Supplementary Table 1 Constructs designed in this study

Construct name	Residue range	Sequence
SUMO-TDP-43	1-414 (full length)	MGSSHHHHHHGSGLVPRGSASMSDSEVNQEAKPEVKPEVKPETHINL KVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLRFLYDGIRIQAD QTPEDLDMEDNDIIEAHREQIGGMSEYIRVTEDENDEPIEIPSEDDGTV LLSTVTAQFPGACGLRYRNPVSQCMRGVRLVEGILHAPDAGWGNLV YVVNYPKDNKRKMDETDASSAVKVKRAVQKTSDLIVLGLPWKTTEQ DLKEYFSTFGEVLMVQVKKDLKTGHSKGFGFVRFTEYETQVKVMSQ RHMIDGRWCDCKLPNSKQSQDEPLRSRKVFVGRCTEDMTEDELREFF SQYGDVMDVFIPKPFRAFAFVTFADDQIAQSLCGEDLIIKGISVHISNA EPKHNSNRQLERSGRFGGNPGGFGNQGGFGNSRGGGAGLGNNQGSN MGGGMNFGAFSINPAMMAAAQAALQSSWGMMGMLASQQNQSGPS GNNQNQGNMQREPNQAFGSGNNSYSGSNSGAAIGWGSASNAGSGSG FNGGFGSSMDSKSSGWGM
SUMO-SegA	311-360	MGSSHHHHHHGSGLVPRGSASMSDSEVNQEAKPEVKPEVKPETHINL KVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLRFLYDGIRIQAD QTPEDLDMEDNDIIEAHREQIGGMNFGAFSINPAMMAAAQAALQSSW GMMGMLASQQNQSGPSGNNQNQGNMQ
SUMO-SegB	286-331	MGSSHHHHHHGSGLVPRGSASMSDSEVNQEAKPEVKPEVKPETHINL KVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLRFLYDGIRIQAD QTPEDLDMEDNDIIEAHREQIGGQGGFGNSRGGGAGLGNNQGSNMG GGMNFGAFSINPAMMAAAQAALQ
SUMO-SegB A315E	286-331	MGSSHHHHHHGSGLVPRGSASMSDSEVNQEAKPEVKPEVKPETHINL KVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLRFLYDGIRIQAD QTPEDLDMEDNDIIEAHREQIGGQGGFGNSRGGGAGLGNNQGSNMG GGMNFGEFSINPAMMAAAQAALQ
SUMO-SegAB	286-360	MGSSHHHHHHGSGLVPRGSASMSDSEVNQEAKPEVKPEVKPETHINL KVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLRFLYDGIRIQAD QTPEDLDMEDNDIIEAHREQIGGQGGFGNSRGGGAGLGNNQGSNMG GGMNFGAFSINPAMMAAAQAALQSSWGMMGMLASQQNQSGPSGN NQNQGNMQ

Supplementary Table 2 Structural alignment details

Figure #	Residues displayed	Residues aligned	# atom pairs	r.m.s.d.
Figure 2a&c	SegA-sym 312-347 & SegA-asym long chain 312-352	312-336	161	1.344
Figure 2f	SegB A315E inner chain & outer chain	288-319	177	2.243
Figure 2a & Supplementary Figure 5a bottom left	SegA-sym 312-347 & SegA-asym short chain 311-346	336-346	70	1.150
Figure 2a & Supplementary Figure 5a bottom middle	SegA-sym 312-347 & SegA-asym short chain 311-346	322-336	88	1.222
Figure 2a & Supplementary Figure 5a bottom right	SegA-sym 312-347 & SegA-slow 311-360	312-336	150	1.776
Supplementary Figure 5c left	SegA-sym 328-333, 341'-346' & SegA-asym long chain 328-333, short chain 341-346	328-333	35	0.810
Supplementary Figure 5c middle	SegA-sym 334-341 both chains & SegA-asym 334-341 both chains	(long chain) 334-341	45	0.873
Supplementary Figure 5c right	SegA-sym 342-347, 327'-333' & SegA-asym long chain 342-352, short chain 327-333	342-347	44	1.568
Supplementary Figure 5d	SegA-sym 328-336, 338'-347' & SegA-slow long chain 328-336, short chain 338-347	328-336	53	0.624
Supplementary Figure 5e	SegA-sym 334-341 both chains & SegA-slow long chain 334-341	336-340	27	0.948
Supplementary Figure 5h (enlarged)	SegA-sym (312-319) & SegB A315E inner chain (312-319)	312-319	39	1.056
Supplementary Figure 5h (enlarged)	SegA-asym long chain (312-319) & SegB A315E inner chain (312-319)	312-319	43	1.463
Supplementary Figure 5h (enlarged)	SegA-asym short chain (312-319) & SegB A315E inner chain (312-319)	312-319	44	1.343
Supplementary Figure 5h (enlarged)	SegB outer chain (312-319) & SegB A315E inner chain (312-319)	315-319	35	1.573

Supplementary Table 3 Validation statistics of the hypothetical SegB A315E G304W model

	SegB A315E G304W (hypothetical model)
R.m.s.d. bonds (Å)	0.007
R.m.s.d. angles (°)	0.574
Molprobity clashscore, all atoms	16.61
Molprobity score	2.47
Poor rotamers (%)	0
Ramachandran outliers (%)	0
Ramachandran allowed (%)	21.8
Ramachandran favoured (%)	79.2
Cβ deviations > 0.25 Å (%)	0
Bad bonds (%)	0
Bad angles (%)	0