

## Supplementary Tables

**Table S1. Yeast-two-hybrid interaction candidate hits.** List and frequency of all candidate proteins identified through yeast-two-hybrid (Y2H) with the baits tau-CTTR and PM-tau-CTTR.

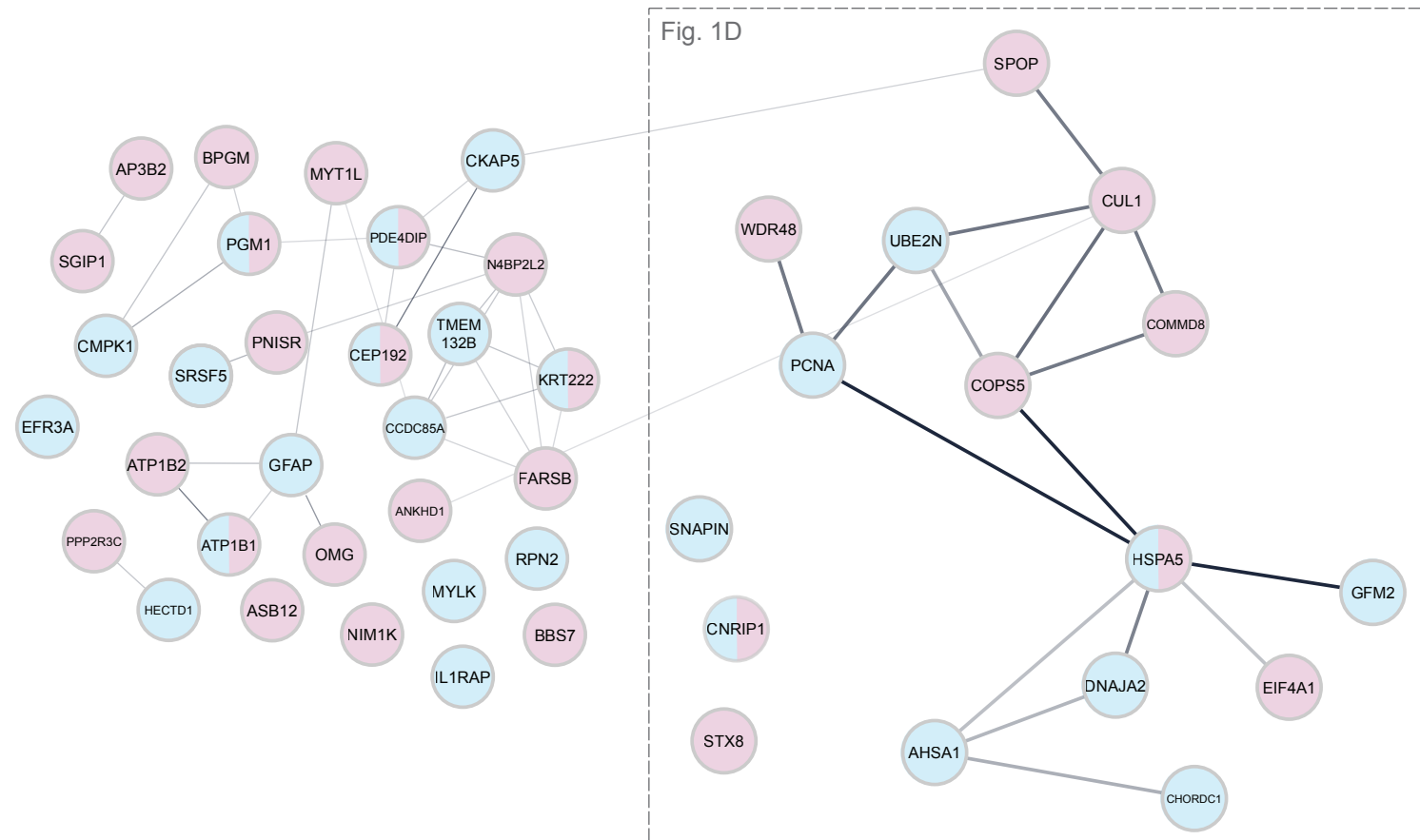
Protein	Description	Entrez Gene ID	Y2H hits/bait	
			tau-CTTR	PM-tau-CTTR
AHSA1	activator of HSP90 ATPase activity 1	10598	1	0
ANKHD1	ankyrin repeat and KH domain containing 1	54882	0	1
AP3B2	adaptor related protein complex 3 subunit beta 2	8120	0	1
ASB12	ankyrin repeat and SOCS box containing 12	142689	0	1
ATP1B1	ATPase Na <sup>+</sup> /K <sup>+</sup> transporting subunit beta 1	481	1	2
ATP1B2	ATPase Na <sup>+</sup> /K <sup>+</sup> transporting subunit beta 2	482	0	2
BBS7	Bardet-Biedl syndrome 7	55212	0	1
BPGM	bisphosphoglycerate mutase	669	0	2
CCDC85A	coiled-coil domain containing 85A	114800	1	0
CEP192	centrosomal protein 192	55125	1	1
CHORDC1	cysteine and histidine rich domain containing 1	26973	1	0
CKAP5	cytoskeleton associated protein 5	9793	3	1
CMPK1	cytidine/uridine monophosphate kinase 1	51727	3	0
CNRIP1	cannabinoid receptor interacting protein 1	25927	2	3
COMMD8	COMM domain containing 8	54951	0	1
COPS5	COP9 signalosome subunit 5	10987	0	8
CUL1	cullin 1	8454	0	1
DNAJA2	DnaJ heat shock protein family member A2	10294	1	0
EFR3A	EFR3 homolog A	23167	1	0
EIF4A1	eukaryotic translation initiation factor 4A1	1973	0	1
FARSB	phenylalanyl-tRNA synthetase subunit beta	10056	0	1
GFAP	glial fibrillary acidic protein	2670	1	0
GFM2	GTP dependent ribosome recycling factor mitochondrial 2	84340	1	0
HECTD1	HECT domain E3 ubiquitin protein ligase 1	25831	2	0
HSPA5	heat shock protein family A member 5	3309	1	2
IL1RAP	interleukin 1 receptor accessory protein	3556	1	0
KRT222	keratin 222	125113	1	2
MYLK	myosin light chain kinase	4638	1	0
MYT1L	myelin transcription factor 1 like	23040	0	1
N4BP2L2	NEDD4 binding protein 2 like 2	10443	0	1
NIM1K	NIM1 serine/threonine protein kinase	167359	1	0
OMG	oligodendrocyte myelin glycoprotein	4974	1	0
PCNA	proliferating cell nuclear antigen	5111	2	0
PDE4DIP	phosphodiesterase 4D interacting protein	9659	1	1
PGM1	phosphoglucomutase 1	5236	1	1
PNISR	PNN interacting serine and arginine rich protein	25957	0	4
PPP2R3C	protein phosphatase 2 regulatory subunit B <sup>gamma</sup>	55012	0	1
RPN2	ribophorin II	6185	1	0
SGIP1	SH3GL interacting endocytic adaptor 1	84251	0	1
SNAPIN	SNAP associated protein	23557	2	0
SPOP	speckle type BTB/POZ protein	8405	0	3
SRSF5	serine and arginine rich splicing factor 5	6430	1	0
STX8	syntaxin 8	9482	0	2
TMEM132B	transmembrane protein 132B	114795	1	0
UBE2N	ubiquitin conjugating enzyme E2 N	7334	2	0
WDR48	WD repeat domain 48	57599	0	2

**Table S2. STRING functional GO term annotation of CTTR interaction candidates.** GO term annotation of candidate interacting proteins of the tau-CTTR and/or PM-tau-CTTR identified through Y2H and interpreted using the STRING functional enrichment tool. Only terms after a redundancy cutoff of 0.293 were shown. FDR values were obtained through the Benjamini–Hochberg procedure. PPI Enrichment Score: 0.00139

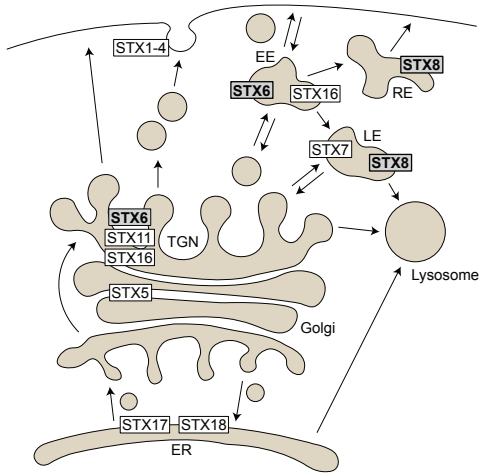
Category	Term ID	Description	Count	Enriched proteins	FDR value
GO Function	GO.0031625	ubiquitin protein ligase binding	5	STX8 UBE2N HSPA5 CUL1 SPOP	5.70E-04
GO Function	GO.0051087	chaperone binding	3	AHSA1 DNAJA2 HSPA5	3.60E-03
GO Function	GO.0051879	Hsp90 protein binding	2	AHSA1 CHORDC1	1.10E-02
GO Process	GO.1903894	regulation of IRE1-mediated unfolded protein response	2	HSPA5 COPS5	1.40E-02
GO Function	GO.0032555	purine ribonucleotide binding	6	EIF4A1 GFM2 DNAJA2 UBE2N CHORDC1 HSPA5	2.80E-02
GO Function	GO.0000149	SNARE binding	2	STX8 SNAPIN	3.40E-02
GO Process	GO.0006281	DNA repair	4	WDR48 UBE2N COPS5 PCNA	4.00E-02

**Table S3. Cloning primer sequences.**

<b>Gene/Plasmid</b>	<b>Primer Sequences (F, forward; R, reverse)</b>
AHSA1 into pENTR-SD-TOPO	F: 5'-CACCATGGCCAAGTGGGGTGAGG R: 5'-AAATAAGCGTGCGCCATAGC
CNRIP1 into pENTR-SD-TOPO	F: 5'-CACCATGGGGGACCTGCCGGG R: 5'-GAGGAAGGACTCCTTGTTCA
COPS5 into pENTR-SD-TOPO	F: 5'-CACCATGGCGGCGTCCGGGAG R: 5'-AGAGATGTTAATTTGATTAACAGTT
CUL1 into pENTR-SD-TOPO	F: 5'-CACCATGTCTCAACCCGGAGCC R: 5'-AGCCAAGTAACTGTAGGTGTC
HSPA5 into pENTR-SD-TOPO	F: 5'-CACCATGAAGCTCTCCCTGGTGG R: 5'-AGCCAACCTCATCTTTTCTGCTGTA
PCNA into pENTR-SD-TOPO	F: 5'-CACCATGTTTCGAGGCGCGCTG R: 5'-AGATCCTTCTTCATCCTCGAT
SNAPIN into pENTR-SD-TOPO	F: 5'-CACCATGGCGGGGGCTGGTTCC R: 5'-TTTGCCTGGGGAGCCAGG
STX6 into pENTR-SD-TOPO	F: 5'-CACCATGTCCATGGAGGACCCCT R: 5'-CAGCACTAAGAAGAGGATGA
STX8 into pENTR-SD-TOPO	F: 5'-CACCATGGCACCGGACCCCTGG R: 5'-GTTGGTCGGCCAGACTGCA
WDR48 into pENTR-SD-TOPO	F: 5'-CACCATGGCGGCCCATCACCGG R: 5'-CGTGGACTTCTGACGGTAAT
STX8-HA into pcDNA3.1	F: 5'-TAAGGATCCCACCATGGCACCGGACCCCTGG R: 5'-TGTGAATTCTAAGCGTAATCTGGAACATCGTATGGGTAGGATCTG TTGGTCGGCCAGACTGCA
pEGFPC1-STX6 FL	F: 5'-GGTGAATTCTATGTCCATGGAGGACCCCT R: 5'-TAAGGATCCTCATCACAGCACTAAGAAGAGG
pEGFPC1-STX6 1-234	F: 5'-GGTGAATTCTATGTCCATGGAGGACCCCT R: 5'-TAAGGATCCCTATTGGCGCCGATCACTGGTC
pEGFPC1-STX6 235-255	F: 5'-GGTGAATTCTTGGTGTGCCATAGCCATCC R: 5'-TAAGGATCCTCATCACAGCACTAAGAAGAGG
pEGFPC1-STX6 1-160	F: 5'-GGTGAATTCTATGTCCATGGAGGACCCCT R: 5'-TAAGGATCCTCATGCCTGCTGCTCCTCAATG
pEGFPC1-STX6 161-255	F: 5'-GGTGAATTCTCAGCAGCAGTTGATCGTGG R: 5'-TAAGGATCCTCATGCCTGCTGCTCCTCAATG
pEGFPC1-STX6 1-71	F: 5'-GGTGAATTCTATGTCCATGGAGGACCCCT R: 5'-TAAGGATCCTCAAATATGCTGATGGTTTCATC
pEGFPC1-STX6 72-255	F: 5'-GGTGAATTCTGAAGCAAATCCTAGAAAATTT R: 5'-TAAGGATCCTCATCACAGCACTAAGAAGAGG



**Fig. S1. Complete STRING networks of CTTR and PM-CTTR interaction candidates.** Ubiquitin-proteasome and molecular chaperons clusters and in individual candidate presented in Fig. 1D are highlighted (broken box).



**Fig. S2. Schematic of secretory pathways and syntaxins.** Illustration of the distinct localizations of individual syntaxins (STX) within the secretory machinery of cells. ER, endoplasmic reticulum; TGN, trans-Golgi network; EE, early endosome; LE, late endosome; RE, recycling endosome.

STX8	----MIMV <b>ILLLLVAIVVVAV</b> -----	[aa216-232]
STX6	-----WCA <b>IAILFAVLLVVLILFLVL</b> ----	[aa235-255]
STX10	-----WCA <b>IAVLVGVLLLVLILLFSL</b> ----	[aa229-249]
STX16	-----MLV <b>ILILFVIIIIVLIVVLVGV</b> ----	[aa302-322]
STX7	-----C <b>IIILILVIGVAIISLIIWGL</b> ----	[aa239-259]
STX5	WLMVK <b>IFLILIVFFIIFVVFL</b> -----	[aa334-354]
STX4	----- <b>IAICVSITVLLAVIIGV</b> TVV-	[aa276-296]
STX3	----L <b>IIIIVLVVLLGILALIIGL</b> -----	[aa264-284]
STX2	-----W <b>IIIAVSVLVVAIIALII</b> GLSVGK-	[aa265-288]
STX1A	----- <b>IMIIICCVILGIVIASTVGGI</b> ---	[aa266-286]
STX1B	----- <b>IMIIICCVVLGVVLASSIGGTLGL</b>	[aa265-288]
STX18	--AGFR <b>VWILFFLVMCSFSLFL</b> -----	[aa310-330]
STX17	---LAALP <b>VAGALIGGMVGGPIGL</b> -----	[aa255-275]
STX17	----- <b>VAGIAAALGGGVLGFTGGKLI</b> ----	[aa255-275]
STX12	---KMC <b>ILVLVLSVIIILILGLII</b> -----	[aa249-269]

**Fig. S3. Alignment of transmembrane domain amino acid sequences of syntaxins.** CLUSTAL O alignment of transmembrane (TM) domain amino acid (aa) sequences of human syntaxins. Isoforms are indicated, followed by aa sequences and position of the TM in the respective full-length protein in brackets. Bolt lettering indicates Isoleucine (I), Leucine (L) and Valine (V) residues in similar positions. Conserved positions are highlighted in grey.