Electronic Supplementary Material (ESI) for RSC Advances.

Electronic Supplementary Information for:

The dynamics of the β-propeller domain in Kelch protein KLHL40 changes upon nemaline myopathy associated mutation

Matteo Lambrughi[#], Matteo Lucchini[#], Marcello Pignataro^, Marco Sola[#], Carlo Augusto Bortolotti[#§⊙]

[#] Department of Life Sciences, University of Modena and Reggio Emilia, Via Campi 103, 41125, Modena (Italy)

^ Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia, Via Campi 103, 41125, Modena (Italy)

[§] CNR-Nano Institute of Nanoscience, via Campi 213/A, 41125 Modena, Italy

[⊙] Corresponding author. Mail to: carloaugusto.bortolotti@unimore.it

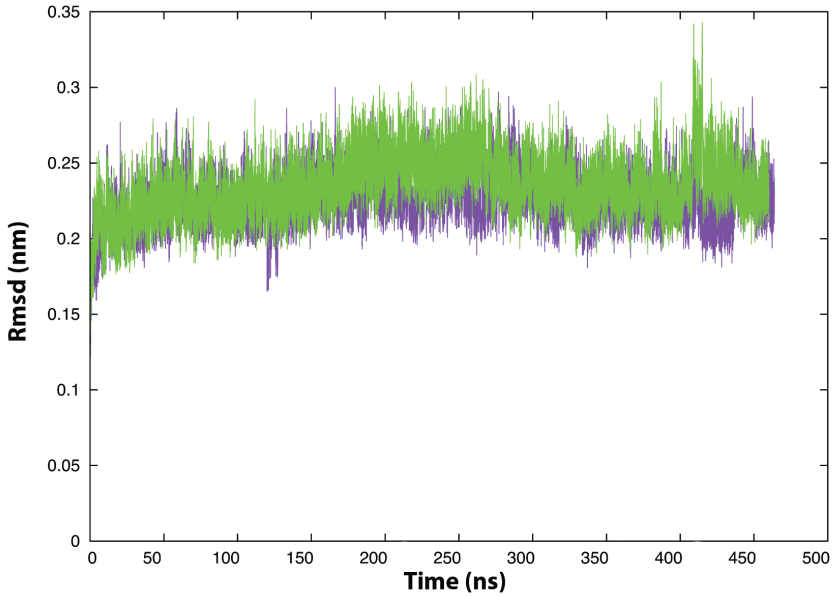


Figure S1. All mainchain atom root mean square displacement (rmsd) profiles of wild-type (purple) and mutant (green) MD simulations . We calculated the main chain rmsd over the simulation time using as a reference the initial crystallographic structure, considering only the secondary structural elements, i.e. the β-sheet core. The last residues in the C-terminal tail (residue 307-315) were not included in the calculation.

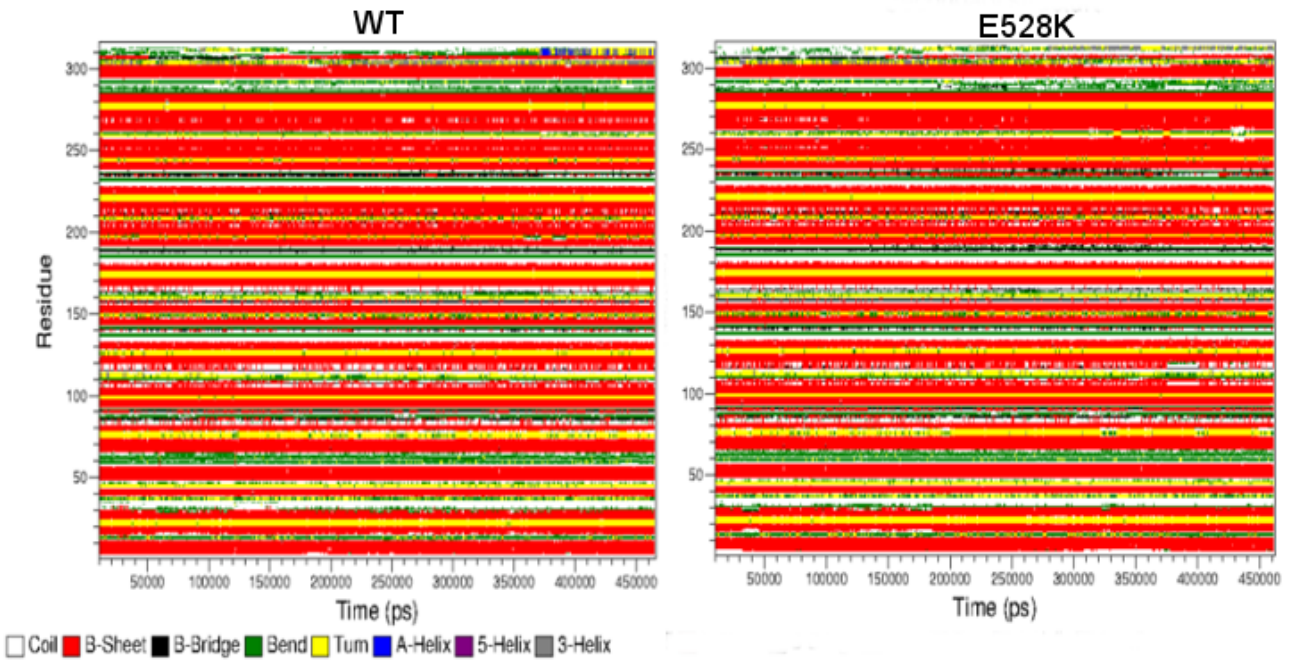


Figure S2. Time-dependent profiles of occurrence and persistence of secondary structure during MD simulations. Left panel Wild-type Kelch domain of KLHL40 rigth panel E528K mutant. The secondary structure elements were calculated by DSSP and they are highlighted with colors: white coil, red b-sheet, black b-bridge, green bend, yellow turn, blue a-helix, purple 5-helix, grey 3-helix.

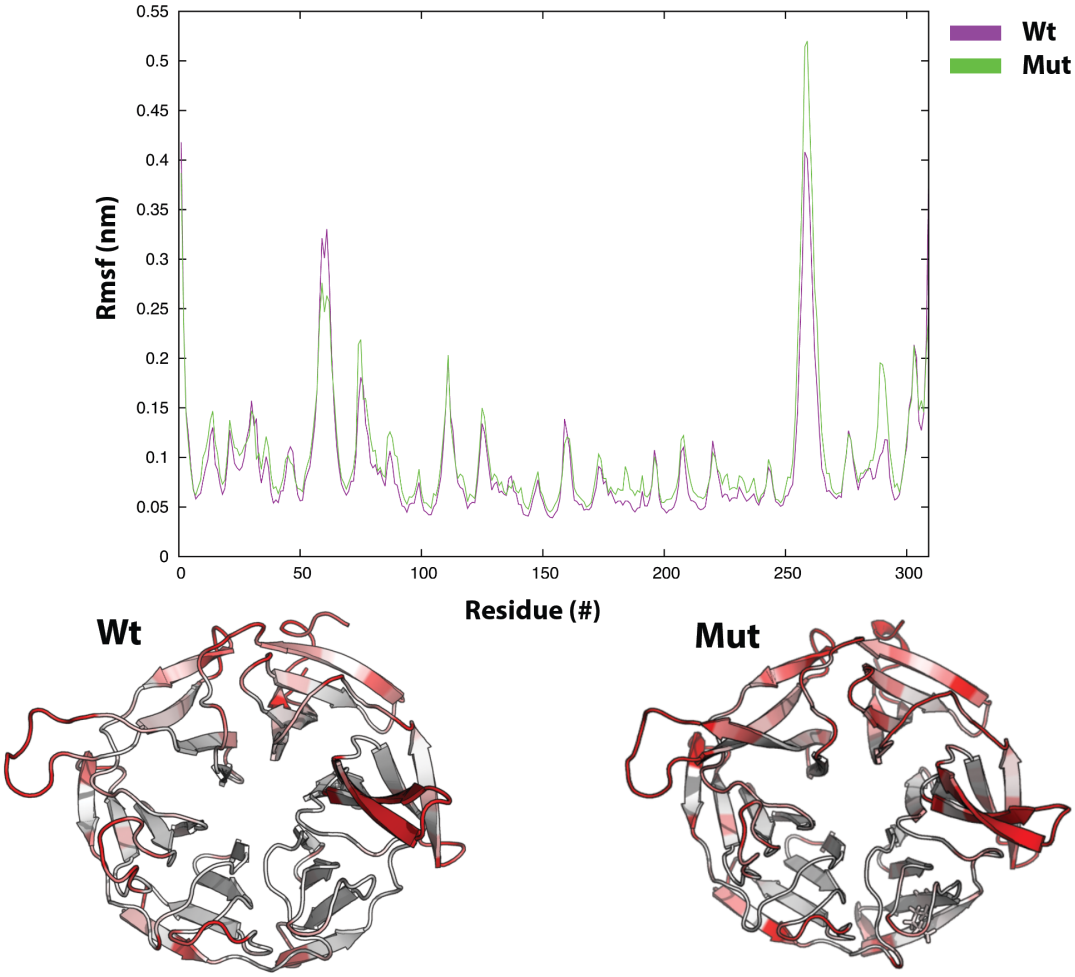


Figure S3. RMSF for the wild-type (purple) and E528K mutant (green) of Kelch domain of KLHL40. The rmsf values are indicated as shade of colors from white (low values) to red (high values) on an average structure from MD simulations.

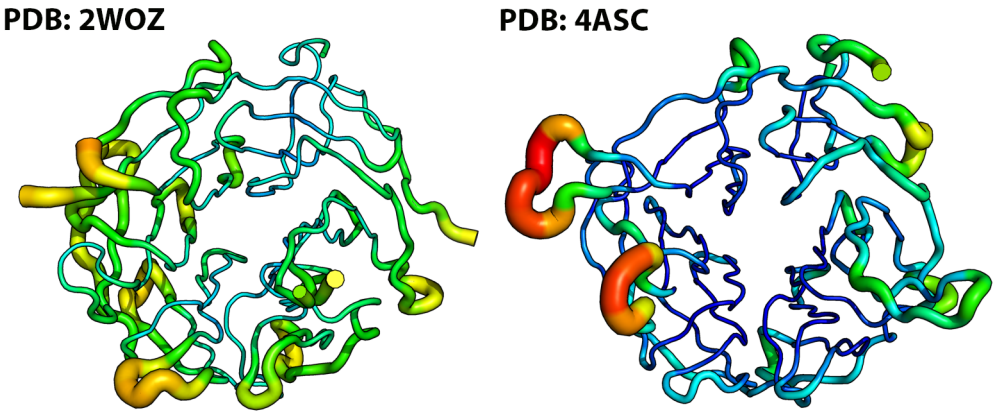


Figure S4. B-factor values from X-ray structure of Kelch domain of KLHL41 (PDB 2WOZ) and KLHL40 (PDB 4ASC). The structures are represented as cartoon, with thickness proportional to the B-factor values. The B-factor values are highlighted by shade of colors from blue (low values) to red (high values).

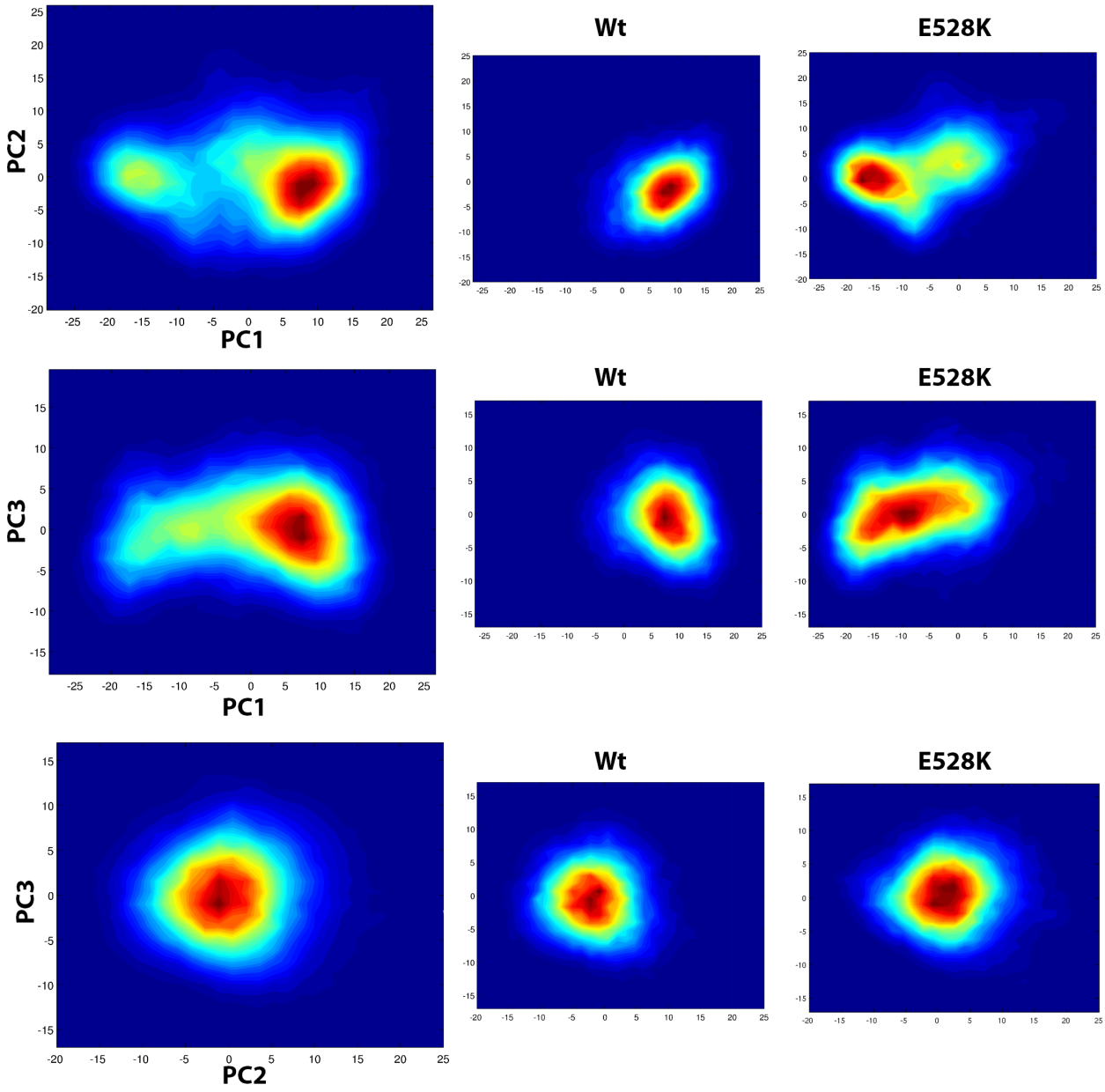
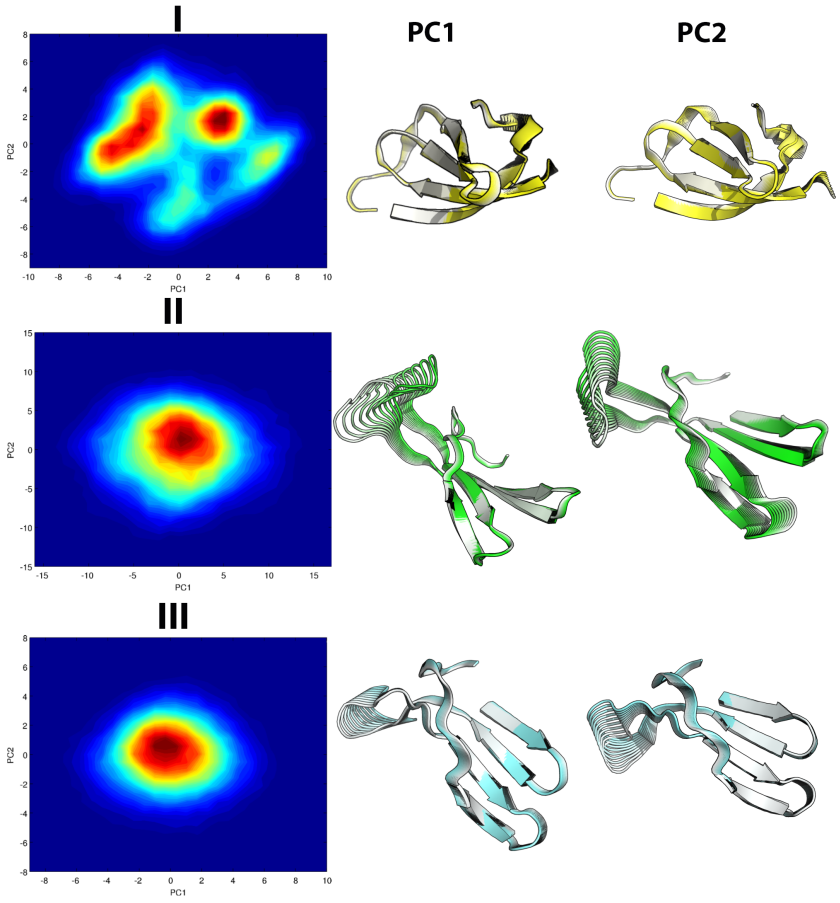


Figure S5. Projections of the combined macro-trajectory (wild-type + mutant) along the first principal components (PCs) derived by principal component analysis (PCA). Two-dimensional projections along the first and second (top panel) the first and third (middle panel) and the second and third (bottom panel) PCs. We carried out the covariance matrix for PCA calculation for all the atom of Kelch domain upon fitting on the Ca atoms of the b-sheet core. The small panels on the right side of the figure show the contribute of wild-type and mutant simulations to the essential subspace. Differential fluctuations between the wild-type and mutant can be observed only on PC1 while PC2 and PC3 describe similar fluctuations.


I
II
III
PC1
PC2
PC1
PC2
PC2
PC1
PC2
PC1

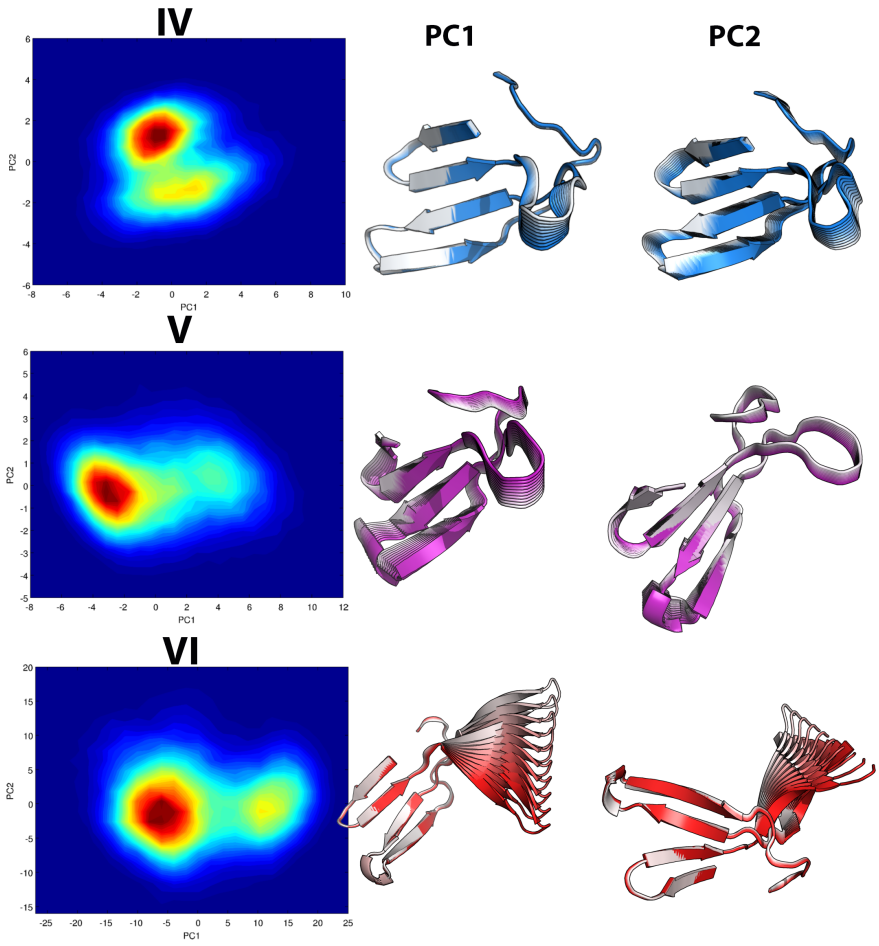


Figure S6. Analysis of the flexibility of each blade of KLHL40. Projections of the combined macro-trajectory (wild-type + mutant) along the first two principal components (PCs) derived by principal component analysis (PCA). We carried out the covariance matrix for PCA calculation for all the atom of each blade (I, II, III, IV, V, VI) of Kelch domain of KLHL40 upon fitting on the Ca atoms of the b-sheet core. In the small inserts on the right side 10 representative structures obtained from the projections of the macro-simulation over the first two PC are shown. Major differences in fluctuations can be observed in blade VI, V and VI showing that the mutation alters not only local motions but it also affects distant regions of the domain.