# Supporting Information

## Deciphering the Influence of Y12L and N17H Substitutions on the Conformation and Oligomerization of Human Calcitonin

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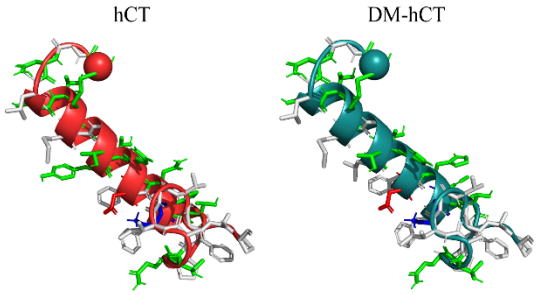


**Fig. S1. The initial structures of hCT and DM-hCT monomers.** The initial structures of the hCT monomer (left panel) and DM-hCT monomer (right panel) used in our simulation are constructed using PyMol mutagenesis based on the NMR-characterized phCT monomer structure (PDBid: 2jxz). Side-chains of each peptide are shown as sticks and colored by residue type: hydrophobic residues (white), negatively charged residues (red), positively charged residues (blue), and polar residues (green). The N-terminal Cα atom is highlighted by a sphere for clarity. The N-terminal Cα atom is highlighted by a sphere for clarity.

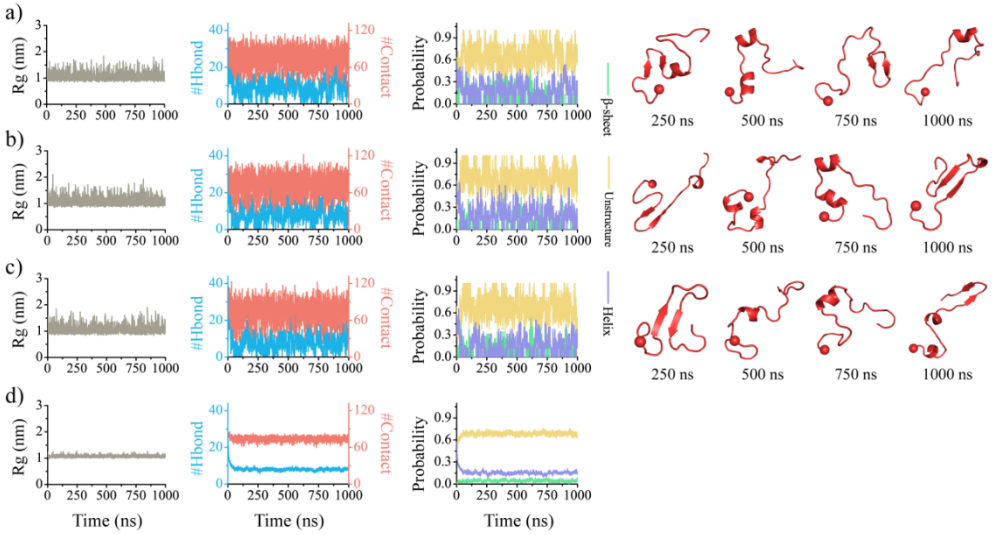


**Fig. S2. Equilibrium and convergence assessments of hCT monomer simulations.** Time evolution of key parameters, including radius of gyration (Rg), number of hydrogen bonds and contacts, and secondary structure content (comprising β-sheet, unstructured, and helix conformations), for three out of fifty independent DMD simulations of the hCT monomer **a-c)**. Snapshots from each independent simulation are presented at 250 ns intervals. The averaged values of radius of gyration, number of hydrogen bonds and contacts, as well as the average content of each secondary structure across all fifty independent DMD simulations as a function of simulation time are shown **d)**. The N-terminal Cα atom is highlighted by a sphere for clarity.

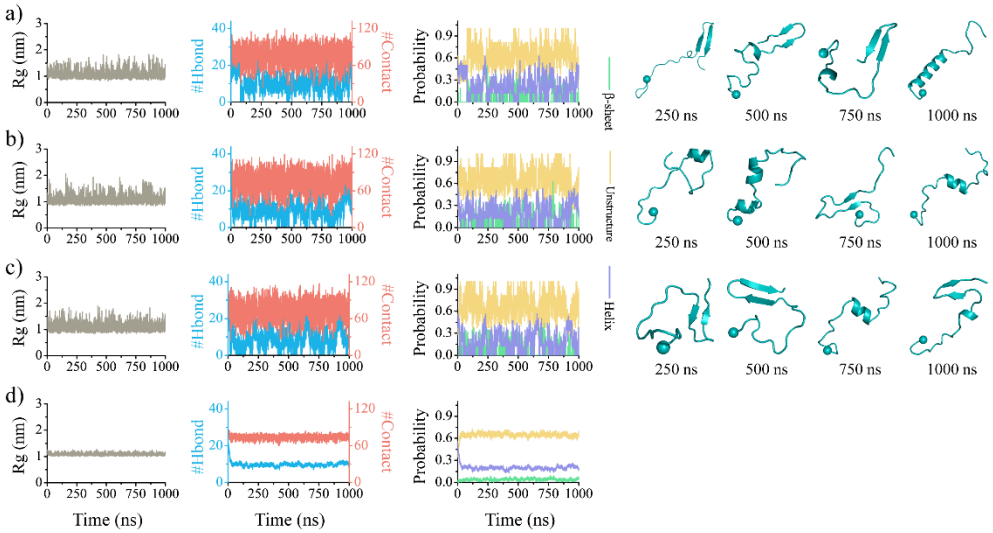


**Fig. S3. Equilibrium and convergence assessments of DM-hCT monomer simulations.** Time evolution of the radius of gyration, number of hydrogen bonds, and contacts, as well as the propensity of secondary structures (including β-sheet, unstructured, and helix conformations) for three out of fifty independent DMD simulations of the DM-hCT monomer **a-c)**. Snapshots from each independent DMD trajectory are presented at 250 ns intervals. The averaged values of radius of gyration, number of hydrogen bonds and contacts, as well as the average content of each secondary structure across all fifty independent DMD simulations as a function of simulation time are shown **d)**. The N-terminal Cα atom is highlighted with a sphere for clarity.

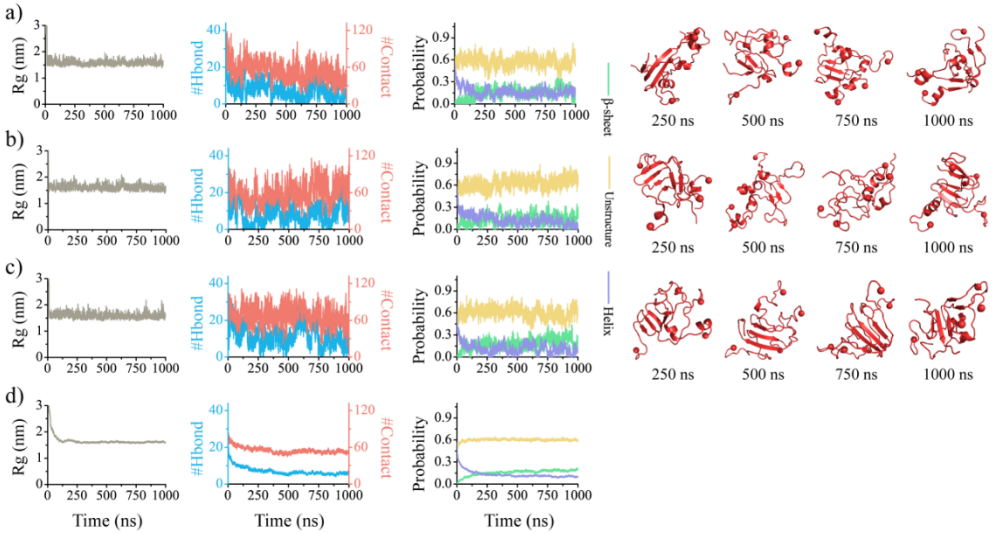


**Fig. S4. Equilibrium and convergence assessments for simulations of four hCT peptides.** Time evolution of radius of gyration, number of hydrogen bonds and contacts, and the content of each secondary structure (including β-sheet, unstructured, and helix) for three out of fifty independent DMD simulations of four hCT peptides **a-c)**. Snapshots from each independent DMD trajectory are presented at 250 ns intervals. The averaged values of radius of gyration, number of hydrogen bonds and contacts, as well as the average content of each secondary structure across all fifty independent DMD simulations as a function of simulation time are shown **d)**. The N-terminal Cα atom of each peptide is highlighted with a sphere for clarity.

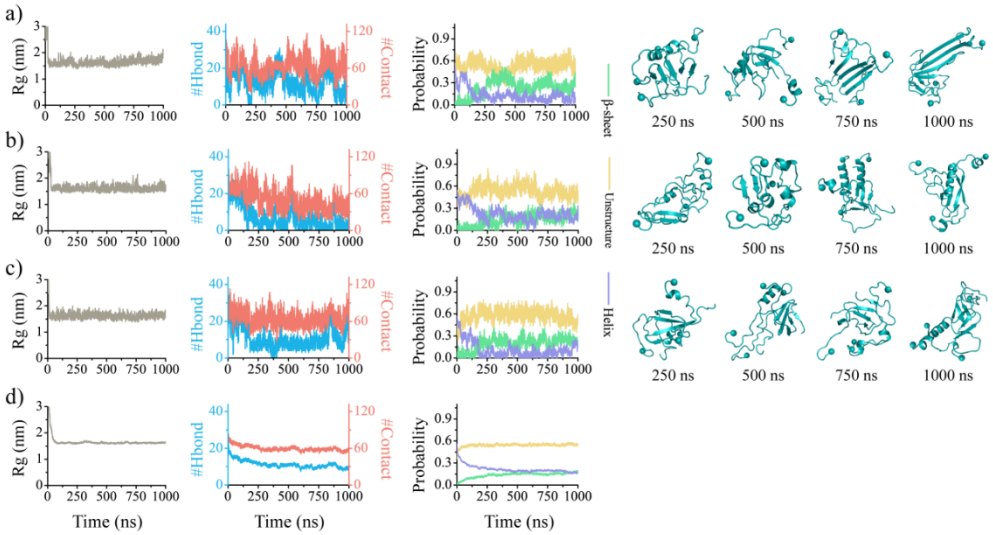


**Fig. S5. Equilibrium and convergence assessments for simulations of four DM-hCT peptides.** Time evolution of radius of gyration, number of hydrogen bonds and contacts, and the content of each secondary structure (including β-sheet, unstructured, and helix) for three out of fifty independent DMD simulations of four DM-hCT peptides **a-c)**. Snapshots from each independent DMD trajectory are presented at 250 ns intervals. The averaged values of radius of gyration, number of hydrogen bonds and contacts, as well as the average content of each secondary structure across all fifty independent DMD simulations as a function of simulation time are shown **d)**. The N-terminal Cα atom of each peptide is highlighted with a sphere for clarity.