Supplementary information

Supplementary Tables 1-5: These tables contain information about constructs and reagents used for this study.

Supplementary Table 1. DNA constructs for recombinant protein production used in this study

Name	Description	Source/reference	Identifier
Individual proteins/subunits			
VPS35L	VPS35L (1-963, full-length) in pAV5a vector	This study	pDB51
VPS26C	VPS26C (1-297, full-length) in pAV5a vector	This study	pDB48
VPS29-His_6	VPS29-Tev-$(GGS)_2$-His_6 in pAV5a vector	This study	pDB47
MBP-CCDC22 NN-CH-VBD	MBP-Tev-CCDC22 (1-118)-$(GGSK)_6$-CCDC22 (436-727) in pMalC2Tev vector	This study	pDB79
MBP-CCDC93 VBD	MBP-Tev-hCCDC93 (442-631) in pMalC2Tev vector	This study	pDB80
MBP-CCDC22 DBD	MBP-Tev-CCDC22 (280-446) in pMalC2Tev vector	This study	pDB81
MBP-CCDC93 DBD	MBP-Tev-CCDC93 (305-433) in pMalC2Tev vector	This study	pDB82
His_6-DENND10	His_6-Tev-DENND10 (1-357, full-length) in pHisTev vector	This study	pDB97, pDK380
MBP-CCDC22 NN-CH-VBD^{R490D}	MBP-Tev-CCDC22 (1-118)-$(GGSK)_6$-CCDC22 (436-727)^{R490D} in pMalC2Tev vector	This study	pDB102
MBP-CCDC22 NN-CH-VBD^{V501R}	MBP-Tev-CCDC22 (1-118)-$(GGSK)_6$-CCDC22 (436-727)^{V501R} in pMalC2Tev vector	This study	pDB103
MBP-CCDC22 NN-CH-VBD$^{R490D/V501R}$	MBP-Tev-CCDC22 (1-118)-$(GGSK)_6$-CCDC22 (436-727)$^{R490D/V501R}$ in pMalC2Tev vector	This study	pDB104
MBP-CCDC93 VBD^{R483E}	MBP-Tev-CCDC93 (442-631)^{R483E}in pMalC2Tev vector	This study	pDB84
MBP-CCDC93 VBD^{A492W}	MBP-Tev-CCDC93 (442-631)^{A492W}in pMalC2Tev vector	This study	pDB105
MBP-CCDC93 VBD$^{R483E/A492W}$	MBP-Tev-CCDC93 (442-631)$^{R483E/A492W}$ in pMalC2Tev vector	This study	pDB106
MBP-CCDC22 DBD$^{A411D/A418D/E422R}$	MBP-Tev-CCDC22 (280-446)$^{A411D/A418D/E422R}$ in pMalC2Tev vector	This study	pDB107
MBP-CCDC22 DBD$^{R425D/R433D/R436D}$	MBP-Tev-CCDC22 (280-446)$^{R425D/R433D/R436D}$ in pMalC2Tev vector	This study	pDB108
MBP-CCDC93 DBD^{E410R}	MBP-Tev-CCDC93 (305-433)^{E410R} in pMalC2Tev vector	This study	pDB86
MBP-CCDC93 DBD^{F403D}	MBP-Tev-CCDC93 (305-433)^{F403D} in pMalC2Tev vector	This study	pDB109

MBP-CCDC93 DBD$^{E410R/F403D}$	MBP-Tev-CCDC93 (305-433)$^{E410R/F403D}$ in pMalC2Tev vector	This study	pDB110
His_6-DENND10^{W30D}	His_6-Tev-DENND10^{W30D} in pHisTev vector	This study	pDB111
His_6-DENND10^{Y32D}	His_6-Tev-DENND10^{Y32D} in pHisTev vector	This study	pDB112

Supplementary Table 2. Sequences of recombinant proteins used in this study.

Only sequences in the final product (i.e., after protease cleavage to remove the affinity tag) are shown and are annotated by corresponding colors.

>VPS35L

MAVFPWHSRNRNYKAEFASCRLEAVPLEFGDYHPLKPITVTESKTKKVNRKGSTSSTSSSSSSSVVDPLSSVLDGTDPLSMFAATADPAALAAAM
DSSRRKRDRDDNSVVGSDFEPWTNKRGEILARYTTTEKLSINLFMGSEKGKAGTATLAMSEKVRTRLEELDDFEEGSQKELLNLTQQDYVNRIEE
LNQSLKDAWASDQKVKALKIVIQCSKLLSDTSVIQFYPSKFVLITDILDTFGKLVYERIFSMCVDSRSVLPDHFSPENANDTAKETCLNWFFKIA
SIRELIPRFYVEASILKCNKFLSKTGISECLPRLTCMIRGIGDPLVSVYARAYLCRVGMEVAPHLKETLNKNFFDFLLTFKQIHGDTVQNQLVVQ
GVELPSYLPLYPPAMDWIFQCISYHAPEALLTEMMERCKKLGNNALLLNSVMSAFRAEFIATRSMDFIGMIKECDESGFPKHLLFRSLGLNLALA
DPPESDRLQILNEAWKVITKLKNPQDYINCAEVWVEYTCKHFTKREVNTVLADVIKHMTPDRAFEDSYPQLQLIIKKVIAHFHDFSVLFSVEKFL
PFLDMFQKESVRVEVCKCIMDAFIKHQQEPTKDPVILNALLHVCKTMHDSVNALTLEDEKRMLSYLINGFIKMVSFGRDFEQQLSFYVESRSMFC
NLEPVLVQLIHSVNRLAMETRKVMKGNHSRKTAAFVRACVAYCFITIPSLAGIFTRLNLYLHSGQVALANQCLSQADAFFKAAISLVPEVPKMIN
IDGKMRPSESFLLEFLCNFFSTLLIVPDHPEHGVLFLVRELLNVIQDYTWEDNSDEKIRIYTCVLHLLSAMSQETYLYHIDKVDSNDSLYGGDSK
FLAENNKLCETVMAQILEHLKTLAKDEALKRQSSLGLSFFNSILAHGDLRNNKLNQLSVNLWHLAQRHGCADTRTMVKTLEYIKKQSKQPDMTHL
TELALRLPLQTRT

>VPS26C

MGTALDIKIKRANKVYHAGEVLSGVVVISSKDSVQHQGVSLTMEGTVNLQLSAKSVGVFEAFYNSVKPIQIINSTIEMVKPGKFPSGKTEIPFEF
PLHLKGNKVLYETYHGVFVNIQYTLRCDMKRSLLAKDLTKTCEFIVHSAPQKGKFTPSPVDFTITPETLQNVKERALLPKFLLRGHLNSTNCVIT
QPLTGELVVESSEAAIRSVELQLVRVETCGCAEGYARDATEIQNIQIADGDVCRGLSVPIYMVFPRLFTCPTLETTNFKVEFEVNIVVLLHPDHL
ITENFPLKLCRI

>VPS29-Tev-$(GGS)_2$-His_6 (corresponding to Q9UBQ0-2, isoform 2 in Uniprot)

MAGHRLVLVLGDLHIPHRCNSLPAKFKKLLVPGKIQHILCTGNLCTKESYDYLKTLAGDVHIVRGDFDENLNYPEQKVVTVGQFKIGLIHGHQVI
PWGDMASLALLQRQFDVDILISGHTHKFEAFEHENKFYINPGSATGAYNALETNIIPSFVLMDIQASTVVTYVYQLIGDDVKVERIEYKKPENLY
FQGGGSGGSHHHHHH

>MBP-Tev-CCDC22 NN-CH (1-118)-$(GGSK)_6$-CCDC22 VBD(436-727)

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNNN
NLGIEGRISEFENLYFQGHMEEADRILIHSLRQAGTAVPPDVQTLRAFTTELVVEAVVRCLRVINPAVGSGLSPLLPLAMSARFRLAMSLAQACM
DLGYPLELGYQNFLYPSEPDLRDLLLFLAERLPTDASEDADQGGSKGGSKGGSKGGSKGGSKGGSKRKLQDCRELESSRRLAEIQELHQSVRAAA
EEARRKEEVYKQLMSELETLPRDVSRLAYTQRILEIVGNIRKQKEEITKILSDTKELQKEINSLSGKLDRTFAVTDELVFKDAKKDDAVRKAYKY
LAALHENCSQLIQTIEDTGTIMREVRDLEEQIETELGKKTLSNLEKIREDYRALRQENAGLLGRVREA

>MBP-Tev-CCDC93 VBD (442-631)

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNNN
NLGIEGRISEFENLYFQGHMTLTSAMTHDEDLDRRYNMEKEKLYKIRLLQARRNREIAILHRKIDEVPSRAELIQYQKRFIELYRQISAVHKETK
QFFTLYNTLDDKKVYLEKEISLLNSIHENFSQAMASPAARDQFLRQMEQIVEGIKQSRMKMEKKKQENKMRRDQLNDQYLELLEKQRLYFKTVKE
FKEEGRKNEMLLSKVKAKAS

>MBP-Tev-CCDC22 DBD (280-446)

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNNN
NLGIEGRISEFENLYFQGHMGAGAKTGAPKGSRFTHSEKFTFHLEPQAQATQVSDVPATSRRPEQVTWAAQEQELESLREQLEGVNRSIEEVEAD
MKTLGVSFVQAESECRHSKLSTAEREQALRLKSRAVELLPDGTANLAKLQLVVENSAQRVIHLAGQWEKHRVPLLAEYRHLRKLQDCRELES

>MBP-Tev-CCDC93 DBD (305-433)

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNNN
NLGIEGRISEFENLYFQGHMSPEKLGTSQLHRRKVISLNKQIAQKTKHLEELRASHTSLQARYNEAKKTLTELKTYSEKLDKEQAALEKIESKAD

PSILQNLRALVAMNENLKSQEQEFKAHCREEMTRLQQEIENLKAERAPRGDEKT

>His6-Tev-DENND10

MGHHHHHHDYDIPTTENLYFQGSMAAAEVADTQLMLGVGLIEKDTNGEVLWVWCYPSTTATLRNLLLRKCCLTDENKLLHPFVFGQYRRTWFYIT
TIEVPDSSILKKVTHFSIVLTAKDFNPEKYAAFTRILCRMYLKHGSPVKMMESYIAVLTKGICQSEENGSFLSKDFDARKAYLAGSIKDIVSQFG
METVILHTALMLKKRIVVYHPKIEAVQEFTRTLPALVWHRQDWTILHSYVHLNADELEALQMCTGYVAGFVDLEVSNRPDLYDVFVNLAESEITI
APLAKEAMAMGKLHKEMGQLIVQSAEDPEKSESHVIQDIALKTREIFTNLAPFSEVSADGEKRVLNLEALKQKRFPPATENFLYHLAAAEQMLKI

>MBP-Tev-CCDC22 NN-CH (1-118)-(GGSK)$_6$-CCDC22 VBD (436-727)^{R490D}

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNN
NLGIEGRISEFENLYFQGHMEEADRILIHSLRQAGTAVPPDVQTLRAFTTELVVEAVVRCLRVINPAVGSGLSPLLPLAMSARFRLAMSLAQACM
DLGYPLELGYQNFLYPSEPDLRDLLLFLAERLPTDASEDADQGGSKGGSKGGSKGGSKGGSKGGSKRKLQDCRELESSRRLAEIQELHQSVRAAA
EEARRKEEVYKQLMSELETLPRDVS**D**LAYTQRILEIVGNIRKQKEEITKILSDTKELQKEINSLSGKLDRTFAVTDELVFKDAKKDDAVRKAYKY
LAALHENCSQLIQTIEDTGTIMREVRDLEEQIETELGKKTLSNLEKIREDYRALRQENAGLLGRVREA

>MBP-Tev-CCDC22 NN-CH (1-118)-(GGSK)$_6$-CCDC22 VBD (436-727)^{V501R}

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNN
NLGIEGRISEFENLYFQGHMEEADRILIHSLRQAGTAVPPDVQTLRAFTTELVVEAVVRCLRVINPAVGSGLSPLLPLAMSARFRLAMSLAQACM
DLGYPLELGYQNFLYPSEPDLRDLLLFLAERLPTDASEDADQGGSKGGSKGGSKGGSKGGSKGGSKRKLQDCRELESSRRLAEIQELHQSVRAAA
EEARRKEEVYKQLMSELETLPRDVSRLAYTQRILEI**R**GNIRKQKEEITKILSDTKELQKEINSLSGKLDRTFAVTDELVFKDAKKDDAVRKAYKY
LAALHENCSQLIQTIEDTGTIMREVRDLEEQIETELGKKTLSNLEKIREDYRALRQENAGLLGRVREA

>MBP-Tev-CCDC22 NN-CH (1-118)-(GGSK)$_6$-CCDC22 VBD (436-727)$^{R490D/V501R}$

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNN
NLGIEGRISEFENLYFQGHMEEADRILIHSLRQAGTAVPPDVQTLRAFTTELVVEAVVRCLRVINPAVGSGLSPLLPLAMSARFRLAMSLAQACM
DLGYPLELGYQNFLYPSEPDLRDLLLFLAERLPTDASEDADQGGSKGGSKGGSKGGSKGGSKGGSKRKLQDCRELESSRRLAEIQELHQSVRAAA
EEARRKEEVYKQLMSELETLPRDVS**D**LAYTQRILEI**R**GNIRKQKEEITKILSDTKELQKEINSLSGKLDRTFAVTDELVFKDAKKDDAVRKAYKY
LAALHENCSQLIQTIEDTGTIMREVRDLEEQIETELGKKTLSNLEKIREDYRALRQENAGLLGRVREA

>MBP-Tev-CCDC93 VBD (442-631)^{R483E}

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNN
NLGIEGRISEFENLYFQGHMTLTSAMTHDEDLDRRYNMEKEKLYKIRLLQARRNREIAILH**E**KIDEVPSRAELIQYQKRFIELYRQISAVHKETK
QFFTLYNTLDDKKVYLEKEISLLNSIHENFSQAMASPAARDQFLRQMEQIVEGIKQSRMKMEKKKQENKMRRDQLNDQYLELLEKQRLYFKTVKE
FKEEGRKNEMLLSKVKAKAS

>MBP-Tev-CCDC93 VBD (442-631)^{A492W}

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNN
NLGIEGRISEFENLYFQGHMTLTSAMTHDEDLDRRYNMEKEKLYKIRLLQARRNREIAILHRKIDEVPSR**W**ELIQYQKRFIELYRQISAVHKETK
QFFTLYNTLDDKKVYLEKEISLLNSIHENFSQAMASPAARDQFLRQMEQIVEGIKQSRMKMEKKKQENKMRRDQLNDQYLELLEKQRLYFKTVKE
FKEEGRKNEMLLSKVKAKAS

>MBP-Tev-CCDC93 VBD (442-631)$^{R483E/A492W}$

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNN
NLGIEGRISEFENLYFQGHMTLTSAMTHDEDLDRRYNMEKEKLYKIRLLQARRNREIAILH**E**KIDEVPSR**W**ELIQYQKRFIELYRQISAVHKETK
QFFTLYNTLDDKKVYLEKEISLLNSIHENFSQAMASPAARDQFLRQMEQIVEGIKQSRMKMEKKKQENKMRRDQLNDQYLELLEKQRLYFKTVKE
FKEEGRKNEMLLSKVKAKAS

>MBP-Tev-CCDC22 DBD (280-446)$^{A411D/A418D/E422R}$

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNN
NLGIEGRISEFENLYFQGHMGAGAKTGAPKGSRFTHSEKFTFHLEPQAQATQVSDVPATSRRPEQVTWAAQEQELESLREQLEGVNRSIEEVEAD
MKTLGVSFVQAESECRHSKLSTAEREQALRLKSRAVELLPDGTANLAKLQLVVENS**D**QRVIHL**D**GQW**R**KHRVPLLAEYRHLRKLQDCRELES

>MBP-Tev-CCDC22 DBD (280-446)$^{R425D/R433D/R436D}$

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNN

NLGIEGRISEFENLYFQGHMGAGAKTGAPKGSRFTHSEKFTFHLEPQAQATQVSDVPATSRRPEQVTWAAQEQELESLREQLEGVNRSIEEVEAD
MKTLGVSFVQAESECRHSKLSTAEREQALRLKSRAVELLPDGTANLAKLQLVVENSAQRVIHLAGQWEKHDVPLLAEYDHLDKLQDCRELES

>MBP-Tev-CCDC93 DBD (305-433)^{F403D}
MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNNN
NLGIEGRISEFENLYFQGHMSPEKLGTSQLHRRKVISLNKQIAQKTKHLEELRASHTSLQARYNEAKKTLTELKTYSEKLDKEQAALEKIESKAD
PSILQNLRALVAMNENLKSQEQEDKAHCREEMTRLQQEIENLKAERAPRGDEKT

>MBP-Tev-CCDC93 DBD (305-433)^{E410R}
MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNNN
NLGIEGRISEFENLYFQGHMSPEKLGTSQLHRRKVISLNKQIAQKTKHLEELRASHTSLQARYNEAKKTLTELKTYSEKLDKEQAALEKIESKAD
PSILQNLRALVAMNENLKSQEQEFKAHCRERMTRLQQEIENLKAERAPRGDEKT

>MBP-Tev-CCDC93 DBD (305-433)$^{F403D/E410R}$
MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKVTVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYAQSGLLAEITPDKAFQDKLYPFTW
DAVRYNGKLIAYPIAVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKSALMFNLQEPYFTWPLIAADGGYAFKYENGKYDIKDVGVDNAGAK
AGLTFLVDLIKNKHMNADTDYSIAEAAFNKGETAMTINGPWAWSNIDTSKVNYGVTVLPTFKGQPSKPFVGVLSAGINAASPNKELAKEFLENYL
LTDEGLEAVNKDKPLGAVALKSYEEELAKDPRIAATMENAQKGEIMPNIPQMSAFWYAVRTAVINAASGRQTVDEALKDAQTNSSSNNNNNNNNN
NLGIEGRISEFENLYFQGHMSPEKLGTSQLHRRKVISLNKQIAQKTKHLEELRASHTSLQARYNEAKKTLTELKTYSEKLDKEQAALEKIESKAD
PSILQNLRALVAMNENLKSQEQEDKAHCREEMTRLQQEIENLKAERAPRGDEKT

>His$_6$-Tev-DENND10 (1-357)^{W30D}
MGHHHHHHDYDIPTTENLYFQGSMAAAEVADTQLMLGVGLIEKDTNGEVLWVDCYPSTTATLRNLLLRKCCLTDENKLLHPFVFGQYRRTWFYIT
TIEVPDSSILKKVTHFSIVLTAKDFNPEKYAAFTRILCRMYLKHGSPVKMMESYIAVLTKGICQSEENGSFLSKDFDARKAYLAGSIKDIVSQFG
METVILHTALMLKKRIVVYHPKIEAVQEFTRTLPALVWHRQDWTILHSYVHLNADELEALQMCTGYVAGFVDLEVSNRPDLYDVFVNLAESEITI
APLAKEAMAMGKLHKEMGQLIVQSAEDPEKSESHVIQDIALKTREIFTNLAPFSEVSADGEKRVLNLEALKQKRFPPATENFLYHLAAAEQMLKI

>His$_6$-Tev-DENND10 (1-357)^{Y32D}
MGHHHHHHDYDIPTTENLYFQGSMAAAEVADTQLMLGVGLIEKDTNGEVLWVWCDPSTTATLRNLLLRKCCLTDENKLLHPFVFGQYRRTWFYIT
TIEVPDSSILKKVTHFSIVLTAKDFNPEKYAAFTRILCRMYLKHGSPVKMMESYIAVLTKGICQSEENGSFLSKDFDARKAYLAGSIKDIVSQFG
METVILHTALMLKKRIVVYHPKIEAVQEFTRTLPALVWHRQDWTILHSYVHLNADELEALQMCTGYVAGFVDLEVSNRPDLYDVFVNLAESEITI
APLAKEAMAMGKLHKEMGQLIVQSAEDPEKSESHVIQDIALKTREIFTNLAPFSEVSADGEKRVLNLEALKQKRFPPATENFLYHLAAAEQMLKI

Supplementary Table 3. DNA oligos used in this study

Purpose	Identifier and sequence, all 5' to 3'
VPS35L	oDB220120-1, CTCGGTCCGAACTCCTAAAAAACCGCCACCatggccgtctttc, forward primer to extract VPS35L and add annealing arm for SLIC oDB220120-2, GCATGCCTCGAGACTGCAGGCTCTAGATTAggtccttgtttgcagagggag, reverse primer to extract VPS35L and add annealing arm for SLIC oDB220120-14, GGTGGCGGTTTTTTAGGAGTTC, reverse primer to open pAV5a oDB220120-15, TAATCTAGAGCCTGCAGTCTCGAG, forward primer to open pAV5a
VPS26C	oDB220120-4, TTTGAAAACCTGTATTTTCAGGGCCATATGGGGACCGCCCTGGACATC, forward primer to extract VPS26C and add annealing arm for SLIC GCTGAAGCTCTGCAGGATATAATCTAGAGCCTGCAGTCTCGAGGCATGC oDB220505-1, GCATGCCTCGAGACTGCAGGCTCTAGATTATATCCTGCAGAGCTTCAGC, reverse primer to extract VPS26C and add annealing arm for SLIC oDB220120-14, GGTGGCGGTTTTTTAGGAGTTC, reverse primer to open pAV5a oDB220120-15, TAATCTAGAGCCTGCAGTCTCGAG, forward primer to open pAV5a
VPS29-His$_6$	oDB220120-11, CTCGGTCCGAACTCCTAAAAAACCGCCACCATGGCTGGGCACAGATTG, forward primer to extract VPS29 and add annealing arm for SLIC oDB220120-12, GATGAGAGCCTCCACTTCCACCGCCCTGAAAATACAGGTTTTCAGGTTTTTTGTATTCGATTCGTTCTACTTTC, forward primer to extract VPS29 and add annealing arm for SLIC oDB220120-13, TTCAGGGCGGTGGAAGTGGAGGCTCTCATCATCATCATCATCATTAATCTAGAGCCTGCAGTCTCGAG, forward primer to open pAV5a and add SLIC annealing arm for VPS29-His6 oDB220120-14, GGTGGCGGTTTTTTAGGAGTTC, reverse primer to open pAV5a
His$_6$-DENND10	cbyo-230123-1, ACTACCGAAAACCTGTACTTCCAG, PCR DENND10opti BamHI fw Cbyo-230123-2, TAAGTGCTCGAGTTAAATCTTCAGCATC, PCR DENND10opti XhoI bw
MBP-CCDC22 Head-VBD^{R490D}	Cbyo-230502-1, CTGGCATATACCCAGCGTATTCTG, Aliblunt for CCDC22_VBDopti R490D FW

	Cbyo-230502-2, ATCGCTAACATCACGAGGCAGGGTTTC, Aliblunt for CCDC22_VBDopti R490D BW
MBP-CCDC22 Head-VBD^{V501R}	Cbyo-230502-3, CGTGGCAATATTCGCAAGCAGAAAGAAG, Aliblunt for CCDC22_VBDopti V501R FW Cbyo-230502-4, AATTTCCAGAATACGCTGGGTATATGC, Aliblunt for CCDC22_VBDopti V501R BW
MBP-CCDC22 Head-VBD$^{R490D/V501R}$	Cbyo-230502-5, TTAGCTTACACGCAACGCATCTTAGAGATCCGTGGCAATATTCGCAAGCAGAAAGAAG, Aliblunt for CCDC22_VBDopti R490D/V501R FW Cbyo-230502-2, ATCGCTAACATCACGAGGCAGGGTTTC, Aliblunt for CCDC22_VBDopti R490D BW
MBP-CCDC93 VBD^{A492W}	Cbyo-230502-6, TGGGAACTGATTCAGTATCAGAAACGTTTTATCGAAC, Aliblunt for CCDC93_VBDopti A492W FW Cbyo-230502-7, ACGGCTCGGAACTTCATCAATTTTAC, Aliblunt for CCDC93_VBDopti A492W BW
MBP-CCDC93 VBD$^{R483E/A492W}$	Cbyo-230502-6, TGGGAACTGATTCAGTATCAGAAACGTTTTATCGAAC, Aliblunt for CCDC93_VBDopti A492W FW Cbyo-230502-8, ACGGCTCGGAACTTCATCAATTTTC, Aliblunt for CCDC93_VBDopti R483E/A492W BW
MBP-CCDC22 DBD$^{A411D/A418D/E422R}$	Cbyo-230502-9, TTAGATGGACAATGGCGTAAACATCGTGTTCCGCTGCTGG, Aliblunt for CCDC22_DBDopti A411D/A418D/E422R FW Cbyo-230502-10, GTGGATGACGCGTTGATCGCTATTTTCAACAACCAGCTGCAG, Aliblunt for CCDC22_DBDopti A411D/A418D/E422R BW
MBP-CCDC22 DBD$^{R425D/R433D/R436D}$	Cbyo-230502-11, GAGTACGATCACTTAGATAAACTGCAGGATTGTCGTGAACTGG, Aliblunt for CCDC22_DBDopti R425D/R433D/R436D FW Cbyo-230502-12, GGCTAATAATGGTACGTCATGTTTTTCCCACTGACCTGCCAG, Aliblunt for CCDC22_DBDopti R425D/R433D/R436D BW
MBP-CCDC93 DBD^{F403D}	Cbyo-230502-13, TAAAGCCCATTGTCGTGAAGAAATGAC, Aliblunt for CCDC93_DBDopti F403D FW Cbyo-230502-14, TCCTCTTGCTCTTGGCTTTTCAGATTTTCATTC, Aliblunt for CCDC93_DBDopti F403D BW
MBP-CCDC93 DBD$^{E410R/F403D}$	Cbyo-230502-15, TAAAGCCCATTGTCGTGAACGTATGAC, Aliblunt for CCDC93_DBDopti E410R/F403D FW Cbyo-230502-14, TCCTCTTGCTCTTGGCTTTTCAGATTTTCATTC, Aliblunt for CCDC93_DBDopti F403D BW
His_6-DENND10^{W30D}	Cbyo-230502-16, ATCCGAGCACCACCGCAACAC, Aliblunt for DENND10 W30D FW Cbyo-230502-17, AACAATCAACCCACAGAACTTCACCATTGGTATC, Aliblunt for DENND10 W30D BW
His_6-DENND10^{Y32D}	Cbyo-230502-16, ATCCGAGCACCACCGCAACAC, Aliblunt for DENND10 W30D FW Cbyo-230502-18, CACACCAAACCCACAGAACTTCAC, Aliblunt for DENND10 Y32D BW

Supplementary Table 4: Guide RNA sequences used for CRISPR/Cas9

Crispr gRNA			
Gene target (Human)	***Guide construct***	***Target sequence***	***Reference***
VPS35L	Guide 1	TGATGAATCTGGTTTCCCCA	This paper
VPS35L	Guide 2	CACTAAGCTGAAGAACCCAC	Singla et al, 2019
VPS29	Guide 1	TAGCTGGCAAACTGTTGCAC	This paper
VPS29	Guide 2	GACTATCTCAAGACTCTGGC	This paper
VPS29	Guide 3	GGACATCAAGTTATTCCATG	This paper

Supplementary Table 5: Antibodies used in this study

Primary antibodies WB, western blot; IF, immunofluorescence staining; FC, Flow Cytometry.			
Target	**Source** (host species)	**Catalog or identifying number**	**Application**
CCDC22	ProteinTech Group (rabbit)	16636-1-AP	WB
CCDC22	Invitrogen (mouse)	MA5-27399	WB
CCDC93	ProteinTech Group (rabbit)	20861-1-AP	WB
CD14-APC	BD Biosciences (mouse)	555399	FC
COMMD1	Novus Biologicals (mouse)	NBP2-03755	WB
COMMD2	Custom made (rat)	UT-R 42 (Li et al., 2015)	WB
COMMD3	Custom made (rat)	UT-R 43 (Li et al., 2015)	WB
COMMD4	Custom made (rabbit)	UT-691 (Li et al., 2015)	WB
COMMD5	ProteinTech Group (mouse)	67043-1-IG	WB
COMMD6	Custom made (rabbit)	051-AP (Starokadomskyy et al., 2013)	WB
COMMD7	Custom made (rat)	UT-R 47 (Li et al., 2015)	WB
COMMD8	Custom made (guinea pig)	UT-GP 135 (Li et al., 2015)	WB
COMMD9	Custom made (rabbit)	192-AP (Starokadomskyy et al., 2013)	WB
COMMD10	Santa Cruz (mouse)	sc-398798	WB
DENND10	Custom made (rabbit)	95-110 (Singla et al., 2019)	WB
FAM21	Custom made (rabbit)	MC2188 (Gomez and Billadeau, 2009)	IF
FLAG	Sigma (mouse)	F1804	WB
HA	Biolegend (mouse)	901502	WB, IF
HA	Cell Signaling (mouse)	2999S	WB
Integrin-β1	Santa Cruz (mouse)	sc-53711	IF
LAMP1	Abcam (rabbit)	Ab24170	IF
Villin	ProteinTech Group (rabbit)	16488-1-AP	FC
VPS26A	Abcam (rabbit)	Ab23892	WB
VPS26C	Millipore (rabbit)	ABN87	WB
VPS29	GeneTex (rabbit)	GTX104768	WB
VPS35	Abcam (goat)	Ab10099	WB
VPS35L	ThermoFisher Scientific (rabbit)	PA5-28553	WB
Secondary antibodies used for immunofluorescence			
Fluorophore	**Source** (target species)	**Catalog number**	
Alexa 488	Invitrogen (mouse)	A11029	
Alexa 555	Invitrogen (rabbit)	A21428	
Phalloidin 488	Invitrogen	A12379	