Supplementary

Terms used for searching in databases and literature:

'*DCTN1* gene', 'dynactin subunit 1', 'Perry syndrome', 'NM_004082:c.212G>A', 'p.Gly71Glu'

References for the supplementary tables

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Figure S1. Spatial relationship of the residue at position 71 of the CAP-Gly domain. Images show the residues located spatially close (4 Å) to Gly71 in the wild-type CAP-Gly domain (left) and the equivalent representation of residues close to Glu71 in the mutant models (right). Gly71 and Glu71 are represented as blue and red spheres (2MPX/Model 3), respectively, or by element (2HKQ/Model 2 and 3E2U/Model 4). In 2MPX/Model 3, the residues in the proximity of position 71 are shown as green spheres. The remaining images are shown in the stick format. The remaining regions of the molecules are represented in cartoon format. The residues of interest are identified using the one letter code. In Model 2, Glu71 is oriented in the opposite direction compared with Model 1 shown in Fig. 1C. Glu71 points toward the β3 strand, which is part of the structural core of the domain. Consequently, both Phe79 and Cys81 rearrange to create room for Glu71. In Model 3, Glu71 is oriented towards the domain surface, as in Model 1, but it is more solvent-exposed in Model 3. Such variation in the environment of Glu71 reflects differences in the loop conformation connecting the β3 and β4 strands between these models, resulting in a less compact environment of Glu71 in Model 3. In Model 4, Glu71 adopts a spatial positioning similar to that adopted in Model 2, but in Model 4, the Glu71 side chain is rotated nearly 90°, respective to Model 2. Å, Angstrom; CAP-Gly, cytoskeleton-associated protein glycine-rich domain; 2MPX, three-dimensional structure of cap-gly domain assembled on microtubules determined by Magic Angle Spinning NMR spectroscopy; 2HKQ, crystal structure of the C-terminal domain of human EB1 in complex with the CAP-Gly domain of human dynactin-1 (p150-Glued); 3E2U, crystal structure of the zink-knuckle 2 domain of human CLIP-170 in complex with p150-Glued.

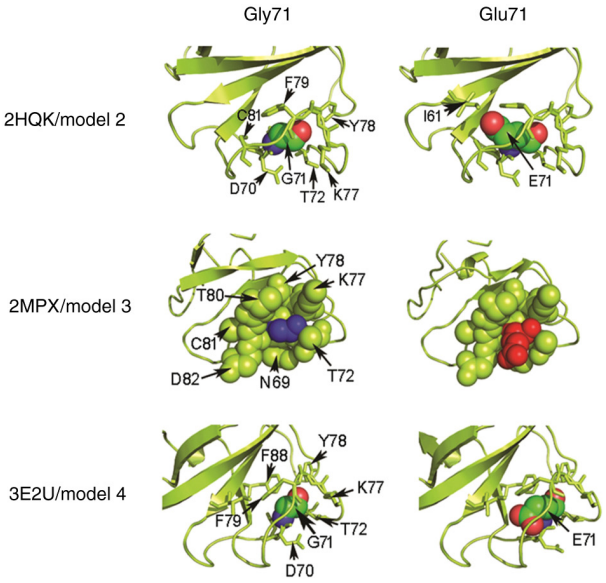

Figure S2. Cavities in the structures of the 2HKQ/Model 2, 2MPX/Model 3 and 3E2U/Model 4. The analysis was performed using the Voronoia program suite (21). The cavities are represented as spheres with mesh format, in blue or green. In the protein structures, the peptide backbone is shown in the cartoon format and the lines indicate residues, except position 71 (Gly or Glu), which is shown as a sphere. The image was generated by PyMOL (20) using data in the cav PDB file generated by Voronoia and the PDB file of respective structures. PDB, protein data bank; 2HKQ, crystal structure of the C-terminal domain of human EB1 in complex with the CAP-Gly domain of human dynactin-1 (p150-Glued); 2MPX, three-dimensional structure of cap-gly domain assembled on microtubules determined by Magic Angle Spinning NMR spectroscopy; 3E2U, crystal structure of the zink-knuckle 2 domain of human CLIP-170 in complex with p150-Glued PDB entries.

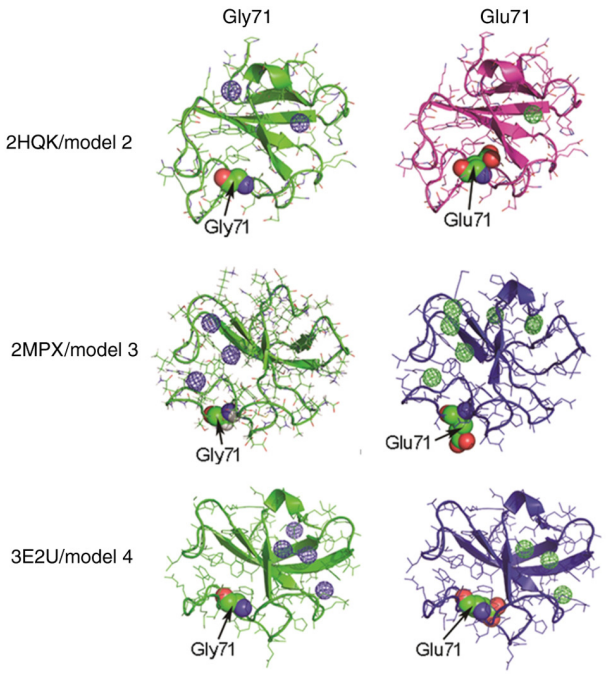

Figure S3. Electrostatic potential maps of the 2HKQ/Model 2, 2MPX/Model 3 and 3E2U/Model 4 protein structures, constructed using Swiss-PdbViewer 4-1-0 software (22). The conventional code represents the charge distribution, where blue and red represent electron-poor and electron-rich regions, respectively. The molecules are represented in a space-filled format, using the CPK color code: Carbon is gray, oxygen is red, nitrogen is blue, sulfur is yellow and hydrogen is white. 2HKQ, crystal structure of the C-terminal domain of human EB1 in complex with the CAP-Gly domain of human dynactin-1 (p150-Glued); 2MPX, three-dimensional structure of cap-gly domain assembled on microtubules determined by Magic Angle Spinning NMR spectroscopy; 3E2U, crystal structure of the zink-knuckle 2 domain of human CLIP-170 in complex with p150-Glued; CPK, Corey-Pauling-Koltun.

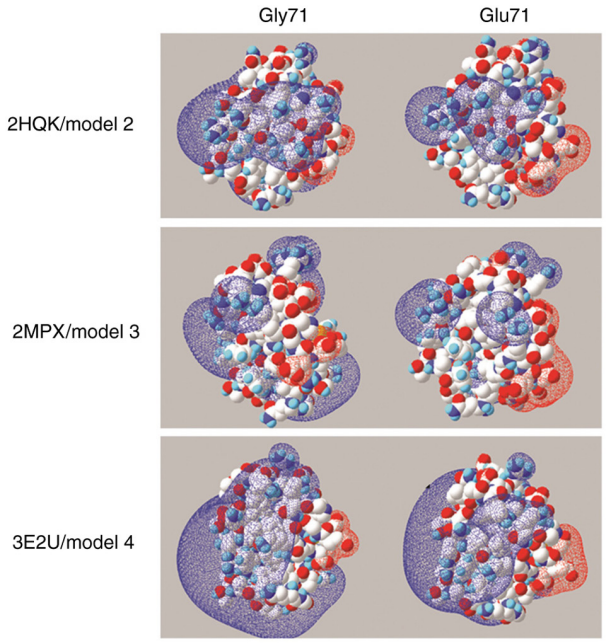

Figure S4. (A) Prediction of aggregation/amyloidogenic-prone sequences in the CAP-Gly domain of p150glued protein. The analysis was performed using the web-based tool AmylPred2, a consensus method for predicting amyloid propensity (21). Consensus-5 indicates that the sequence was predicted to be prone to aggregate as amyloid by at least 5 of the 10 algorithms applied by AmylPred2. The three segments identified as consensus-5 are highlighted in dark blue, red and light gray in the CAP-Gly domain sequence. The pattern of secondary structure elements in the protein is shown at the top. The regions folded as β strands are represented as arrows and the short helix near the C-terminus is represented as a short cylinder. The downward red and blue arrows indicate the Gly59 and Gly71 residues, respectively. The conserved GKNDG motif is highlighted with a black bar. The result of each algorithm is shown below consensus-5. (B) Location of the consensus-5 sequences identified by AmylPred2 analysis in the CAP-Gly domain of p150glued protein. The regions are shown in the same color pattern as aforementioned in A. The β-strands 1-4 and Gly59 and Gly71 residues are indicated by arrows. The image on the right side is rotated 180°, respective to the left image. Graphical images were generated by PyMOL (20) using the coordinates contained in protein data bank no. 3E2U. CAP-Gly, cytoskeleton-associated protein glycine-rich domain; GKNDG motif, Glycine-Lysine-Asparagine-Aspartic acid-Glycine motif; Amyl Patt, amyloidogenic pattern; Av P Densit, average packing density; β-str Cont, β-strand contiguity; Hexa C Ener, hexapeptide configuration energy; N-term, N-terminus; C-term, C-terminus.