Molecular dynamics study with mutation shows that N-terminal domain (NTD) structural re-orientation in NPC1 is required for proper alignment of cholesterol transport

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This PDF file includes:

Supplementary Figures. S1 to S6

Caption for Supplementary Movie

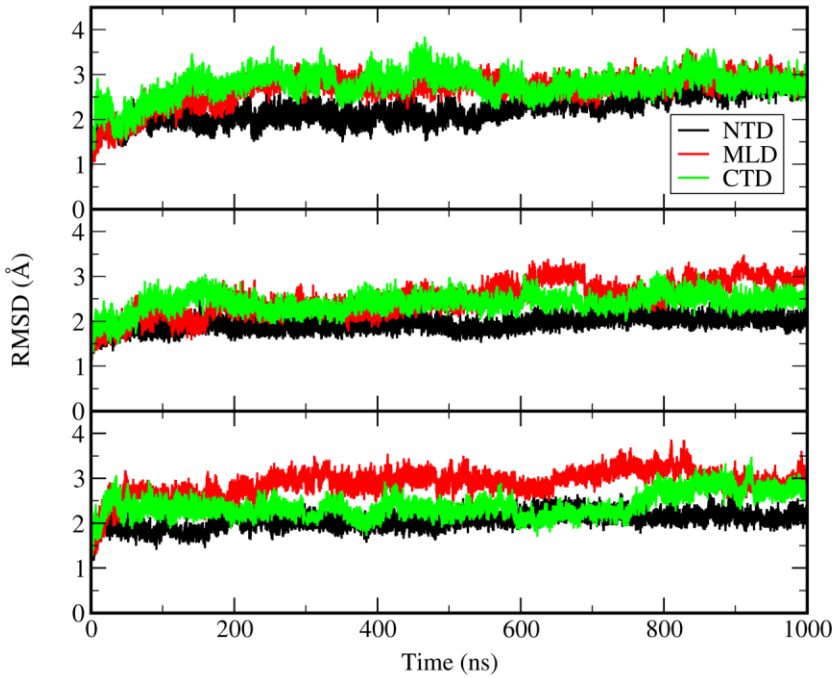

Figure S1. The time evolution of the RMSD of each domains for the three trajectories shown in Figure 2.

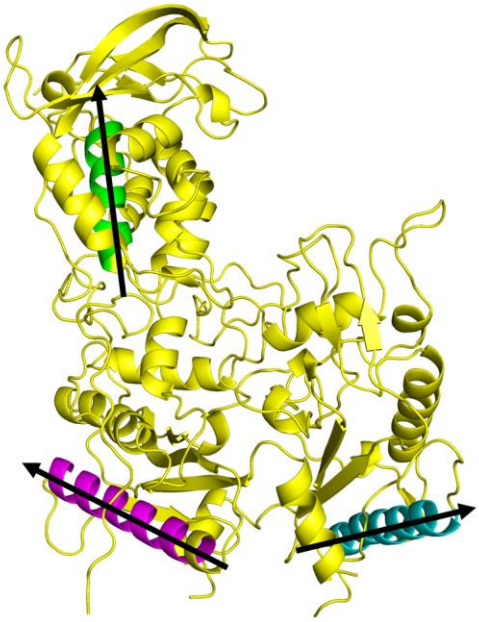

Figure S2. The three helixes we selected for angle calculation between domains during the simulation. The residue number of each helix are Ser99~Thr112, Glu575~Asn593, and Phe1051~Met1069 in NTD, CTD, and MLD domains respectively.

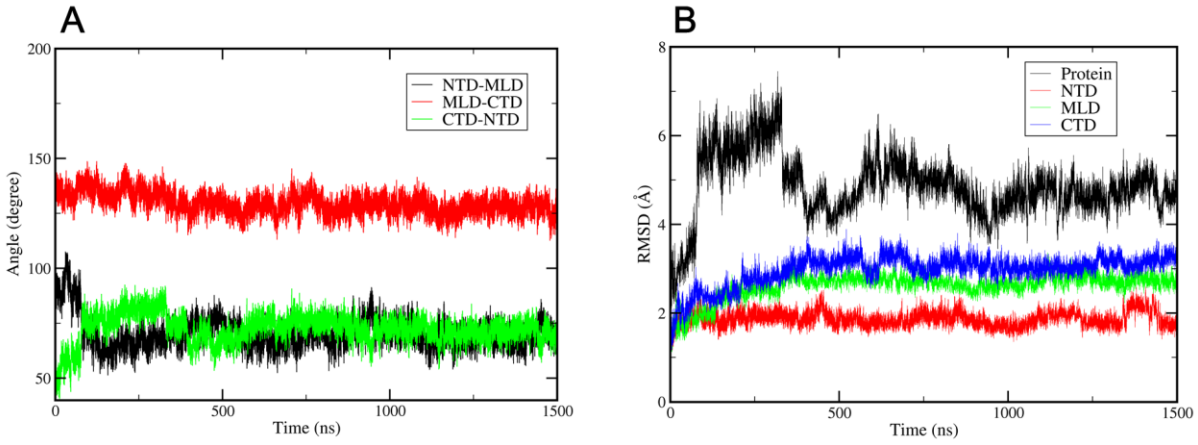

Figure S3. The angle (A) and RMSD (B) time profile of the mutated NPC1 simulation with no cholesterol in the NTD. This RMSD is from the trajectory that was run up to 1.5 μs. The RMSD of the whole system is shown as black line. The RMSD of NTD, MLD, and CTD are shown as red, green, and blue lines respectively.

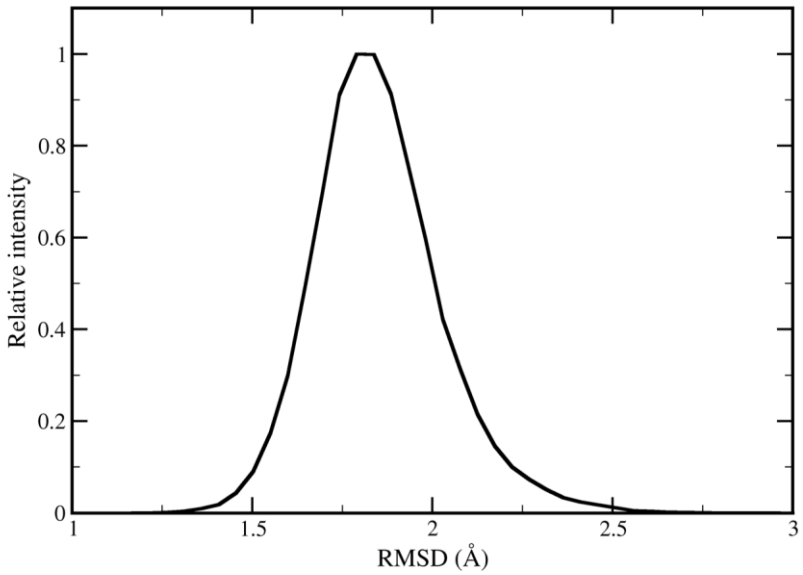

Figure S4. The distribution of RMSD of the NPC2 binding two protruding loops in MLD from the simulation trajectory using the X-ray structure (PDB ID: 5KWY) as a reference.

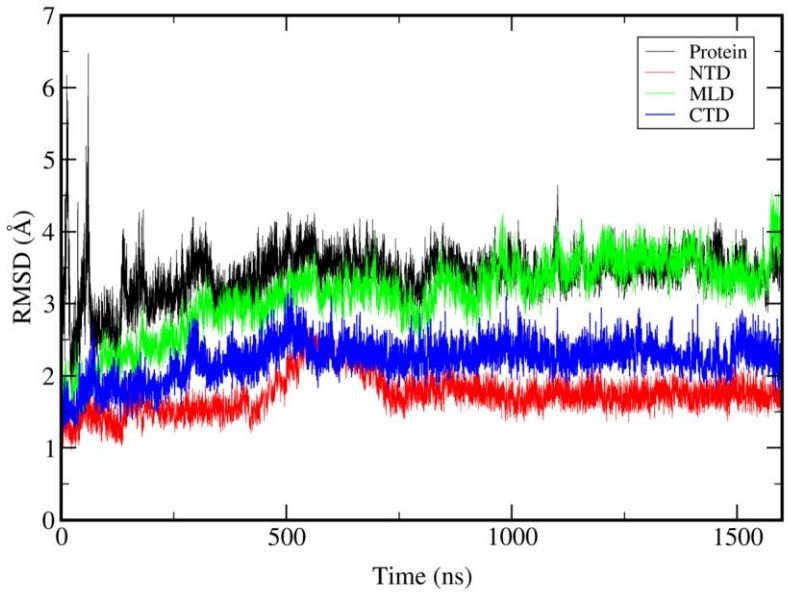

Figure S5. The RMSD time profile of the mutated NPC1 simulation with cholesterol in the NTD. This RMSD is from the trajectory that was run up to 1.6 μs. The RMSD of the whole system is shown as black line. The RMSD of NTD, MLD, and CTD are shown as red, green, and blue lines respectively.

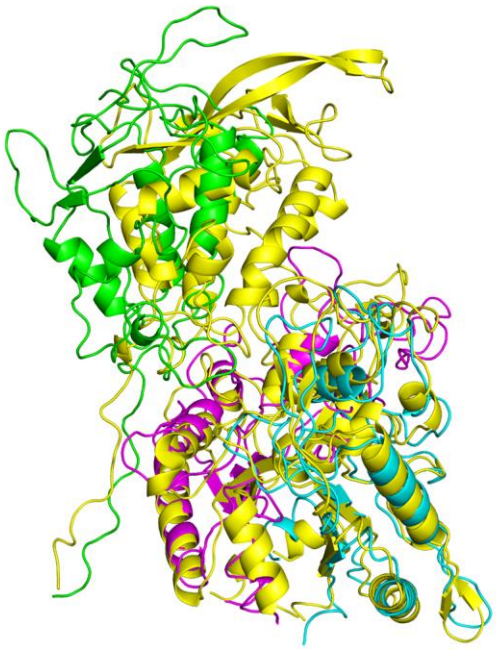

Figure S6. Superposition of the initial structure (yellow) over the simulation structure extracted at 400 ns. The time step of this simulation is 2.0 fs. Tilting of the NTD away from the MLD is observed in this simulation even though the degree of the tilting is not as steep as the simulation trajectory using 4.0 fs time step. The NTD, CTD, and MLD domains from the simulation are shown in green, magenta, and cyan respectively.

List of Supplementary material

Video S1. The movie of wild type NPC1 with no cholesterol on NTD starting from the initial structure. The length of the simulation in movie is 1.0 μs.