Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting information

Lanosterol reduces the aggregation propensity of ultraviolet-damaged human γD-crystallins: a molecular dynamics study

Hong Zhou,[1#] Youyun Li,[1#] Ying Yang,[1] Shengtang Liu,[1] Zaixing Yang[1*]

1. State Key Laboratory of Radiation Medicine and Protection, School for Radiological and Interdisciplinary Sciences (RAD-X), Collaborative Innovation Center of Radiation Medicine of Jiangsu Higher Education Institutions, Soochow University, Suzhou 215123, China

[#] These authors contributed equally;

[*]Corresponding authors: zxyang@suda.edu.cn (Z. Yang)

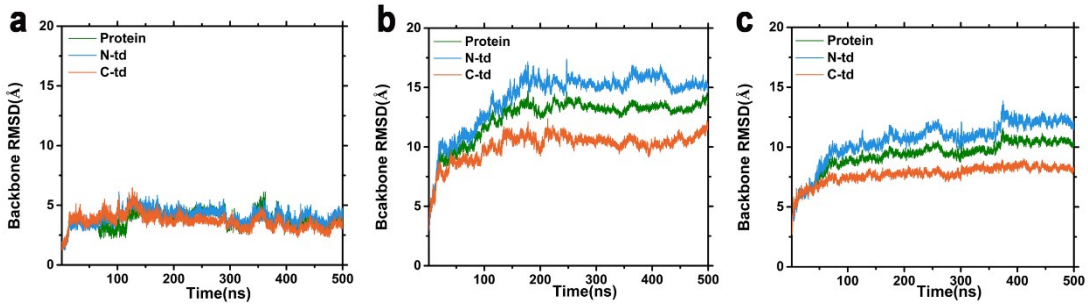

Figure S1. The root mean square deviation (RMSD) of the entire HγD-Crys (protein), N terminal (N-td), and C terminal (C-td) during 500 ns molecular dynamics simulations; (a) for wild-type and (b) and (c) for Trp > KN mutant HγD-Crys in the absence and presence of lanosterol systems, respectively. All quantities are averaged over three independent trajectories.

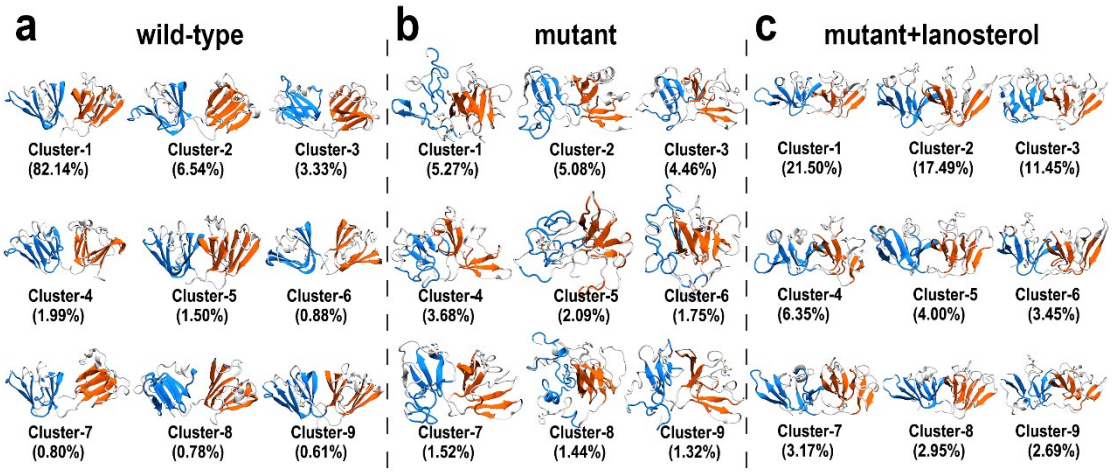

Figure S2. The representative configurations of the first nine clusters for the (a) wild-type, (b) mutant, and (c) mutant + lanosterol systems, respectively. The percentages in the parentheses show the corresponding proportion of each cluster. For each system, a total of 30,000 configurations were collected from its three independent 1000 ns MD trajectories at the time interval of 100 ps to perform clustering analyses. The sampled configurations can be separated into 35, 512, and 117 clusters for the wild-type, mutant, and mutant + lanosterol systems, respectively.

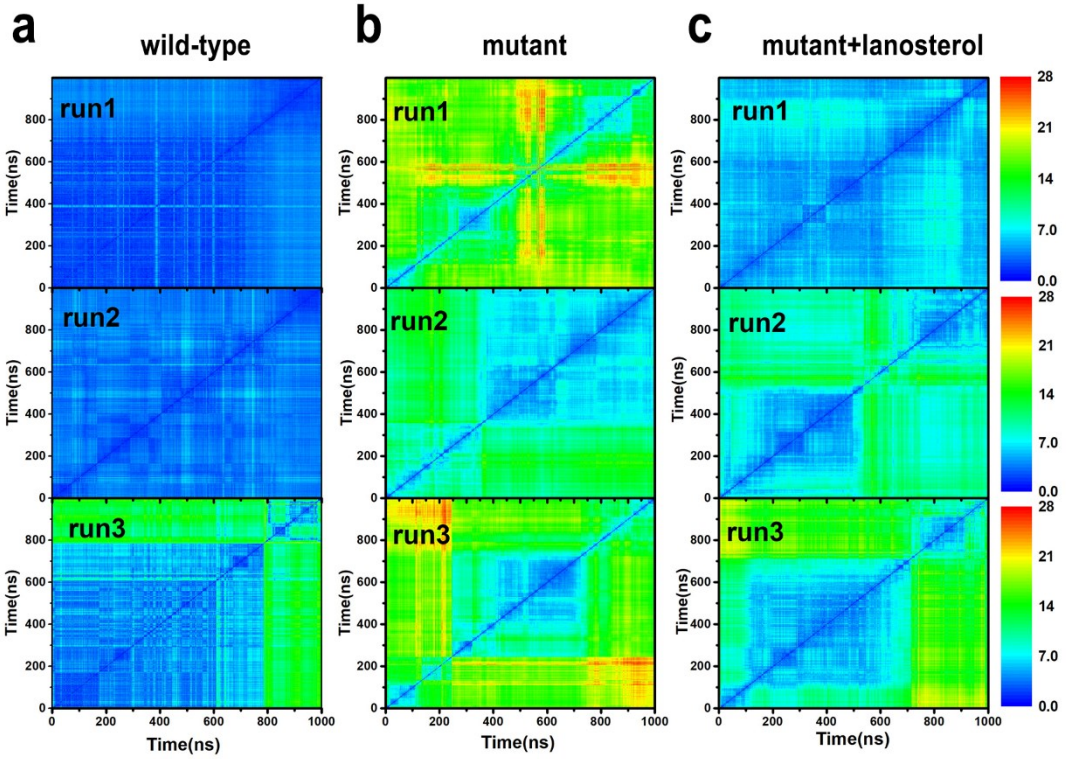

Figure S3. All-to-all RMSD matrix of heavy atoms. The matrix elements were calculated every 1 ns over the three 1000 ns MD trajectories of wild-type, mutant, and mutant + lanosterol systems (a-c). The color scale was the RMSD value (in Å) shown on the right.

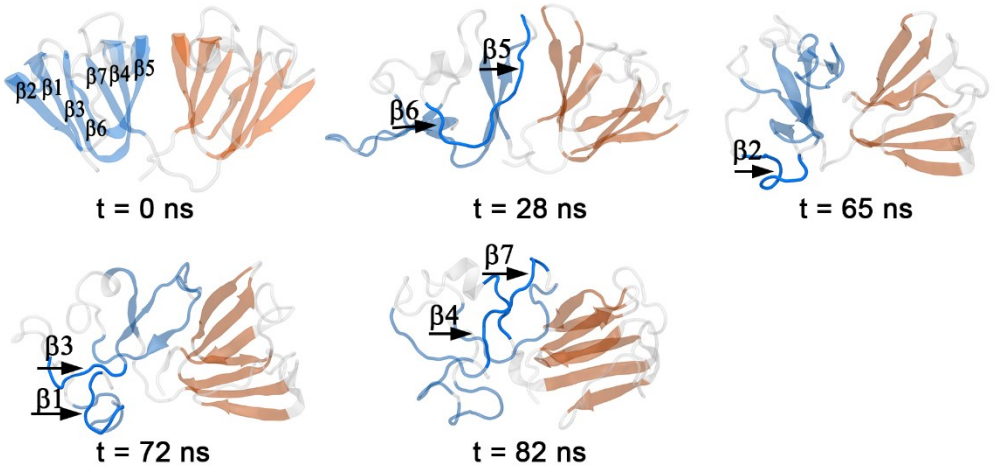

Figure S4. Some key intermediate structures to show the unfolding pathways of Trp > KN mutant HγD-Crys from a representative trajectory. The unfolded *β*-strands along with the simulation time are indicated by an arrow.

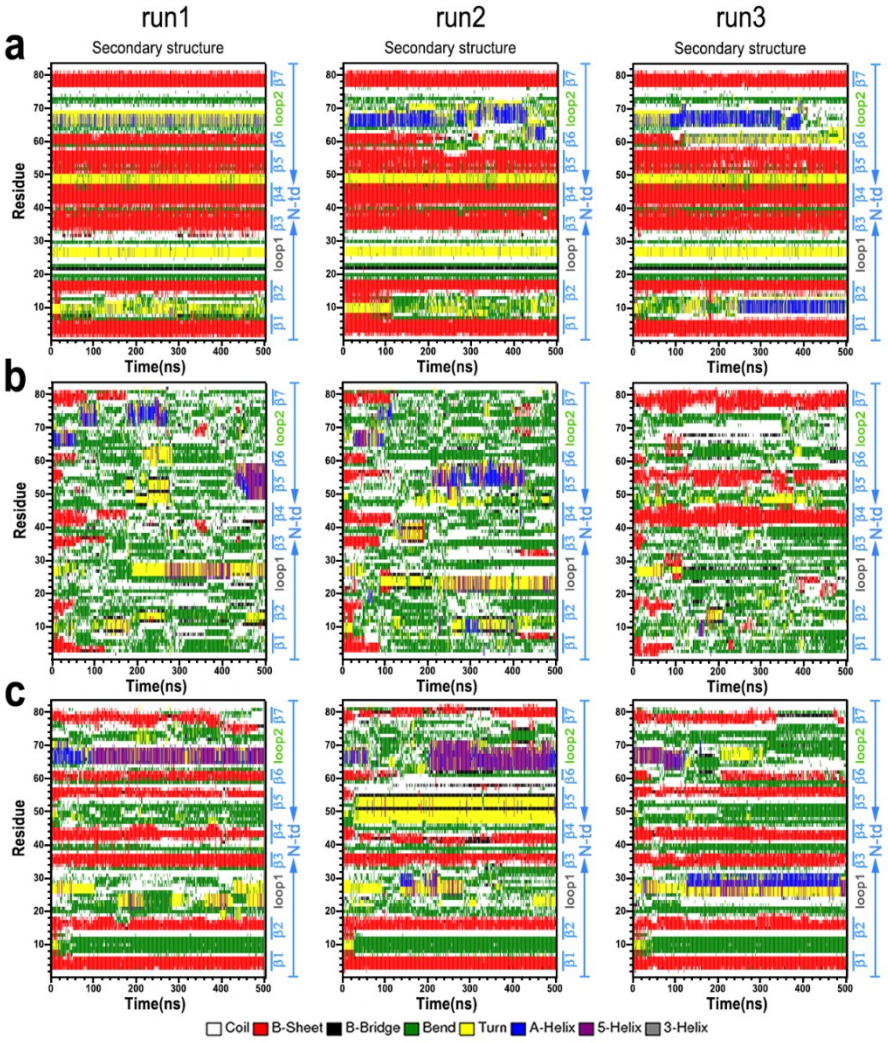

Figure S5. The time evolution of the secondary structure of each residue in the N-td for all three independent trajectories of the wild-type (a), Trp > KN mutant HγD-Crys in the absence (b) and presence (c) of lanosterol. The secondary structures of the residues are assigned according to the DSSP definition.

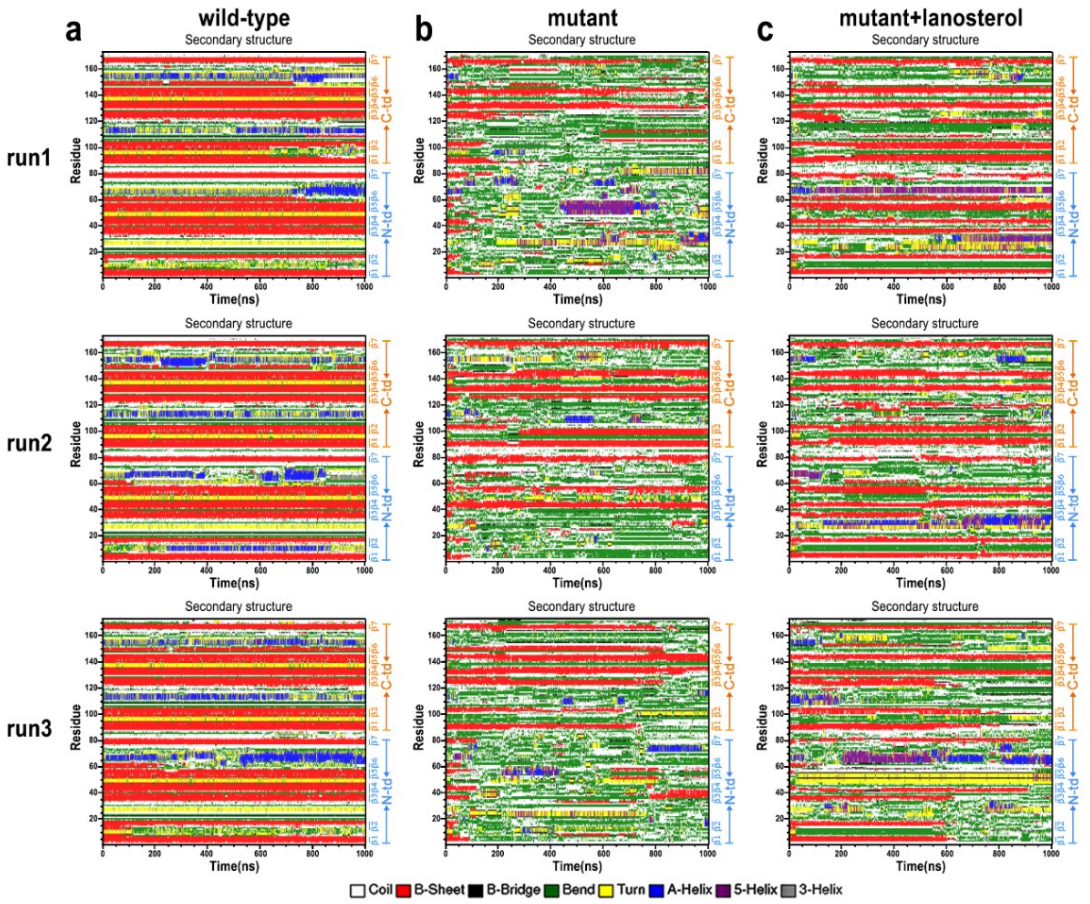

Figure S6. The time evolution of the secondary structure of each residue of the three independent 1000 ns trajectories for the wild-type (a), mutant (b), and mutant + lanosterol systems (c).

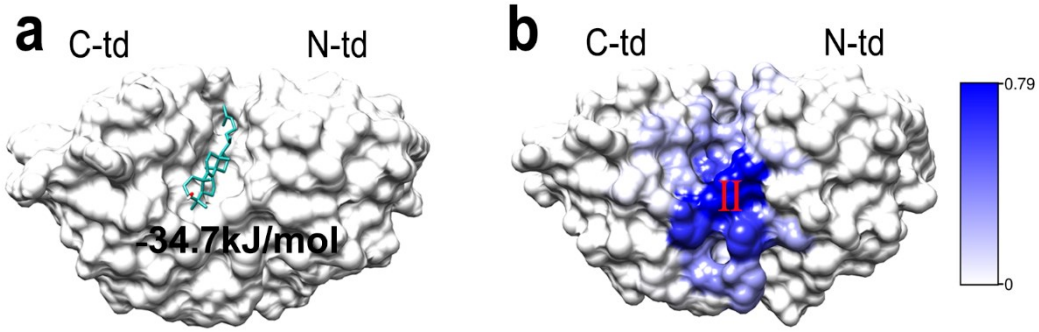

Figure S7. (a) The most energy favorable binding configuration of lanosterol to HγD-Crys in the docking simulations. Lanosterol and protein are represented as cyan stick and white surface, respectively. (b) The contact probability between lanosterol and HγD-Crys protein. A residue is considered in contact with lanosterol when any heavy atom of this residue is within 5.0 Å of any heavy atom of lanosterol.