

Supplementary Material

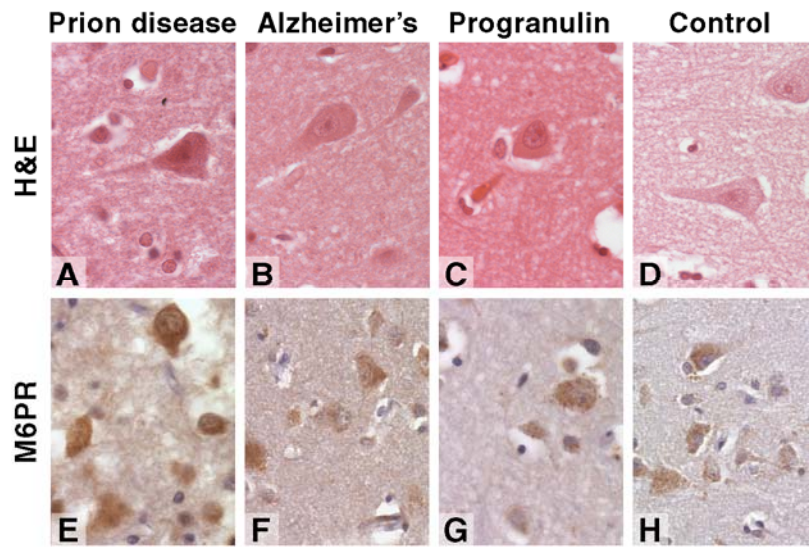


Figure S1. Enlarged endosomal phenotype not present in disease-control brains.

Frontal cortex sections from prion disease (A, E), Alzheimer's disease (B, F), frontotemporal dementia with progranulin mutation (C, G) and age-matched controls (D, H). Representative images of haematoxylin and eosin staining (H&E, A – D) and immunohistochemical staining against mannose-6-phosphate receptor (M6PR, E – H) are shown. Cytoplasmic M6PR-positive vacuoles, as visible in frontal cortical neurons of FTD-3 brains (Fig. 2 of the manuscript), are not observed. Scale bar represents 60 μ m.

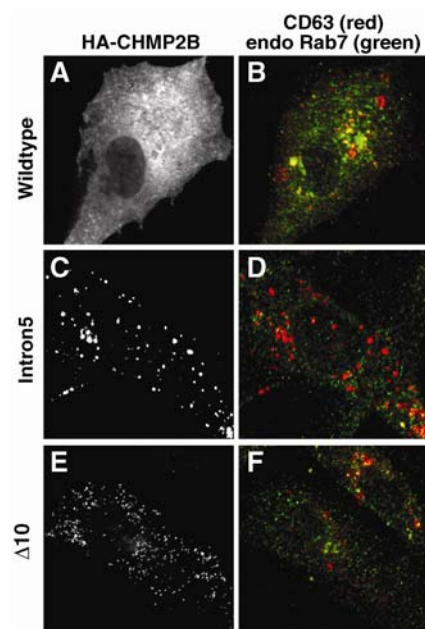


Figure S2. Impaired recruitment of endogenous Rab7 onto endosomes in mutant CHMP2B expressing cells.

SK-N-SH cells were transfected with HA-CHMP2B^{Wildtype} (A, B), HA-CHMP2B^{Intron5} (C, D) or HA-CHMP2B^{Δ10} (E, F), and then immunostained for HA, Rab7 (green) and CD63 to visualise endosomes (red). Quantification (Fig. 8 of the manuscript) showed that expression of mutant CHMP2B led to a reduction in the percentage of CD63-positive endosomes that recruited Rab7. Scale bar = 10 μ m.

Diagnosis	Sex	Age at death	PMI (h)
FTD-3	F	69	18
	F	61	NK
	F	76	NK
	M	59	NK
Control	F	65	30
	F	68	216
	F	79	38
	M	71	120
	M	57	79
	F	68	45
	M	71	39
	M	36	NK
	F	78	168
MAPT	M	71	120
	M	68	31
	M	48	65
	F	63	22
PGRN	F	66	115
	F	68	100
AD	F	85	120
	F	79	96
	M	79	120
fCJD	F	49	96
	F	46	96
	M	43	216
iCJD	M	37	120
sCJD	M	86	120
	M	67	96
	F	59	120
vCJD	F	56	120
	M	18	144
	F	36	120
GSS	M	64	168
FFI	M	60	144

Table S1. Patient information for M6PR brain immunohistochemistry.

AD, Alzheimer's disease; MAPT, frontotemporal dementia with MAPT mutations; GRN, frontotemporal dementia with GRN mutations; fCJD, familial Creutzfeldt-Jakob disease; iCJD, iatrogenic CJD; sCJD, sporadic CJD; vCJD, variant CJD; GSS, Gerstmann-Sträussler-Scheinker syndrome; FFI, fatal familial insomnia; PMI, post-mortem interval in hours; NK, not known.

Primer	Sequence
CHMP2B common forward primer	GACATCTTTGACGGTTCTGA
CHMP2B ^{Wildtype} specific reverse primer	GAGCTTTGGCCATCTTTC
CHMP2B ^{Intron5} specific reverse primer	GAAAAGATGATGTTTCATACCTTTC
CHMP2B ^{Δ10} specific reverse primer	CAGCTGATGGAGCTTTC
FAM-labelled Taqman probe	TTCCAATTCATCAAGAAC

Table S2. Nucleotide sequences for primers and probe used for quantitative real-time PCR of *CHMP2B* transcripts.