Characterization of the structure, dynamics and allosteric networks of human NPP1 in its free form and substrate–bound complex from molecular modeling

Electronic Supplementary Information

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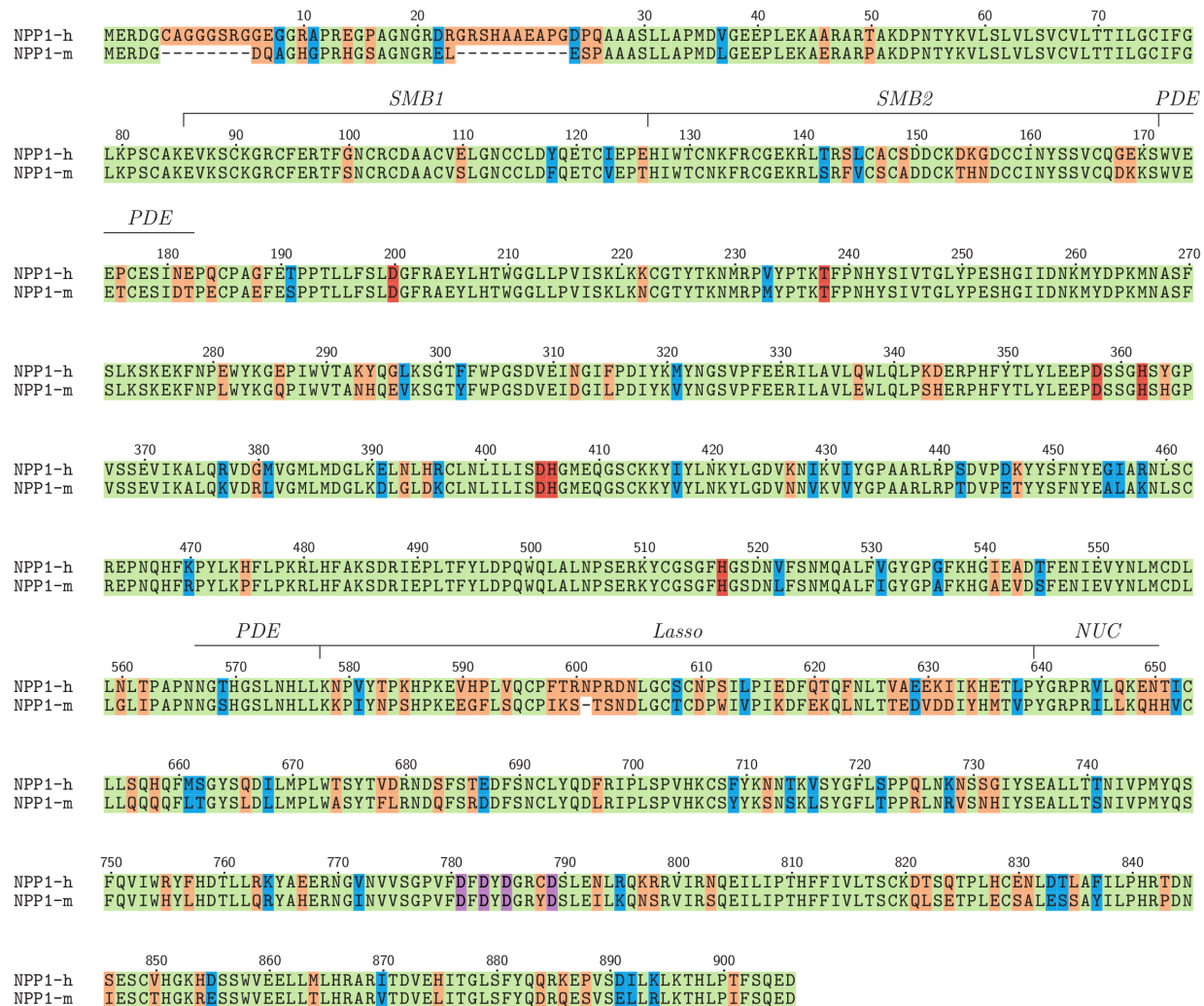
FIGURE S1: Sequence alignment of NPP1-h (Uniprot: P22413) and NPP1-m (Uniprot: P06802). The conserved residues are colored in green, similar residues are in blue and diverging residues are in orange. The Zinc coordinating residues are highlighted in red, and the Calcium coordinating residues are in purple. The similarity and the identity between NPP1-h and NPP1-m sequences are 88.9% and 80.2%, respectively.

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TABLE S1: ColVar parameters used between the Zincs and the coordinating residues of NPP1-h. The other parameters are: width=1 and upperWallConstant=100.

Residue number	Zinc	UpperBoundary
His380	Zn1	2.43
His535	Zn1	2.47
Asp376	Zn1	2.61
Asp218	Zn2	2.17
Asp423	Zn2	2.22
His424	Zn2	2.55
Thr256	Zn2	2.52

Video file **S2.mov** (separate file in Electronic Supplementary Information): Illustration of the ATP mobility in the binding site of NPP1-h, from the NPP1-h-ATP trajectories. The mesh represents the hydrophobic pocket near the adenosine moeity of the ATP.

Video files **S3.mov** and **S4.mov** (separate files in Electronic Supplementary Information): the first 5 normal modes resulting from the PCA analysis of trajectories for NPP1-h (S3.mov) and NPP1-h-ATP (S4.mov).
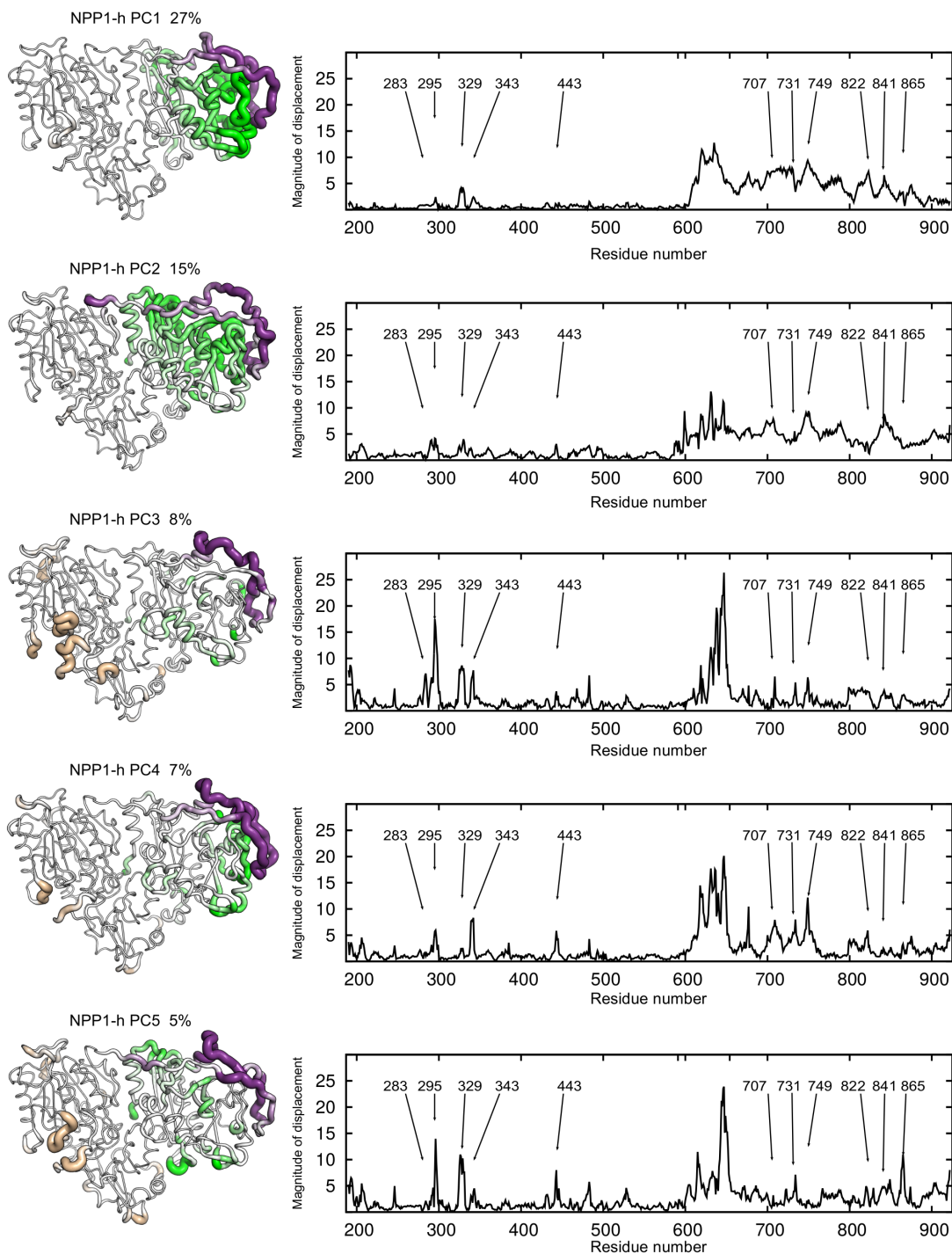
FIGURE S5: Average amplitude of motion for each residue of NPP1-h involved in the first five PCA normal modes from the PCA analysis of NPP1-h trajectories. The PCA analysis was realized using trajectories aligned on the PDE domain. NPP1-h color code is the same as that in Fig. 1.
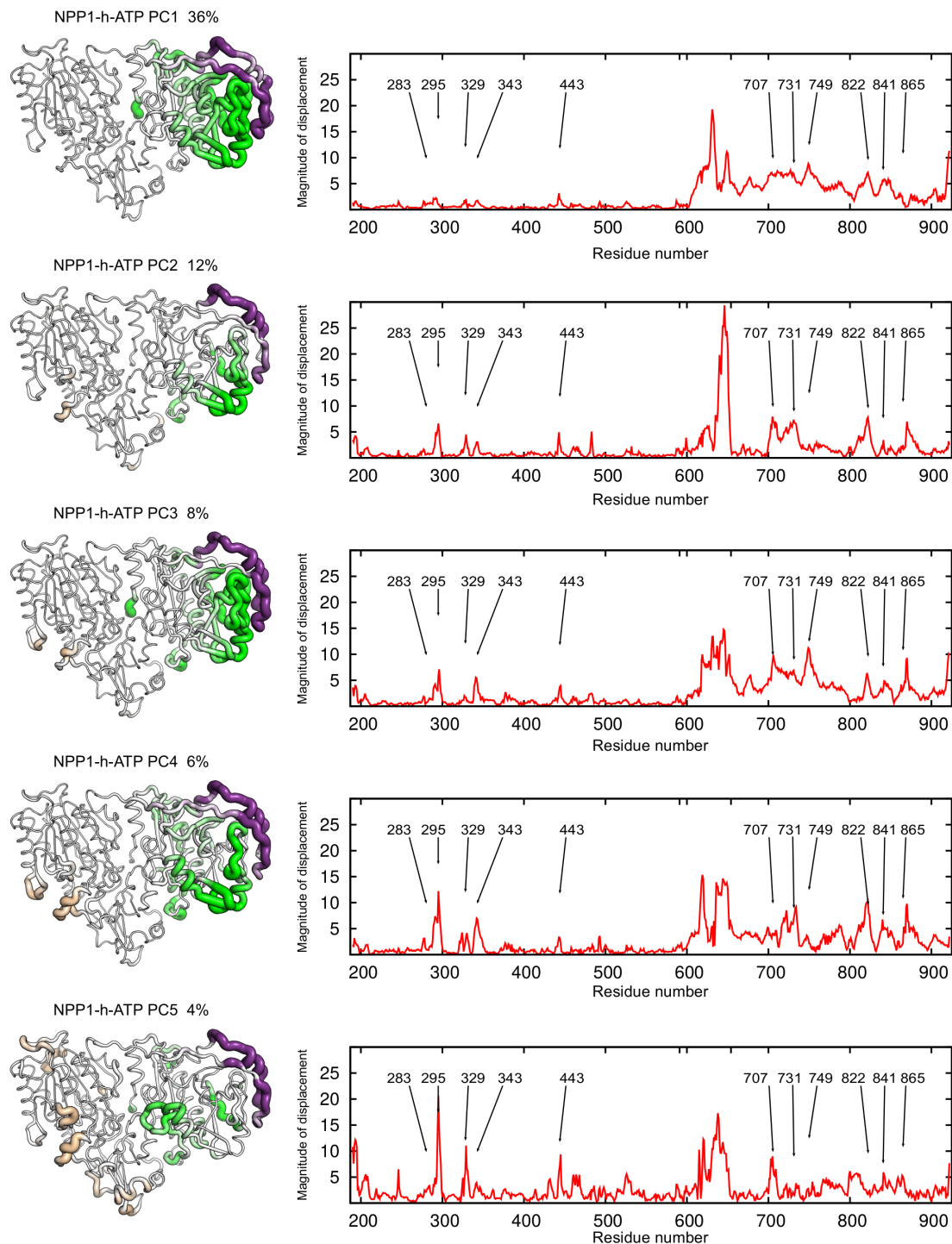
FIGURE S6: Average amplitude of motion for each residue of NPP1-h involved in the first five PCA normal modes from the PCA analysis of NPP1-h-ATP trajectories. The PCA analysis was realized using trajectories aligned on the PDE domain. NPP1-h color code is the same as that in Fig. 1.
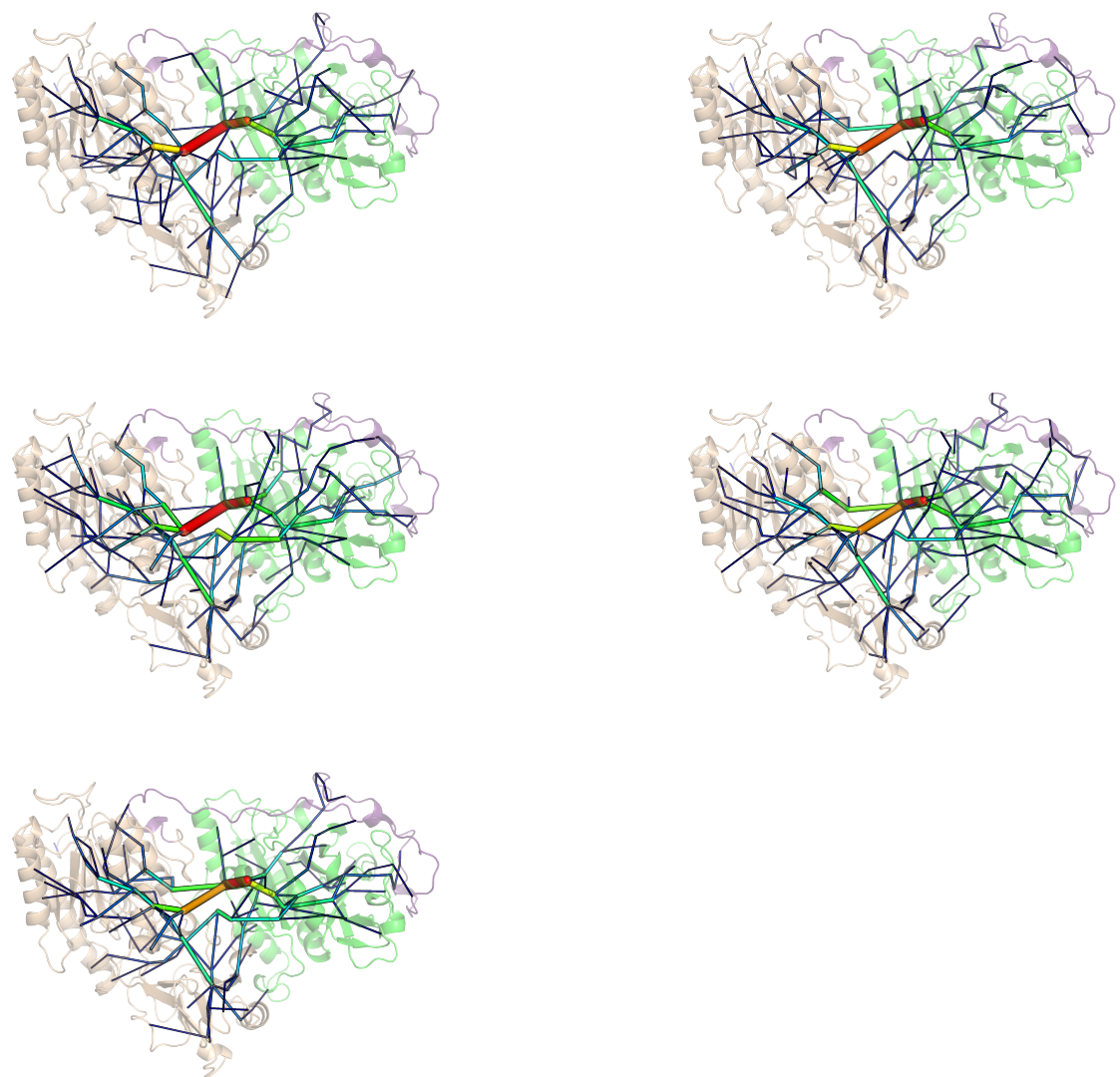
FIGURE S7: Critical edges in NPP1-h according to each individual trajectories. Edges are represented as sticks, and NPP1-h as shaded cartoon. Edges are scaled in size and and color from blue to cyan, to yellow, to green, to red with higher prevalences denoted by a large red stick. NPP1-h color code is the same as that in Fig. 1.
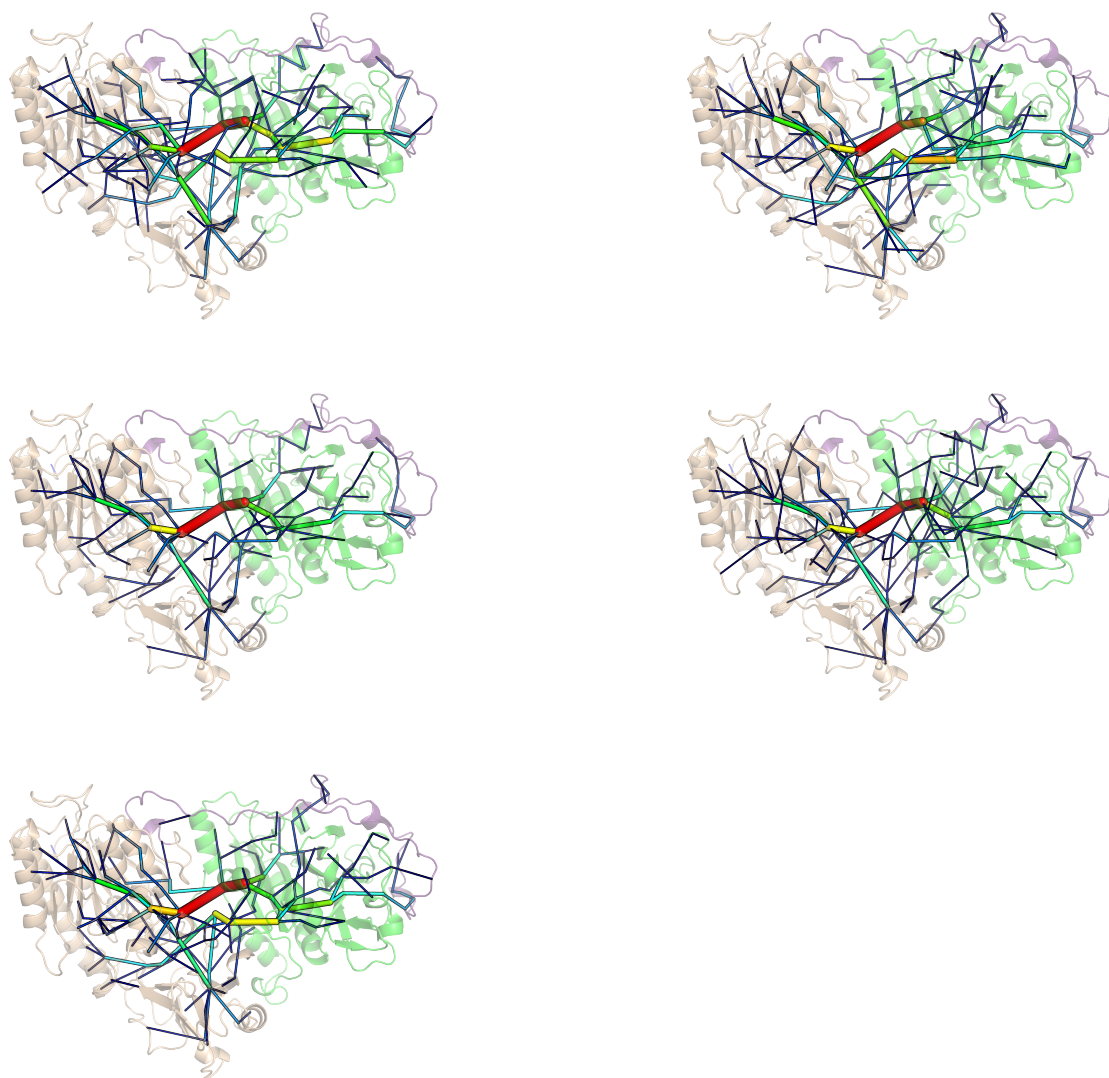
FIGURE S8: Critical edges in NPP1-h-ATP according to each individual trajectories. Edges are represented as sticks, and NPP1-h as shaded cartoon. Edges are scaled in size and and color from blue to cyan, to yellow, to green, to red with higher prevalences denoted by a large red stick. NPP1-h color code is the same as that in Figure 1.
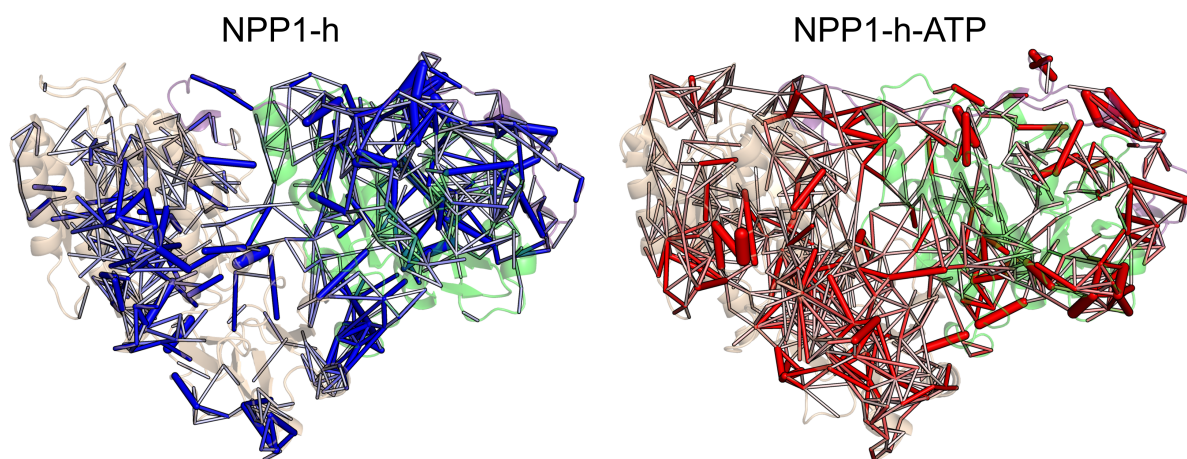
NPP1-h   NPP1-h-ATP

FIGURE S9: Coefficients of variation between the nodes for NPP1-h (*left*) and NPP1-h-ATP (*right*). The coefficients of variation are represented by sticks scaled in size and color from small and white for small values of coefficient to large and dark blue (or red) for higher values of coefficient. NPP1-h color code is the same as that in Fig. 1.
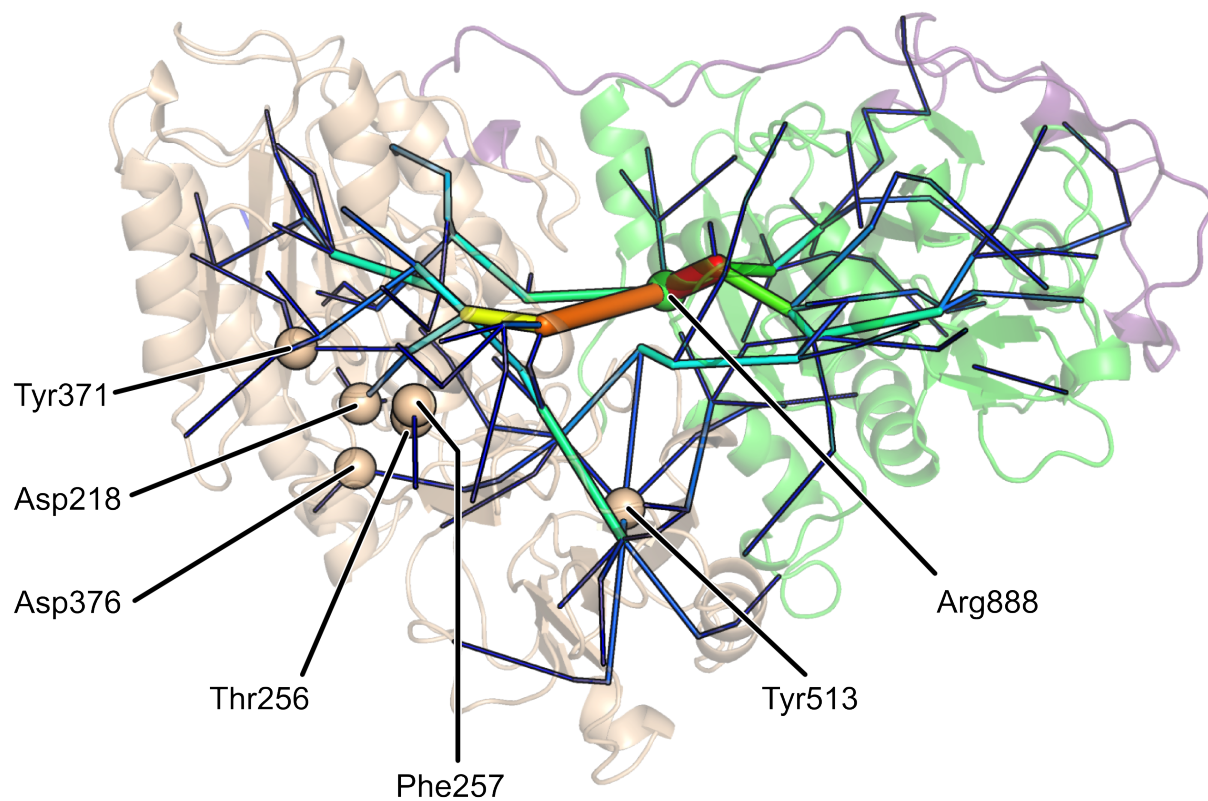
FIGURE S10: Residues identified as important for NPP1-h activity from mutagenesis or disease-associated mutations and involved in critical edges of NPP1-h . The residues are represented as spheres. Edges are represented as sticks, and NPP1-h as shaded cartoon. Edges are scaled in size and and color from blue to cyan, to yellow, to green, to red with higher prevalences denoted by a large red stick. NPP1-h color code is the same as that in Fig. 1.
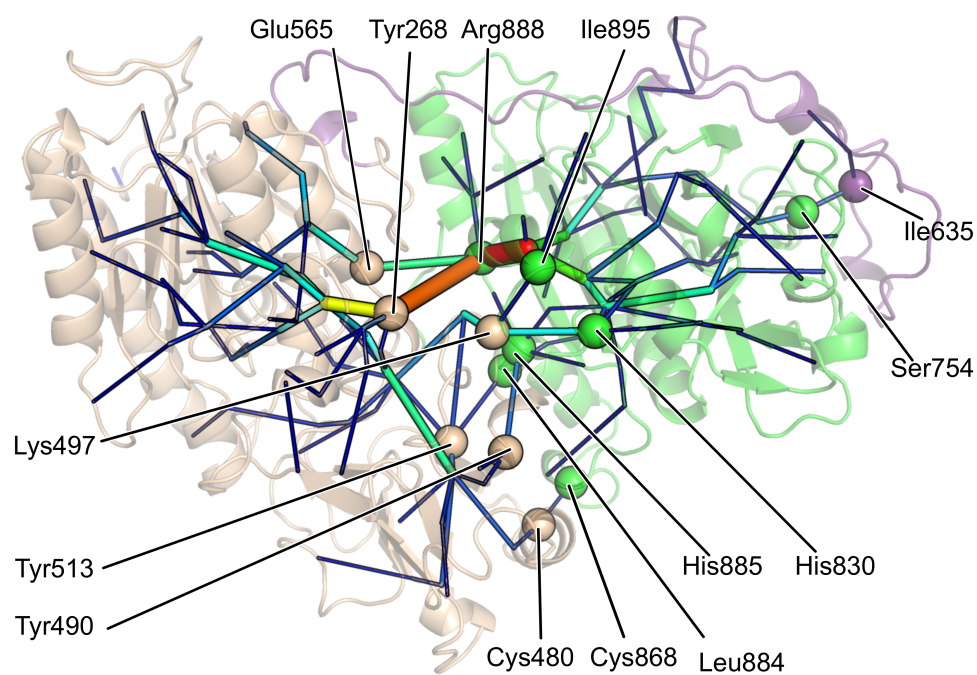
FIGURE S11: Residues involved in interdomain critical edges of NPP1-h . The residues involved in interdomain edges are represented as spheres. Edges are represented as sticks, and NPP1-h as shaded cartoon. Edges are scaled in size and and color from blue to cyan, to yellow, to green, to red with higher prevalences denoted by a large red stick. NPP1-h color code is the same as that in Fig. 1.