Supporting Information

Human Neuronal Calcium Sensor-1 Protein Avoids Histidine Residue to Decrease pH Sensitivity

Yehong Gong[1], *Yuzhen Zhu*[2], *Yu Zou*[1], *Buyong Ma*[3], *Ruth Nussinov*[3,4], *Qingwen Zhang*[1,*]

[1]College of Physical Education and Training, Shanghai University of Sport, 399 Chang Hai Road, Shanghai, 200438, China

[2]Physical Education College, Shanghai Normal University, 100 Gui Lin Road, Shanghai, 200234, China

[3]Basic Science Program, Leidos Biomedical Research, Inc. Cancer and Inflammation Program, National Cancer Institute, Frederick, Maryland 21702, United States

[4]Sackler Inst. of Molecular Medicine, Department of Human Genetics and Molecular Medicine, Sackler School of Medicine, Tel Aviv University, Tel Aviv 69978, Israel

This material includes 7 Supplemental figures.

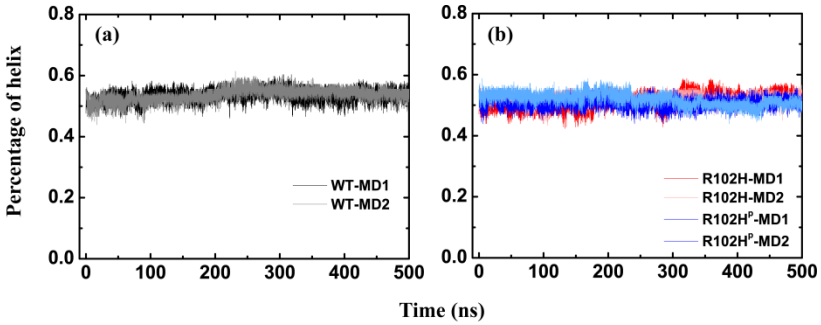

Figure S1 Time evolution of the percentage of helix for WT NCS-1 (black and gray curves), its R102H mutant NCS-1 (red and pink curves) and its R102H^{p} mutant (blue and light blue curves) in two different MD trajectories (WT-MD1 and WT-MD2 for the WT NCS-1, R102H-MD1 and R102H-MD2 for the R102H mutant, and R102H^{p}-MD1 and R102H^{p}-MD2 for the R102H^{p} mutant).

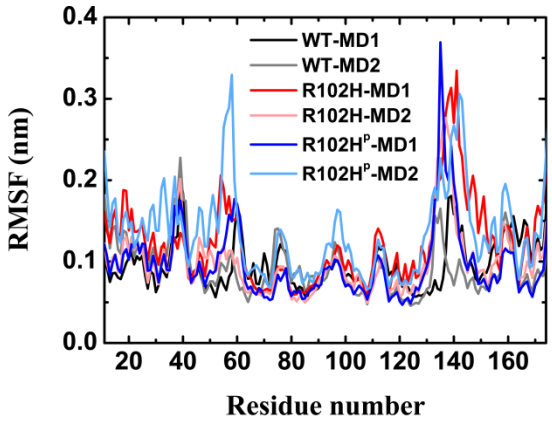

Figure S2 Cα-RMSF of the core structure for WT NCS-1, the R102H mutant, and the R102H^{p} mutant in the two independent MD runs. The Cα-RMSF values were calculated using the last 100 ns data of each MD trajectory for all systems.

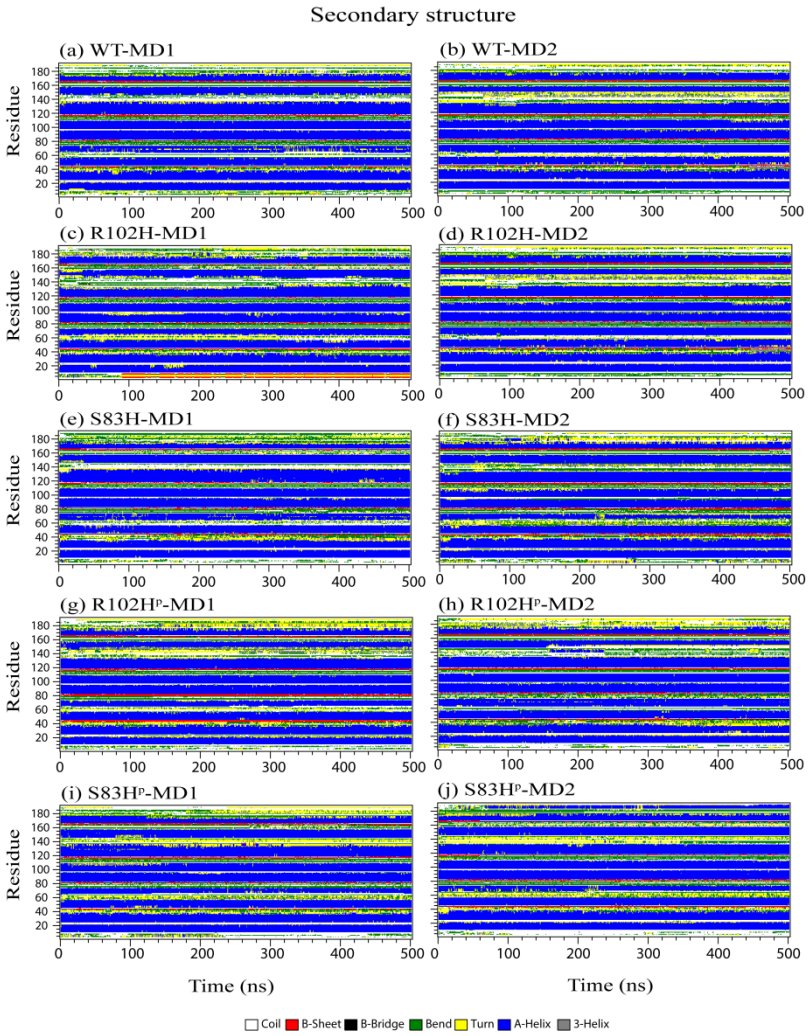

Figure S3 Secondary structure profiles of the WT NCS-1 (a, b), the R102H mutant (c, d), the S83H mutant (e, f), the R102H^{p} mutant (g, h) and the S83H^{p} (i, j) NCS-1 protein as a function of simulation time in the all 500 ns MD simulations.

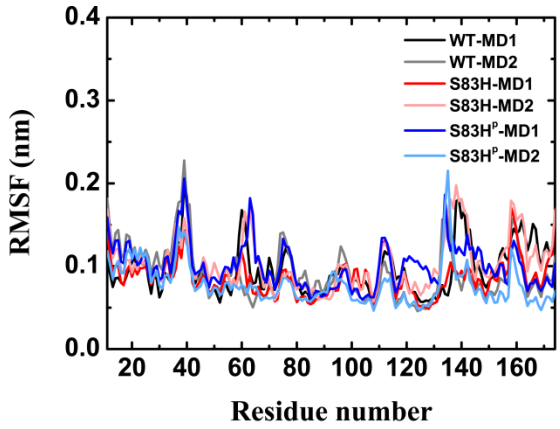

Figure S4 Cα-RMSF of the core structure for WT NCS-1, the S83H mutant, and the S83H^{p} mutant in the two independent MD runs. The Cα-RMSF values were calculated using the last 100 ns data of each MD trajectory for all systems.

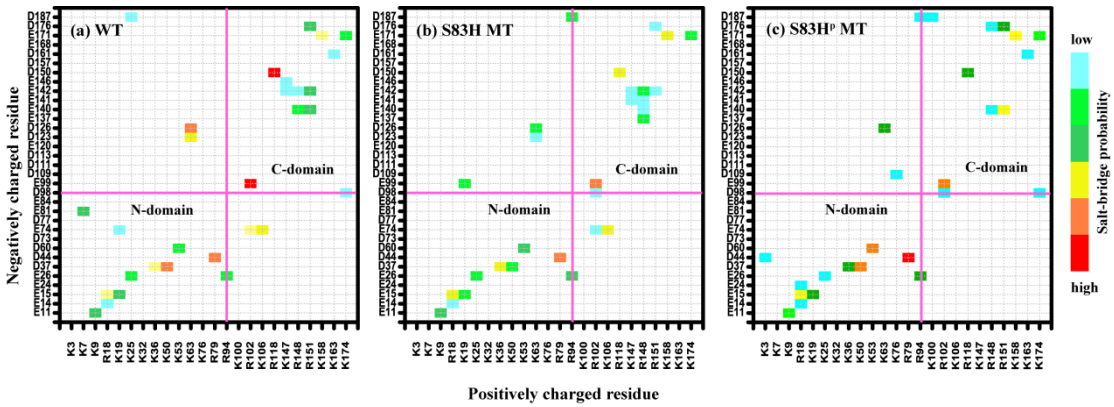

Figure S5 S83H and S83H^{p} mutations shift the salt-bridge network of WT NCS-1. Salt-bridge probability maps for (a) WT NCS-1, (b) the S83H mutant, and (c) the S83H^{p} mutant.

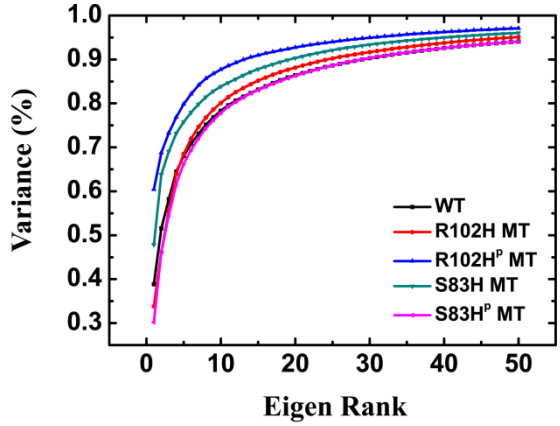

Figure S6 The accumulation of variance. Only two PCs are need to capture more than 40% of the variance and the first four PCs captured around 40% information of all systems.

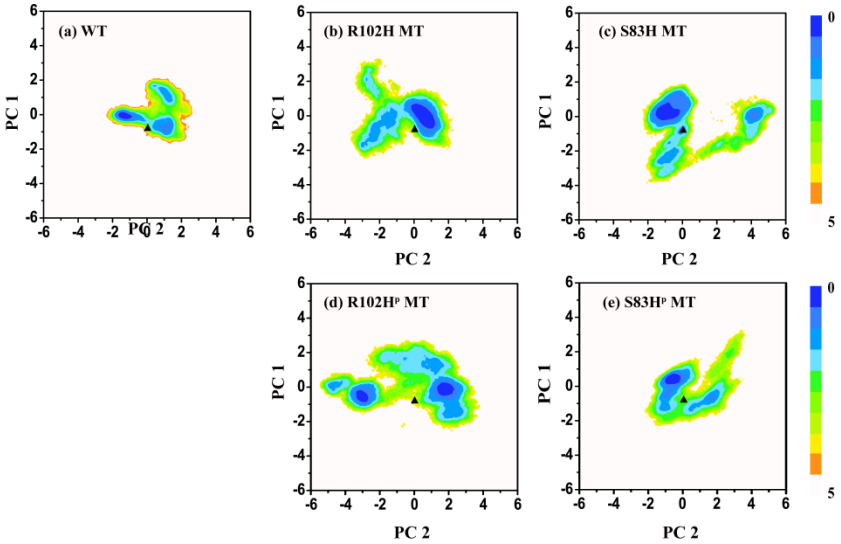

Figure S7 Free-energy surface (in kcal/mol) of the WT (a) and the R102H (b), S83H (c) , $R102H^{p}$ (d), and $S83H^{p}$ (e) mutants as a function of PC1 and PC2, with 2LCP mapped on.