIANE	WEEWRRRKEK	LLKELIRKGI	PHHFRAIVWQ
TBC1D14	-PKQNVKKNL	DFEPLSTTAL	ILEDSPANLP	AKPAEEAQKH	RQQYEEVMVQ	AKKRELKEAQ	RRKKQLEERC	RVEESIGNAV	LTWNNEILPN	WETMWS--R	KVRDLWWQGI	PPSVRGKVS
TBC1D12	--QSSRRKNF	EFEPLSTTAL	ILEDSPNLP	AKSVEEALRH	RQYDEMVAE	AKKREIKEAH	KRKRIMKERF	KQENIASAM	VIWINEILPN	WEVMRST--R	RVRELWWQGL	PPSVRGKVS
TBC1D2A	-----	--ALQWEAGE	ASSDS-IELS	PISKYDEYGF	LTVPDYEVED	LKLLAKIQAL	ES-RSHLLG	LEAVDRP---	LRER--WAAL	G---DLVPSA	ELKQLLRAGI	PREHRPRVWR
TBC1D2B	-----	--ALQVESQE	QPEQAFVKPH	LVSEYDIYGF	RTVPEDDEEE	-KLVAKVRAL	DL-KTLYLTE	NQEVSTG---	VKWENYFAST	VN-REMMCSP	ELKNLIRAGV	PEHRSKVWK
RUTBC3	-----	--SIWPQEIL	AKYTQKEESA	EQPEFYDEF	GFRVYKEEGD	EPGSSLLANS	PLMEDAPQRL	RWDAHLEFTH	NHDVGDLTWD	KIAVSLPRSE	KLRSLVLAGI	PHGMRPQLNM
TBC1D6	-----	-----MQPA	ERSRVPRIDP	YGFERPEFD	DAAYEKFFSS	YLVTLTRRAI	KWSLLQ---	-----	---GGVPRSR	TVKRYVRKGV	PLEHRARVWM	
TBC1D9A	-----	---YSRPSSL	VSSSPQRSTS	SDADGQRFN	LNGNSVPTAT	QTLMTMYRRR	SP-EEFNPKL	AKEFLKE---	QAWKIHFAEY	GQGICMYRTE	KTRELVLKGI	PESMRGELWL
TBC1D9B	-----	---SSPAPQ	EGSEQPASPA	SPLSSRQSF-	-CAEQAPTAS	QGLLKLQKN	SPMEDLQAGK	AKEKMKKE---	ESWHIHFFEY	GRGVMYRTE	KTRDLVVRGI	PETLRGELWM
TBC1D8B	---LRCGAAS	TQYHDISTEL	AISSESTEPS	DNFEVQSLTS	QRECSKTVNT	EALMTVFPHPQ	NL-ETLNSKM	LKEKMKKE---	QSWKILFAEC	GRGVSMFRTE	KTRDLVVRGI	PETLRGELWM
TBC1D8	---SADDDM	ASLVFHSTSM	CSDHRFGDLE	MMSQNSEES	EKEKSPLMHP	DALVTAFAQS	GS-QSPDSRM	SREQIKI---	SLWNDFHVEY	GRTVCMFRTE	KIRKLVAMGI	PESLRGRLWL
TBC1D30	-----	--MRQDKLTGS	LRRGGRCLKR	QGGVGTILS	NVLKKRSCIS	RTAPRLLCTL	EPGVDTKLKF	TLEPSLG---	-----Q	NGFQQWYDAL	KAVARLSTGI	PKEWRRKVL
TBC1D7	-----	---MTEDSQRF	RSVYVEKVG	RGVEEKSLE	ILLKDDRLDT	EKLCTFSQRF	PLPSMYR---	-----	-----A	LVWKVLLIIL	PPHHESHAKV	
TBC1D20	-----	-MALRSAQGD	GPTSGHWDGG	AEKADFNAK	KKPVAEIHQA	LNSDPTDVAA	LRRMAISEGG	LLTDEIRRKV	WPKLLNVNAN	DPPPISGKNL	RMQSKDYQVQ	LLDVRSLRR
TBC1D24	--VTPDASVY	SDIVGKIVGK	HSSSCLPLPE	FVDNTQVPSY	CLNARGEGAV	RKILLCLANQ	FDPDISFCPAL	PAVALLLHY	SIDEAECFEK	ACRILACNDP	GRRLIDQSFL	AFESSCMTFG
TBC1D23	----LFRLLI	QYHEPELCSY	LDTKKITPDS	YALNWLGLSF	ACYCSTFVQ	AIWDGYLQQA	DPFFIYFLML	IILVNAKEVI	LTQESDSKEE	VIKFLNTPS	SLNIEDIEDL	FSLAQYYCSK
TBC1D19	PEHLKEPLVY	MRKAQGSWEK	RILKSLNSMC	TELSIPLARK	RPVGEQKELL	NKWNEMGTDE	PDLSLFRPVY	APKDFLEVL	NLRNPNYENG	DSLFRTHLG	LIQVPLKVKD	IPELKECFVE
TBC1D21	-----	---MT	TLSPENLSA	RQSASFILVK	KKPVAEIHQA	LNSDPTDVAA	LRRMAISEGG	LLTDEIRRKV	WPKLLNVNAN	DPPPISGKNL	RMQSKDYQVQ	LLDVRSLRR
TBCK	-----SFG	QGRDRSLLD	DTTDTLSLQ	LRNRLKDVGG	EAFYPLEDD	QSNLPHSNNS	NELSAATLP	LIIEKDETEY	QLNRIILFDR	LLKAYPYKKN	QIWKEARVDI	PPLMRGLTWA
TBC1D22A	-----P	RPEAEPSP	SGDLRLVKSV	SEHTSCPAE	SASDAAPLQ	SQSLPHSATV	TLGG-TSDPS	TLSSSALSER	EASRLDKFKQ	LLAGPNTDLE	ELRRLSWSGI	PKVPRPMTWK
TBC1D22B	-----	RSQSTSDVP	AN-YKVIKSS	SDAQLSRNSS	DTCLRNPLHK	QQSLPLRPII	PLVARISDQN	ASGAPPMTVR	EKRTRLEKFRQ	LLSSQNTDLD	ELRKCSPWGV	PREVRPITWR
TBC1D13	-----IPC	EGGLRCLCWK	ILLNYLPLER	ASWTSILAKQ	RELYAQFLRE	MIIQPGIAKA	NMGVSREDVT	FEDHPLNPNP	DSRWNTYFKD	NEVLLQIDKD	VRRLCDPISF	FQRATDYPCL

	125	135	145	155	165	175	185	195	205	215	225	235	
TBC1D15	FILGTFWDS	TKEERTQLQK	QKTDEYFRMK	LQWKSISQ--	----EQEKR	NSLRDYRSL	IEKDVNRTR	TNKFVEGQDN	-PGLILHDI	MTYCMYDFD	LG----	YVQ	GMSDILSPILL
TBC1D17	FILGYLSWEG	TAEEHKAHIR	KKTDEYFRMK	LQWKSIVSP--	----EQERR	NSLLHGYSRL	IERDVSRTDR	TNKFVEGPN	-PGLGLNDI	LLTYCMYHFD	LG----	YVQ	GMSDILSPILL
TBC1D16	FILRYYSHE	TSEEREALRL	QKRKEYSEIQ	QKRLSMTP--	----EEH	RAFWRNVQFT	VDKDVVTRDR	NNQFFRGEDN	-PNVESMRR	LLNYAVYNPA	VG----	YSQ	GMSDILVAPIL
RUTBC1	AHTLREIQDP	SQEKPAQAGEL	EAGEFLAAVC	AAA-----	----YTIEL	LDTVALNLHR	IDKDVQRCDR	NYWYFTPPN-	---LERLRDV	MCSYVWEHLD	VG----	YVQ	GMSDILAPLL
RUTBC2	KHGQADSEDN	LSEEPEMESL	FPALASLAVT	TSANEVSPVS	SSGVTYSPEL	LDLYTVNLHR	IEKDVQRCDR	NYWYFTPAN-	---LEKLRN	MCSYIWQHIE	IG----	YVQ	GMSDILAPLL
TBC1D5	IKIHIITNP-	-----RK	VVGQQDLMIN	NPLSQDEG--	----SLWNK	FFQDKELRSM	IEQDVKRTFP	EMQFFQQENV	---RKITDV	FCYARENEQ	LL----	YKQ	GMHEILAPIV
TBC1D10A	YISG-----	-----	-GKVKLQQNP	GK---FD--	----ELDMS	-PGDPKWLVD	IERDLHRQFP	FHEMFVSRGG	-HGQQDFRV	KAYTLRPE	EG----	YVQ	AQAPIAAVLL
TBC1D10B	YISN-----	-----	-SKELLEQNP	GK---FE--	----ELERA	-PGDPKWLVD	IEKDLHRQFP	FHEMFAARGG	-HGQQDYRT	KAYTYRPD	EG----	YVQ	AQAPVAAVLL
TBC1D10C	LCG-----	-----	-AHVCQKNSP	GT---YQ--	----ELAEA	-PGDPQWMT	IGRDLHRQFP	LHEMFVSPQG	-HGQQQLQV	KAYTLRPE	QG----	YVQ	AQGPVAAVLL
TBC1D3C	VLLN-----	-----	-TEEMKLNKP	GR---YQ--	----IMKEK	GKRSEHIQR	IDRDVSGTLR	KHIFFRDRYG	-TKQRELLH	LLAYEYNPE	VG----	YCR	DLSHIAALFL
TBC1D3B	VLLN-----	-----	-IEEMKLNKP	GR---YQ--	----IMKEK	GKRSEHIQR	IDRDISGTLR	KHMFFRDRYG	-TKQRELLH	LLAYEYNPE	VG----	YCR	DLSHIAALFL
USP6	VLLN-----	-----	-IQEIKLNKP	GR---YQ--	----IMKER	GKRSEHIHR	IDLDVVRTTLR	NHVFFRDRYG	-AKQRELYT	LLAYSEYNPE	VG----	YCR	DLSHIAALFL
RN-TRE	LLE-----	-----	-IPKMKETR	DL---YS--	----KLKHR	ARGCSPDIRQ	IDLDVNRTR	DHIMFRDRYG	-VKQQLFHV	LAAYSIYNTE	VG----	YVQ	GMSQITALLL
TBC1D1	FIAE-----	-----	-QFHLKHQFP	SKQQPKDV--	----PYKEL	LKQLTSQQA	ILLIDLGRTP	THPYFSAQLG	-AGQLSINI	LKAYSLLDQE	VG----	YVQ	GLSFVAGILL
TBC1D4	FIAL-----	-----	-QYRLRHRLP	NKQQPPDI--	----SYKEL	LKQLTAQQA	ILLVDLGRTP	THPYFVSVLQ	-PGQLSFINL	LKAYSLLDKE	VG----	YVQ	GISFVAGVLL
RabGAP-1	LLAG-----	-----	-CHNDHLVE	K-----	----YRIL	ITKESPDQA	ITRDINRTFP	AHDYFKDTGG	-DGQDSLKYI	CKAYSVDDEE	IG----	YVQ	QSFIAAVLL
TBC1D18	LLAG-----	-----	-CHNDQAMLD	R-----	----YRIL	ITKDSAQESV	ITRDINRTFP	AHDYFKDTGG	-DGQESLYKI	CKAYSVDDED	IG----	YVQ	QSFIAAVLL
EVI5	LACS-----	-----	-AQS-MPIKD	Q-----	----YSEL	LKMTSPCEKL	IRRDIAARTYP	EHNFFKEKDS	-LGQEVLFNV	MKAYSVDRE	VG----	YVQ	GSAFIVGLLL
EVI5L	LACS-----	-----	-ATD-MPVKN	Q-----	----YSEL	LKMSSPCEKL	IRRDIAARTYP	EHEFFKGQDS	-LGQEVLFNV	MKAYSVDRE	VG----	YVQ	GSAFIVGLLL
TBC1D14	LAINGNELNIT	HELFDICLAR	AKERWRSLS	TGSEVENE--	----DAGFS	AADREASLEL	IKLDISRTRFP	NLCIFQ-QGG	-PYHDMHSI	GAYTCYRPD	VG----	YVQ	GMSFIAAVLI
TBC1D12	LAVGNELNIT	PELYEIFLSR	AKERWKSFS	TSS--END--	----TEGVS	VADREASLED	IKLDISRTRFP	SLYIFQ-KGG	-PYHDMHSI	GAYTCYRPD	VG----	YVQ	GMSFIAAVLI
TBC1D2A	WIVH-----	-----	-LRVQHLHT-	--PGCYQE--	----LLSRG	QAREHPAARQ	IELDLNRTRFP	NNKHFTCPTS	-SFPDKRRV	LAFSWQNPT	IG----	YVQ	GLNRFAAIAL
TBC1D2B	WCVD-----	-----	-RHRTRFKDN	TEPGHFQT--	----LLQKA	LEKQNPASKQ	IELDLRLRTP	NNKHFTCPTS	-EGIQKLRV	LAFSWRNPD	IG----	YVQ	GLNRFAAIAL
RUTBC3	RISG-----	-----	-ALQKRNSE	LSYR-----	----EIVKNS	SNDETIAAKQ	IEKDLRLRTP	SNACFASMG	-IGVPRRRV	RALAWLYPE	IG----	YVQ	GTGMVAACL
TBC1D6	VISG-----	-----	-AQAMDQNP	GY-----	----HQLLQ	GERNPRLEDA	IRTDLNRTRFP	DNVFKRKTDD	PCLQRTYNY	LLAYGHHNQ	VG----	YVQ	GMNFIAGYLI
TBC1D9A	LISG-----	-----	-AINFKATH-	--PGYYED--	----LVEKS	MGKYNLATEE	IERDLHRSLP	--EHPAFQNE	-MGIAARRV	LAYAFRNPN	IG----	YVQ	AMNIVTSVLL
TBC1D9B	LISG-----	-----	-AWNFMVTH-	--PGYYAE--	----LVEKS	TGKYSLATEE	IERDLHRSLP	--EHPAFQNE	-LGIAARRV	LAYAFRNPT	IG----	YVQ	AMNIVTSVLL
TBC1D8B	LISG-----	-----	-AVNDMATN-	--PDYYTE--	----VVEQS	LGTCNLATEE	IERDLRRSLP	--EHPAFQSD	-TGISAARRV	LAYAYRNPK	IG----	YVQ	AMNIVTSVLL
TBC1D8	LISG-----	-----	-AVTDLASH-	--PGYYGN--	----LVEES	LGKCCLVTEE	IERDLHRSLP	--EHPAFQNE	-TGIAARRV	LAYAHRNPK	IG----	YVQ	AMNIVTSVLL
TBC1D30	TIAD-----	-----	-HYLHSIAID	WDKTRMFT--	----FNERS	NPDDDSMGIQ	IVKDLHRTGC	SSYCGQEAQ	--DRVVKRV	LAYARWNKT	VG----	YVQ	GFNIAALIL
TBC1D7	MMYR-----	-----	-----	-----	----KE	QYLDVLHALK	VVRFVSDATP	QAEVYLRMYQ	--LESGLPR	SPSFPLEPDD	EV----	FLA	IAKAMEEMVE
TBC1D20	FPPG-----	-----	MPEEQREGLQ	EELIDIILL--	----ILERNP	QLHYQGYHD	IVVTFLLVVG	ERLATSLEK	LSTHHLRDFM	DPTMDNTHI	LN----	YLM	PIIQVNP
TBC1D24	DIVN-----	KYCQAAHKLM	VAVSDVLQV	YADWQRWLF	ELPLCFYFAR	FDFVFLVEGYK	VLYRVALAIL	KFFHKVRAG	PLESDSVKQD	IRTFVRDIAK	TV----	SPE	KLEKAFAIR
TBC1D23	TPAS-----	-----	FRKDNHHLFG	STLLGIKDDD	----ADLSQ	ALCLAISVSE	ILQANQLQGE	GVRFFVVD	PAEQYNAGHL	STAFHLSDSL	MLQNPSEFA	SVKS	LEAQK
TBC1D19	LGLNIGQLG-	IDDSTQVPPE	LFENFHVRIG	QKVLAEQDSA	AAQQYIRQGS	PTALRAELWA	LILNINSSQE	DVLYVEQLKT	NVIQHDLVD	SLYKDVKLT	ASND--DYF	VFE	YLYQVL
TBC1D21	KIQP-----	-----	-----	-----	----LLENL	HRNFTETRNN	IARDIQKIYD	KDPLGNVLID	---KKRLEKI	LLSYVCNTQ	AE----	YVQ	GFHEMMLFQ
TBCK	AILG-----	-----	-VEGAIAHAK-	-----	----YDAID	KDTPIPTDRQ	IEVDIPRCHQ	YDELILSSPEG	---HAKFRRV	LKAWVSHPD	LV----	YVQ	GLDSICAEFL
TBC1D22A	LISGYLFAN-	-VDRRPAITQ	RKQKRYFAFI	EHY-----	----YDSRN	DEVHQDTYRQ	IHIDIPRMS	-EALILQPK-	--VTEIFERI	LFIWAIRHPA	SG----	YVQ	GINDIVTFFF
TBC1D22B	LISGYLFAN-	-TERRKLTQ	RKREYFVFI	EQY-----	----YDSRN	EEHQDTYRQ	IHIDIPRTP	LIPLFQQLP-	--VQEIFERI	LFIWAIRHPA	SG----	YVQ	GINDIVTFFF
TBC1D13	LILD-----	-----	-PQNFETLR	KRVEQTTLKS	----QTVAR	RSQVTNMSSP	HKNSVPSLNL	EYEVLPNGCE	-AHWEVVERI	LFIYAKLNPG	IA----	YVQ	GMNEIVGPLY

	245	255	265	275	285	295	305	315	325	335	345	355
TBC1D15	YVME-----			-NVDFAWCF	ASYMDG---	MHQNFEEQMQ	G MKTQLIQG-			-STLLRLLDS	GFCFSYLESQ-	
TBC1D17	YVIQ-----			-NVDFAWCF	CGFMEL----	VQGNFEEESQE	TMKRQLGR-			-LLLLRVLDP	LLCDFLDSQ-	
TBC1D16	AEVL-----			-DESDFWCF	VGLMQN----	TIFVSSPRDE	DMEKQLLY-			-RELLRRLTHV	RFYQHLVSLG	
RUTBC1	VTLD-----			-NDQLAYSQF	SHLMQR----	MSQNFPNG-G	AMDTHFANM-			-RSLIQILDS	ELFELMHQNG	
RUTBC2	VILD-----			-DVALASQF	TELMKR----	MNQNFPHG-G	AMDTHFANM-			-RSLIQILDS	ELFELMHQNG	
TBC1D5	FVLHCDHQAF	LHASESAQPS	EEMKTVLNPE	YLFDHAYAVF	SQLMETAEPW	FSTFEHDGQK	GKETLMTPIP	FARPQDLGPT	IAIVTKVNQI	QDHLKKKHI	ELYMHLNRL-	
TBC1D10A	MHMP-----			-AQ-AFWCL	VQICEK---Y	LPGYYSEKLE	AIQLDGEI-			-FSLLQKVSP	VAHKHLRSQ-	
TBC1D10B	MHMP-----			-AQ-AFWCL	VQICDK---Y	LPGYYSAGLE	AIQLDGEIF-			-FALLRRASP	LAHRHLRRQ-	
TBC1D10C	MHLP-----			-PE-AFWCL	VQICEV---Y	LPGYYGPHME	AVRLDAEVF-			-MALLRRLLP	HVHKHLQQV-	
TBC1D3C	LYLP-----			-ED-AFWAL	VQLLASERHS	LQGFHSPNGG	TVQGLQDQQ-			-EHVVATSQP	KTMGHQDKK-	
TBC1D3B	LYLP-----			-ED-AFWAL	VQLLASERHS	LQGFHSPNGG	TVQGLQDQQ-			-EHVVATSQS	KTMGHQDKK-	
USP6	LYLP-----			-ED-AFWAL	VQLLASERHS	LPGFHSFNGG	TVQGLQDQQ-			-EHVVPKSPQ	KTMWHQDKE-	
RN-TRE	MYMN-----			-ED-AFWAL	VKLFSGPKHA	MHGFFVQGF	KLLRFQEH-			-EKILNKFLS	KLKQHLDSQ-	
TBC1D1	LHMS-----			-EE-AFKML	KFLMFDG--	LKQYRPDMI	ILQIQMYQ-			-SRLLDHYHR	DLYNHLEEH-	
TBC1D4	LHMS-----			-EQ-AFEML	KFLMYDLG--	FRKQYRPDM	SLQIQMYQ-			-SRLLDHYHR	DLYNHLEEN-	
RabGAP-1	LHMP-----			-EQ-AFVSL	VKIMFDYG--	LRELFKQNF	DLHCKFYQ-			-ERLMQEIYP	DLYNHFLDI-	
TBC1D18	LHMP-----			-EQ-AFCVL	VKIMFDYG--	LRDLYRNNFE	DLHCKFYQ-			-ERLMQEQLP	DLSHFSDL-	
EVI5	MQMP-----			-EE-AFCVF	VKLMQDYR--	LRELFKPSMA	ELGLCMYQF-			-ECMIQEHL	ELFVHFQSQ-	
EVI5L	MQMP-----			-EE-AFCVF	VRLMQEYR--	LRELFKPSMA	ELGLCIYQF-			-EYMLQEQLP	DLNTHFRSQ-	
TBC1D14	LNLD-----			-TAD-AFIAF	SNLLNKP--C	QMAFFRVDHG	LMLTYFAAF-			-EVFFEENLP	KLFAHFPKN-	
TBC1D12	LNLE-----			-EAD-AFIAF	ANLLNKP--C	QLAFFRVDHS	MMLKYFATF-			-EVFFEENLS	KLFLHFKSY-	
TBC1D2A	LVLE-----			-EESAFWCL	VAIVET--IM	PADYYCNTLT	ASQVDQRV-			-QDLLSEKLP	RLMAHLGQH-	
TBC1D2B	LYLE-----			-QED-AFWCL	VTIVEV--FM	PRDYTKTLL	GSQVDQRVF-			-RDLMSEKLP	RLHGHEFY-	
RUTBC3	LFLE-----			-EDAFWMM	SAIIE--LL	PASYFSTLL	GVQTDQRV-			-RHLIVQYLP	RLDKLLQEH-	
TBC1D6	LITN-----			-NEESFWLL	DALVGR---I	LPDYSPAML	CLKTDQEV-			-GELVRAKLP	AVGALMERLG	
TBC1D9A	LYAK-----			-EE-AFWLL	VALCER--ML	P-DYYNTRVV	GALVDQGVF-			-EELARDYVP	QLYDCMQDL-	
TBC1D9B	LYGS-----			-EE-AFWLL	VALCER--ML	P-DYYNTRVV	GALVDQGVF-			-EELTRDFLP	QLSEKMQDL-	
TBC1D8B	LYAK-----			-EE-AFWLL	VAVCER--ML	P-DYFNRRII	GALVDQAVF-			-EELIRDHLP	QLTEHMTDM-	
TBC1D8	LYTK-----			-EE-AFWLL	VAVCER--ML	P-DYFNHRVI	GALVDQSVF-			-EELIKGHL	ELAEHMNDL-	
TBC1D30	EVME-----			GNEDALKIM	IYLIDK--VL	PESYFVNLR	ALSVDMAVF-			-RDLRMLKLP	ELSQHLDTLQ	RTANKESGGG
TBC1D7	DSVD-----			---CYNIT	RRFVNG---	LNTKYRDSL	QLPKAFEQY-			---LNLEDG	RLTLHLMCS	
TBC1D20	HDFMQS----			-AVGTIFAL	SWLITWFG-H	VLSDFRHVVR	LYDFFLACH-			---PLMPIYFA	AVIVLYREQE	
TBC1D24	LFSR-----			--KEIQLQM	ANEKALKQKG	ITVKQKRQFV	HLAVHAENFR			SEIVSVREMR	DIWSVPER-	
TBC1D23	QSIESG----			SIAGGEHLG	MGSGREEEDM	YMMVLAHFL	QKNKEYVSIA	SG----		GFMALQQHLA	DINVDGPENG	YG----
TBC1D19	LCFSR-----			DTSVLSHFAP	NSASPPKSYI	RGKLGLEEYA	VFYPPNGVIP			-FHGFSMYVA	PLCFLYHEPS	K----
TBC1D21	LMVE-----			-HDHETFWLF	QFFLQK----	-TEHSCVINI	GVAKNLDM-			-STLITFLDP	VFAEHLKKG-	
TBCK	YLNFN-----			-NEALAYAM	SAFIPKY--L	YNFFLKDNSH	VIQEYLVTF-			-SQMIAFHDP	ELSNHLEIG	
TBC1D22A	VVFICEYIEA	EEVDTVDVSG	VPAEVL	NIADTYN	SKLLDG----	IQDNYTFAQP	GIQMKVKML-			-EELVSRIDE	QVHRHLDQH-	
TBC1D22B	VVFLSEYVE-	EDVENFDVTN	LSQDMLR	SIADSFQ	SKLLDG----	IQDNYTFAQP	GIQKVKKAL-			-EELVSRIDE	QVHNHFRRY-	
TBC1D13	YTFATDPNS-			EWKE	HAADTFQ	TNLMAEIRDN	FIKSLDSDSQ			-YSTLKDKDV	ELYLKLQEQ-	

	365	375	385	395	405	415	425	435	445	455	465	475
TBC1D15	--DSGYLYFC	FRWLLIRFKR	EFS-----	FLDILRLNEV	MWTE--LPCT	NPHLLLCAL	ESEKQOI-W	EKHYGKFNIL	KHINELS--M	KIIVEDILCK	AEAISLQIVK	CKELPQAVCE
TBC1D17	--DSGSLCFC	FRWLLIWFKR	EFP-----	FPDVLRLNEV	LWTG--LPGP	NLHLLVACAI	LDMERDTL-M	LSGFGSNLIL	KHINELT--M	KLSVEDVLTR	AEALHRQLTA	CPELPHNVQE
TBC1D16	--EDGLQMLFC	HRWLLLCFKR	EFP-----	EAEALRIWEA	CWAHY--QTD	YHFLFIQVAI	VAIYGDDV-I	EQQLATDQML	LHFGNLA--M	HMNGELVLRK	ARSLLYQFRL	LPRIPCSLLHD
RUTBC1	--DYTHFYFC	YRWFLLDFKR	ELL-----	YEDVFAVNEA	IWAARHISSE	HVFLFIALAL	VEAYREII-R	DNNMDFTDII	KFFNERA--E	HHQAQEILRI	ARDLVKHKVM	LIENK-----
RUTBC2	--DYTHFYFC	YRWFLLDFKR	ELV-----	YDDVFLVNET	IWAAKHVSSA	HYVLFIALAL	VEVYRDII-L	EENNMDFTDII	KFFNEMA--E	RHNTKQVLKL	ARDLVYKVQT	LIENK-----
TBC1D5	--EIAPQIYG	LRWVRLLFGR	EFP-----	LQDLLVVDA	LFADG--LSL	GLVDYIFVAM	LYIIRDAL-I	SSNYQTCLGL	LMHYPPFIG-D	VHSLILKALF	LRDPKRNPRP	VTYQFHPNLD
TBC1D10A	--KIDPLLYM	TEWFMCAFSR	TLP-----	WSSVLRVNDM	FFCEG---V	KIIFRVGLVL	LKHALGSP-E	KVKACQGGYE	TIERLRS--L	SPKIM-QEAF	LVQEVVELPV	TERQIEREHL
TBC1D10B	--RIDPVLVM	TEWFMCIFAR	TLP-----	WASVLRVNDM	FFCEG---V	KIIFRVGLVL	LRHTLGSV-E	KLRSCQGMYE	TMEQLRN--L	PQQCM-QEDF	LVHEVTNLPV	TEALIERENA
TBC1D10C	--GVGPLLYL	PEWFLCLFAR	SLP-----	FPTVLRVDA	FLSEG---A	RVLFRVGLTL	VRLALGTA-E	QRGACPGLE	TLGALRA--I	PPAQL-QEEA	FMSQVHSVVL	SERDLQREIK
TBC1D3C	--DLCGQCSP	LGCLIRILID	GIS-----	LGLTLRLNDV	YLVEG---E	QALMPITRIA	FKVQKQRL-T	KTSRCG--PW	ARFCNRF--V	DTWAR-DEDT	VLKHLR---A	SMKKLTRKKG
TBC1D3B	--DLCGQCSP	LGCLIRILID	GIS-----	LGLTLRLNDV	YLVEG---E	QALMPITRIA	FKVQKQRL-T	KTSRCG--PW	ARFCNRF--V	DTWAR-DEDT	VLKHLR---A	SMKKLTRKKG
USP6	--GLCGQYAS	LGCLLRNLID	GIS-----	LGLTLRLNDV	YLVEG---E	QALMPITRIA	FKVQKQRL-T	KTSRCG--LW	ARLRNQF--F	DTWAM-NDDT	VLKHLR---A	STKKLTRKQG
RN-TRE	--EIYTSFYT	MKWFQCFD	RTP-----	FTLNLRIIDI	YIFEG---E	RVLTAMSYTI	LKLHKHKL-M	KLSMEE--LV	EFFQETL--A	KDFFF-EDDF	VIEQLQ---I	SMTELKRAKL
TBC1D1	--EIGPSLYA	APWFLTMFAS	QFP-----	LGFVARVFDI	IFLQG---T	EVIFKVALSL	LGSHKPLI-L	QHENLETIVD	FIKSTLP--N	LGLV--QMEK	TINQVFEMDI	A-KQLQAYEV
TBC1D4	--EISPSLYA	APWFLTLFAS	QFS-----	LGFVARVFDI	IFLQG---T	EVIFKVALSL	LSSQETLI-M	ECSFENIVE	FLKNTLP--D	MNTS--EMEK	IITQVFEMDI	S-KQLHAYEV
RabGAP-1	--SLEAHMYA	SQWFLTLFTA	KFP-----	LYMVFHIIDL	LLCEG---L	SVIFNVALGL	LKTSKDDL-L	LTD-FEGALK	ALRVQLP--K	RYRAEENARR	LMELACNIVK	RYRSENAKK
TBC1D18	--NLEAHMYA	SQWFLTLFTA	KFP-----	LQMVFHIIDL	LLCEG---L	NIIHFVALAL	LKTSKEDL-L	QAD-FEGALK	FFRQQLP--K	RYRAEENARR	LMEQACNIKV	PTKKLKKYK
EVI5	--SFHTSMYA	SSWFLTIFLT	TFP-----	LPIATRFIDI	FMSEG---L	EIVFRVGLAL	LQMNQAL-M	QLD-MEGMLQ	HFQKVIP--H	QFDG--VPDK	LIQAAYQVKY	NSKKMKKLEK
EVI5L	--SFHTSMYA	SSWFLTLFLT	TFP-----	LPVATRVFDI	FMSEG---L	EIVFRVGLAL	LQVNQAL-M	QLD-MEGMSQ	YFQRVIP--H	QFDS--CPDK	LVLKAYQVKY	NPKMKRLEK
TBC1D14	--NLTPDIYL	IDWIFTLYSK	SLP-----	LDLACRIWDV	FCRDG---E	EFLFRGTALGI	LKLFEDIL-T	KMD-----F	IHMAQFL--T	RLPEDLPAAE	LFASIATIQM	QSRNKKWAQV
TBC1D12	--SLTPDIYL	IDWIFTLYSK	SLP-----	LDLACRIWDV	FCRDG---E	EFLFRGTALGI	LRLYEDIL-L	QMD-----F	IHIAQFL--T	KLPEDITSEK	LFSCIAAIQM	QNSTKKWTQV
TBC1D2A	--HVDLSLVT	FNWFLVVFAD	SLI-----	SNILLRVDA	FLYEG---T	KVVFRYALAI	FKYNEKEI-L	RLQNGLEIYQ	YLRFFTK--T	ISNSRKLMI	AFNDMNPFRM	KQLRQLRMVH
TBC1D2B	--KVDYTLIT	FNWFLVVFVD	SVV-----	SDILFKIIDS	FLYEG---P	KVIFRFALAL	FKYKEEEI-L	KLQDSMSIFK	YLYRFTR--T	ILDKARKLISI	SFGDLNPFPL	RQIRNRRAYH
RUTBC3	--DIELSLIT	LHWFLTAFAS	VVD-----	IKLLLRINDL	FFYEG---S	RVLFQTLTGM	LHLKEEL-I	QENSASIFN	TLSDIPS--Q	MEAEALLGV	AMRLAGSLTD	VAVETQRRKH
TBC1D6	--VLWTLIVS	SNWFLCLFVD	ILP-----	VEVLRINDC	LFNEG---S	KIIFRVGLVL	IKQHQLI-L	EATSVDPICD	KFKQITKGSF	VMECHTFMQK	IFSEPGSLM	ITVAKLRESC
TBC1D9A	--GV-ISTIS	LSWFLTLFSL	VMP-----	FESAVVVVDC	FFYEG---I	KVIFQALAV	LDANVDKL-L	NCKDDGEAMT	VLGRYLD--S	VTNKDSTLPP	IPHLHSLSD	DVEPYPEVDI
TBC1D9B	--GV-ISSIS	LSWFLTLFSL	VMP-----	FESAVVIVDC	FFYEG---I	KVILQVALAV	LDANMEQL-L	GCSDEGEAMT	MLGRYLD--N	VVNKQSVSPP	IPHLRALLSS	SDDPPAEVDI
TBC1D8B	--TF-FSSVS	LSWFLTLFIS	VLP-----	IESAVNVVDC	FFYDG---I	KAILQLGLAI	LDYNLDKL-L	TCKDDAEAVT	ALNRFFD--N	VTNKDSPLPS	NVQQGSNVSD	EKTSHTRVDI
TBC1D8	--SA-LASVS	LSWFLTLFSL	IMP-----	LESAVNVVDC	FFYDG---I	KAIFQLGLAV	LEANAEDL-C	SSKDDGQALM	ILSRFLD--H	IKNEDSPGPP	VGSHHAFFSD	DQEPYPVTDI
TBC1D30	YEPPLTNVFT	MQWFLTLFAT	CLP-----	NQTVLKIIDS	VFFEG---S	EIILRVSLAI	WAKLGEQI-E	CCETADEFYS	TMGRLTQEML	ENLLQSHL	MQTVYSMAFP	PPQLAELRE
TBC1D7	---AAPKLPY	DLWFKRCFAG	CLP-----	ESSLQRVNDK	VVSGS---C	KILVFAVEI	LTLTKIKV-M	ALNSAEKITK	FLENIPQ---	-----DSSDA	IVSKAIDLWH	KHCGTPVHSS
TBC1D20	VLDCDCDMAS	VHLLSQIPQ	DLPY-----	ETLISRAGDL	FVQFP---P	SELAREAAQ	QQAERTAA-S	TFKDFELASA	QRPDMVLQ	RFRGLLRPED	RTKDVLTKPR	TNRVVKLAVM
TBC1D24	--FALCQPLLL	VSSLQHGYSL	ARFY-----	FQCEGHEPTL	LLIKT---TQ	KEVCGAYLST	DWSERNKFGG	KLGGFTEGEC	FVFRLLQPEVQ	RYEWVVIKHP	ELTKPPLMA	AEPTAPLSHS
TBC1D23	--HWIASTSG	SRSSINSVDG	ESPNGSSDRG	MKSLVNKMTV	ALKTK---S	VNVREKVISF	IENTSTPVDR	HVSSSDRVGK	PYRGVKPVFS	IGDEEYD	EIDSSMSDD	DRKEVVNIQT
TBC1D19	LYQIFREMYV	RFFFLRLHSIS	SHPSG----	IVSLCLLFET	LLQTY---LP	QLFYHLREIG	AQPLRISFKW	MVRAFSGYLA	TDQLLLWDR	ILGYNSEIL	AVLAAVFAF	RAVNLMEVTS
TBC1D21	--GAGAVQSL	FPWFQCFQR	AFKS-----	FDDVWRLNEV	LLTGKPCR	NFQVVLVAYSM	LQMVREQL-L	QESMGDDIL	LACNLI---	DLADELISA	ACVVYAEIQL	KDVPQTLKDF
TBC1D22A	--EVEYQFA	FRWMMNLLMR	EVP-----	LRCITRLNDT	YQSEP-DGFS	HFLHYVCAAF	LVRWRKEI-L	EE-KDFQELL	LFQNLPL--T	AHWDDIEDISL	LLAEAYRLKF	AFADAPNHYYK
TBC1D22B	--EVEYQFA	FRWMMNLLMR	ELP-----	LRCITRLNDT	YQSEP-EGFS	HFLHYVCAAF	LIIKWRKEI-L	DE-EDFQGLL	MLLQNLPL--T	IHWGNEEIGL	LLAEAYRLKY	MFADAPNHYYR
TBC1D13	--NIKQPFA	FRWLTLLLSQ	EFL-----	LPDVIRIIDS	LFADD--NRF	DELLLVCCAM	LMLIREQL-L	EGDFTVNMRL	LQDYPIT---	-----DVCQ	ILQKAKELQD	SK-----

Supplementary Figure 2: Alignment of TBC1D10 subfamily. Conserved amino acids are labelled in green. Amino acids that are identical in two members are labelled in yellow.

	5 15 25 35 45 55 65 75
TBC1D10A	-----
TBC1D10B	METGTAPLVA PRRRHGAPAA PSPPPRGSRA GPVVVAVAGP PVTTATSAPV TLVAPGEARP AWVPGSAETS APAPAPAPAP
TBC1D10C	-----

	85 95 105 115 125 135 145 155
TBC1D10A	-----
TBC1D10B	APAVTGSTVV VLTLEASPEA PKPQLPSGPE SPEPAAVAGV ETSRALAAGA DSPKTEEARP SPAPGPGTPT GTPTRTPSRT
TBC1D10C	-----

	165 175 185 195 205 215 225 235
TBC1D10A	-----
TBC1D10B	APGALTAKPP LAPKPGTTVA SGVTARSASG QVTGGHGAAA ATSAASAGQAP EDESGPPTGP SGTCEAPVAV VIVTPAPEPA
TBC1D10C	-----

	245 255 265 275 285 295 305 315
TBC1D10A	-----
TBC1D10B	ENSQDLGSTS SLGPGISGPR GQAPDTLSYL DSVSLMSGTL ESLADDVSSM GSDSEING-L ALRKTDKYGF LGGQYSGSL
TBC1D10C	-----

	325 335 345 355 365 375 385 395
TBC1D10A	-----
TBC1D10B	LEEVELEVLR QRESKWLDML NNWDKWMAKK HKKIRLRQK GIPPSLRGRA WQYLSGGKVK LQONPGKFEF LDMSPGDPKW
TBC1D10C	-----

	405 415 425 435 445 455 465 475
TBC1D10A	-----
TBC1D10B	LDVIERDLHR QPFHEMFVS RGGHGQODLF RVLKAYTLYR PEEGYCQAQA FIAAVLLMHM PAFQAFWCLV QICEKYLPGY
TBC1D10C	-----

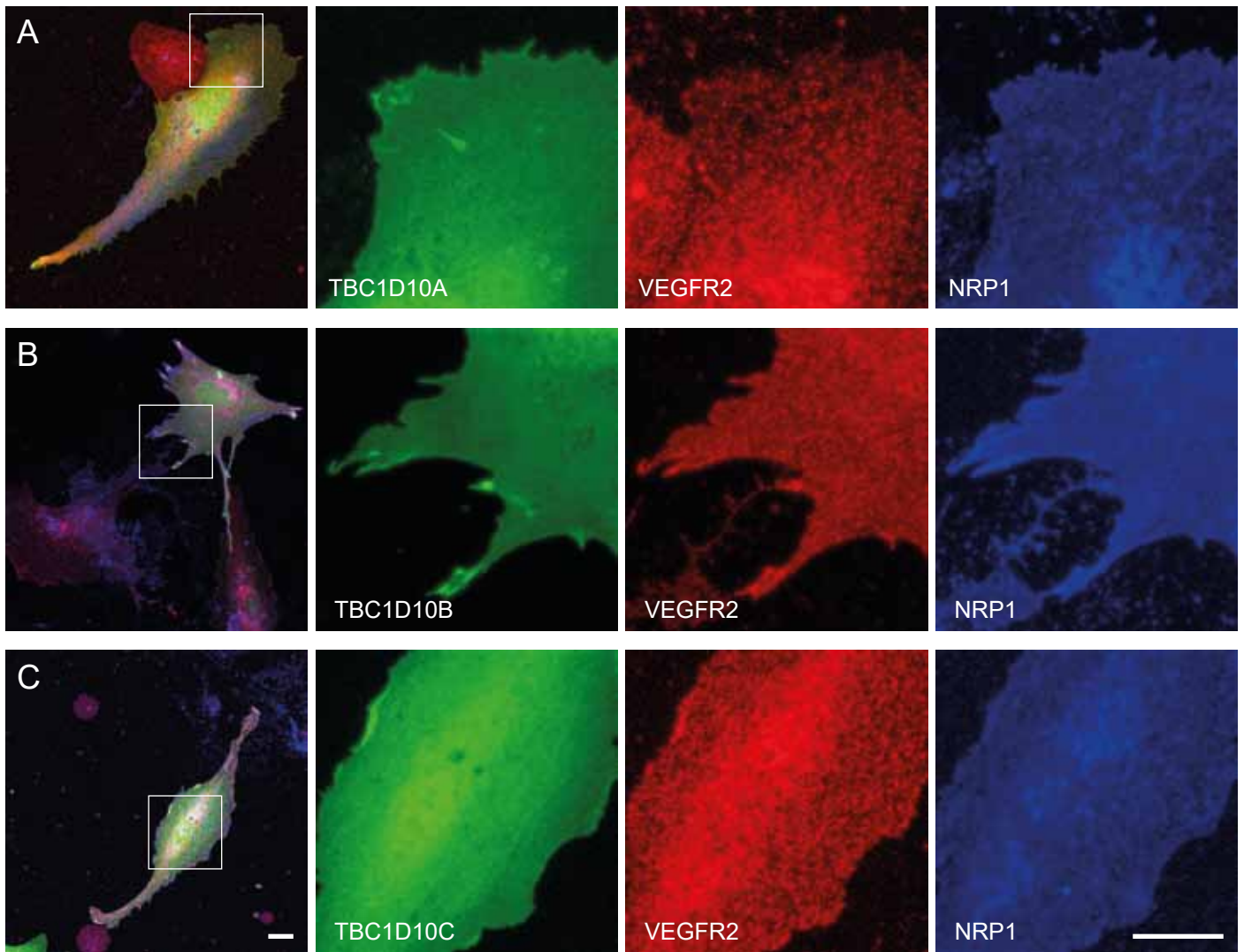
	485 495 505 515 525 535 545 555
TBC1D10A	-----
TBC1D10B	YSAGLEAIQL DGHILFSLIQ KVSFVAHKHL SRQKIDPLLY MTEWFMCIFS RILPWSSVLR VWDMPFCEGV KIIIFRVGLVL
TBC1D10C	-----

	565 575 585 595 605 615 625 635
TBC1D10A	-----
TBC1D10B	LKHALGSPEK VKACQGYET IERLRSLSPK IMQAFVLQVE VVELPVTERQ IEREHLIQR RWQETRGELQ CRSPRRLHGA
TBC1D10C	-----

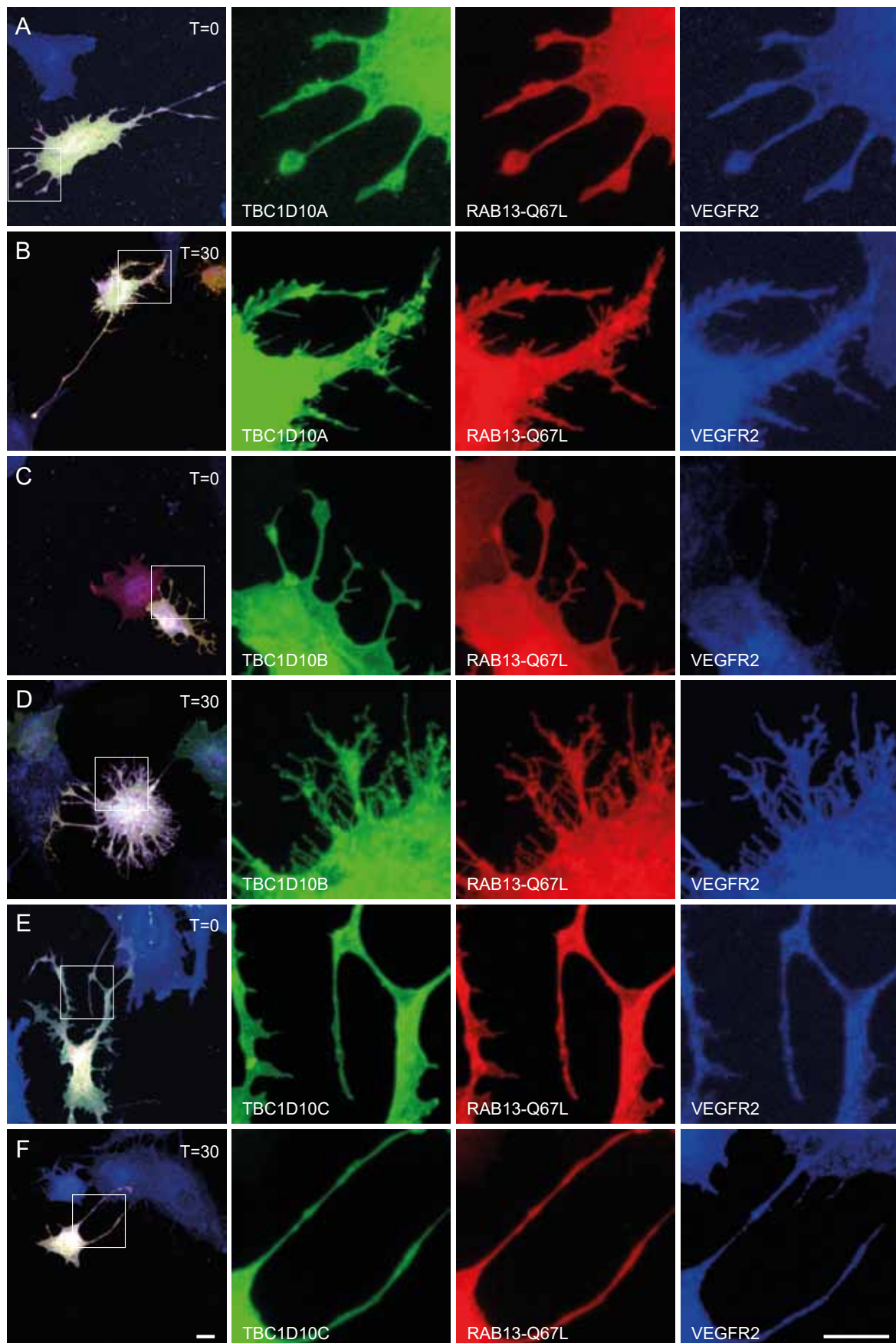
	645 655 665 675 685 695 705 715
TBC1D10A	-----
TBC1D10B	KAILDAEPGP RPALQPS--- -PSIRLPLDA PLFGSKAKPK ----- -PKQAQK
TBC1D10C	-----

	725 735 745 755 765 775 785 795
TBC1D10A	-----
TBC1D10B	EQRKQMKGRG QLEKPPAPNQ AMVVAAGDA CPPQHVPPKD SAPKDSAPQD LAPQVS--- AHRSQESLT
TBC1D10C	-----

	805
TBC1D10A	-----
TBC1D10B	SQSESDTYL AEARQAYF
TBC1D10C	-----
	STSFLETRF



Supplementary Figure 3: VEGFR2, NRP1, and TBC1D10A-C localize to the plasma membrane in unstimulated PAE cells. PAE cells stably expressing VEGFR2 and NRP1 were transiently transfected with TBC1D10A (A), TBC1D10B (B), and TBC1D10C (C). Cells were fixed without stimulation with VEGF-A165a and immunostained for VEGFR2 and NRP1. Scale bar: 10 μ m.



Coexpression of TBC1D10A/ B/ C with a constitutive active form of RAB13. (A) Coexpression of RAB13-Q67L with TBC1D10A induces filopodia in unstimulated cells that are positive for VEGFR2. (B) Thirty minutes after stimulation with VEGF A165a. (C) Coexpression of TBC1D10B with RAB13-Q67L. Filopodia in unstimulated cells are negative for VEGFR2. (D) Thirty minutes after stimulation with VEGF A165a, filopodia contain VEGFR2. (E) Coexpression of TBC1D10C with RAB13-Q67L. Filopodia in unstimulated cells are positive for VEGFR2. (F) Thirty minutes after stimulation with VEGF A165a, filopodia contain VEGFR2. Scale bar: 10 μ m.