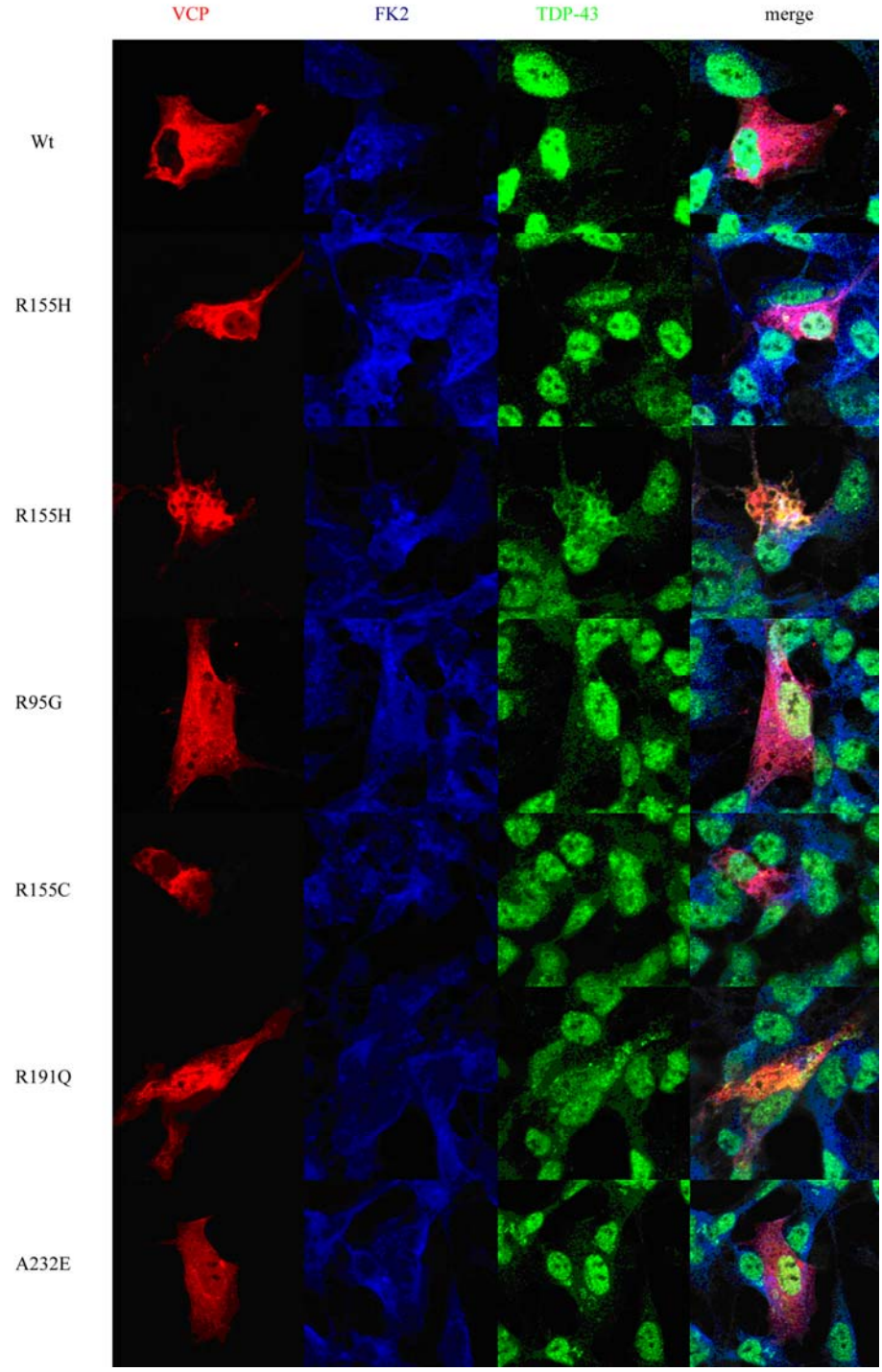
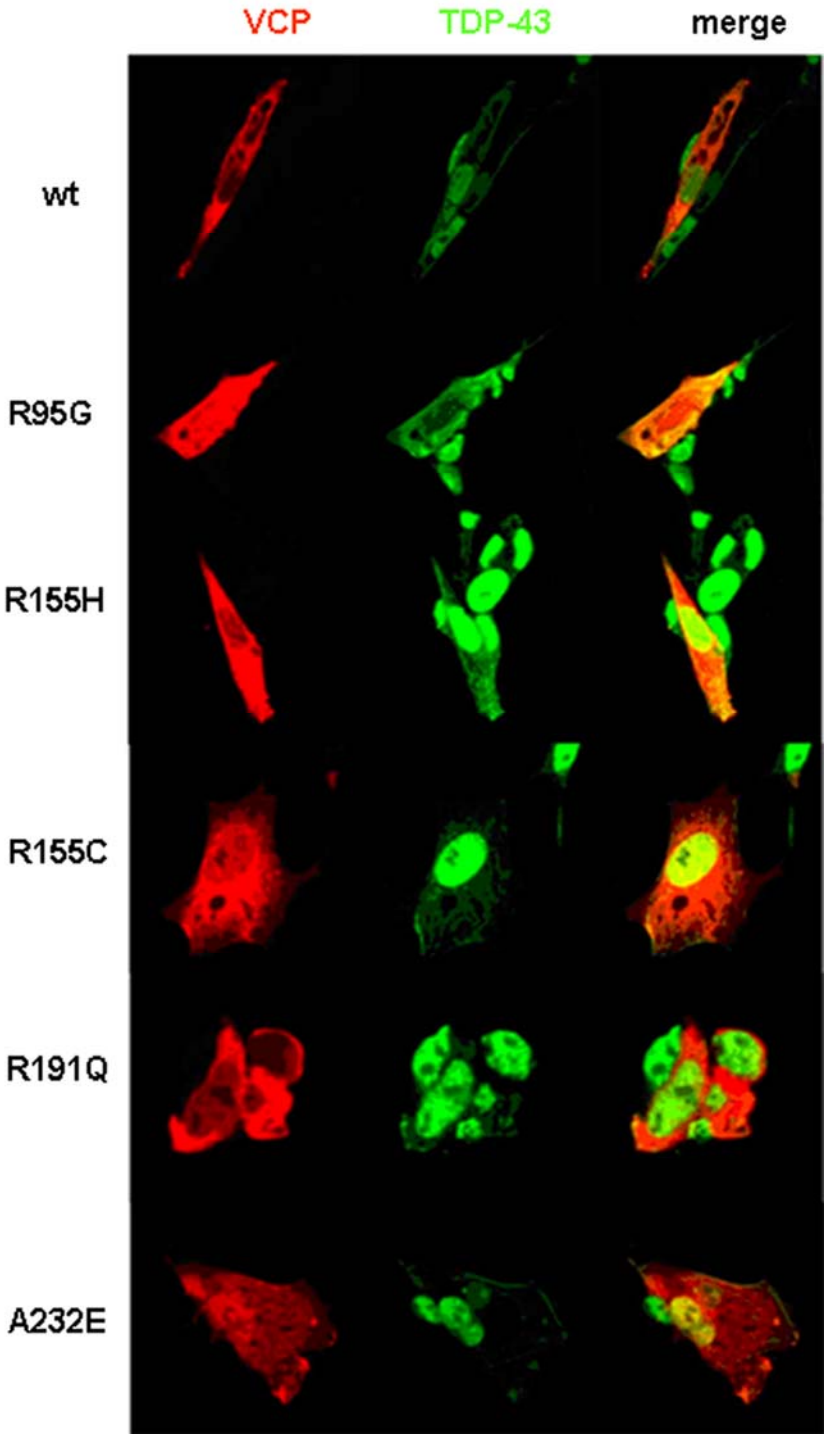
Supplementary Material

Diagnosis	Sex	Age (years)	PMI (hours)	Brain Weight (grams)	Agonal State	FTLD-U Subtype (2)	TDP-43 proteinopathy
FTLD-*VCP*	M	47	7	1185	inanition	4	+
FTLD-*GRN*	M	64	21	1050	myocardial infarction	3	+
FTLD-U	F	67	2	990	myocardial infarction	1	+
NL-1	F	92	6	1120	myocardial infarction	NA	-
NL-2	F	78	18	1290	duodenal cancer	NA	-
AD-1	F	93	17	1070	pneumonia	NA	-
AD-2	F	89	4.6	1050	aspiration pneumonia	NA	-

Supplementary Table 1. Demographic information of cases. FTLD-*VCP;* frontotemporal lobar degeneration *with valosin-containing* R1555H mutation; FTLD-*GRN*; FTLD with progranulin mutation (A9D); FTLD-U, sporadic FTLD with ubiquitin-immunoreactive inclusions; AD, Alzheimer's disease; NL, normal aged control subject; PMI, post-mortem interval.

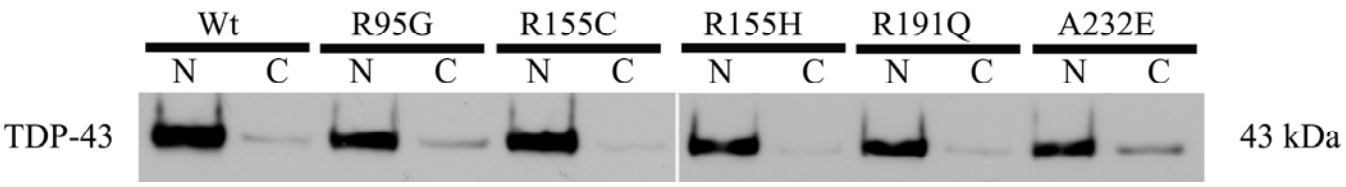


Supplementary Figure 1. Ubiquitin and TDP-43 distribution in overexpressed wild-type and mutant *VCP*. SHSY-5Y cells transiently transfected with monomeric dsRED-VCP constructs (red), TDP-43 (green) and FK2 (blue).



Supplementary Figure 2. PI3 kinase inhibitor (LY294002) treated cells show cytosolic distribution of TDP-43. At 24 hours post-transfection after 5 hour incubation LY294002 (50μM); dsRED-VCP constructs (red) and TDP-43 (green).

A



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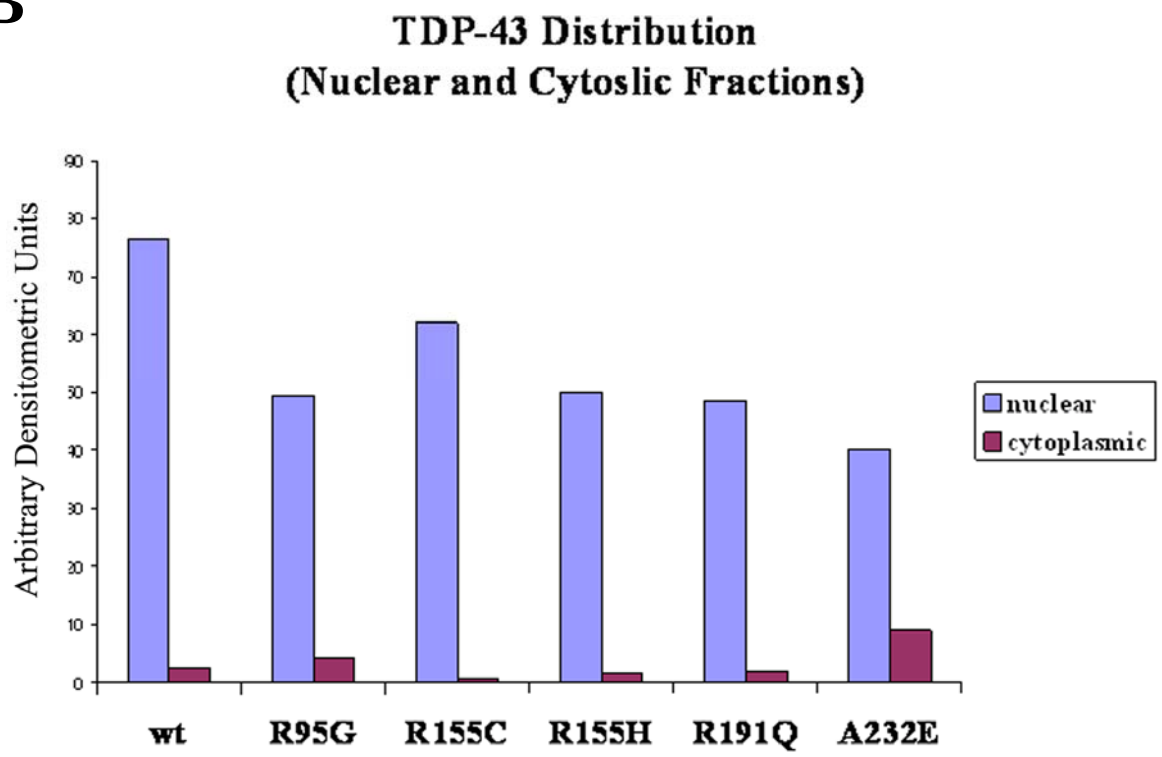

Supplementary Figure 3. Mutations in VCP disrupt nuclear localization of TDP-43.

A) Western blot analysis of nuclear (N) and cytosolic (C) fractions. **B)** Denoitometric analysis of TDP-43 comparing wild-type and all mutant nuclear and cytosolic localization.