Supplementary table 1: The segments chosen for structural studies.

Sequence	Residue no.	Morphology under EM	Structure	Reason to choose
GNNQGSN	300-306	Microcrystals	5WKD	High density of Asn and Gln residues
NFGAFS	312-317	Microcrystals	5WHN	Aromatic residues next to each other
NFGEFS	312-317	Microcrystals	5WKB	Familiar mutation A315E
NFGTFS	312-317	Microcrystals	5WHP	Familiar mutation A315T
NFGpTFS	312-317	Microcrystals	6CF4	Phosphorylation of Familiar mutation A315T
AMMAAA	321-326	Microcrystals	6CEW	A324E reduces TDP-43 aggregation
AAAQAALQS	324-332	Microcrystals/fibrils		ZipperDB (AAAQAA rank no.3; AQAALQ rank no. 8)
AALQSS	328-333	Microcrystals	6CB9	ZipperDB (rank no.10)
SWGMMGMLASQ	333-343	Microcrystals	6CFH	M337E reduces TDP-43 aggregation
ASQQNQ	341-346	Microcrystals		ZipperDB (rank no.5), high NQ density
GNNQNQ	351-356	Microcrystals		ZipperDB (rank no.6), high NQ density
GNNSYS	370-375	Microcrystals	5WIA	ZipperDB (rank no.4)
GSASNAG	386-392	Microcrystals		ZipperDB (GSASNA rank no. 2; SASNAG rank no.7)
GFNGGFG	396-402	Microcrystals	5WIQ	Aromatic residues next to each other
SKSSGW	407-412	Aggregates/fibrils		ZipperDB (rank no.1)

Supplementary table 2: Familial variants of TDP-43, annotated as lying either in predicted LARKS[1] or in a LARKS of known structure[2].

The familiar variants reported in LCD of TDP-43 (Chiang, C. *et al*., *Sci. Rep.* **6,** 21581, 2016)			
G287S[1]	**G290A[1]**	**S292N[1]**	**G294V[1]**
G294A[1]	**G295S[1]**	**G295C[1]**	**G295R[1]**
G298S[1]	**M311V[1]**	**A315T[2]**	**A315E[2]**
A321G	A321V	Q331K	S332N
G335D[1]	**M337V[1]**	Q343R	N345K
G348C	G348V	G348R	N352S
N352T	R361S	R361T	P363A
G368S[1]	**Y374X[1]**	**N378D[1]**	**N378S[1]**
S379P[1]	**S379C[1]**	**A382T[1]**	**A382P[1]**
I383V[1]	**G384R[1]**	**W385G[1]**	**N390S[1]**
N390D[1]	**S393L[1]**		

[1]: lie in predicted LARKS ; [2]: lie in observed LARKS; The variants annotated as 1 or 2 were labeled in bold.