Table e-2: Methods not described in detail in the text

Method	Description
Expression and purification of recombinant proteins	Protein expression in *E. coli* BL21(DE3)CodonPlus (Stratagene, La Jolla, CA, USA) and purification of His_6-tagged proteins was performed as described[14]. GST-tagged proteins were expressed in *E. coli* and purified on Glutathione-Uniflow Resin columns (Clontech). GST was cleaved from proteins using PreScission Protease (Amersham), according to recommendations of the manufacturer.
Biophysical characterization	Circular dichroism spectroscopy in the far UV range for FLNc d23-24 wt and FLNc d23-24 p.K2676Pfs*3 mut proteins was performed as described[23, 24]. Size-exclusion chromatography coupled to multi-angle light scattering (SEC-MALS) was performed using a Superdex 200 10/300 GL column (Cytiva). Protein samples were dialysed against gel filtration buffer (0.1 M potassium chloride and 10 mM potassium phosphate, pH 7.3) overnight at 4 °C. The same buffer was used for column equilibration and subsequent measurements. 100 µl of 1 mg/ml protein samples were applied to a column using the 1260 Infinity HPLC system (Agilent Technologies) coupled to a MiniDawn Treos detector (Wyatt Technologies. An RI-101 detector (Shodex) was used for refractive index determination and Astra 7 software package (Wyatt Technologies) for data analysis.
Cross-linking of FLNc polypeptides	Dimerization of mutant FLNc was examined by chemical cross-linking experiments, using previously established protocols[4]. Cross-linking of recombinant wild-type and mutant FLNc polypeptides was performed in absence or presence of ethylene glycolbis(succinimidylsuccinate) (EGS). Reaction mixtures were analyzed by SDS–PAGE and Western blotting. Dimer formation was analyzed using specific antibodies against respective immunotags.
Proteolytic susceptibility studies	Proteolytic susceptibility was investigated using thermolysin (Sigma, St. Louis, MO, USA). Recombinant proteins were diluted to 10 µM in 50 mM NaH_2PO_4, 300 mM NaCl, 250 mM imidazole, pH 8.0, 5 µg/ml. Thermolysin was added and the mixture was incubated at 37 °C. At each incubation interval, the reaction was stopped by adding 0.2 vol. 5x SDS sample buffer. The samples were analyzed by SDS-PAGE using 10% polyacrylamide gels.