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

Supplemental Information

TAB1 binding induced p38α conformation change: an accelerated molecular dynamics simulation study

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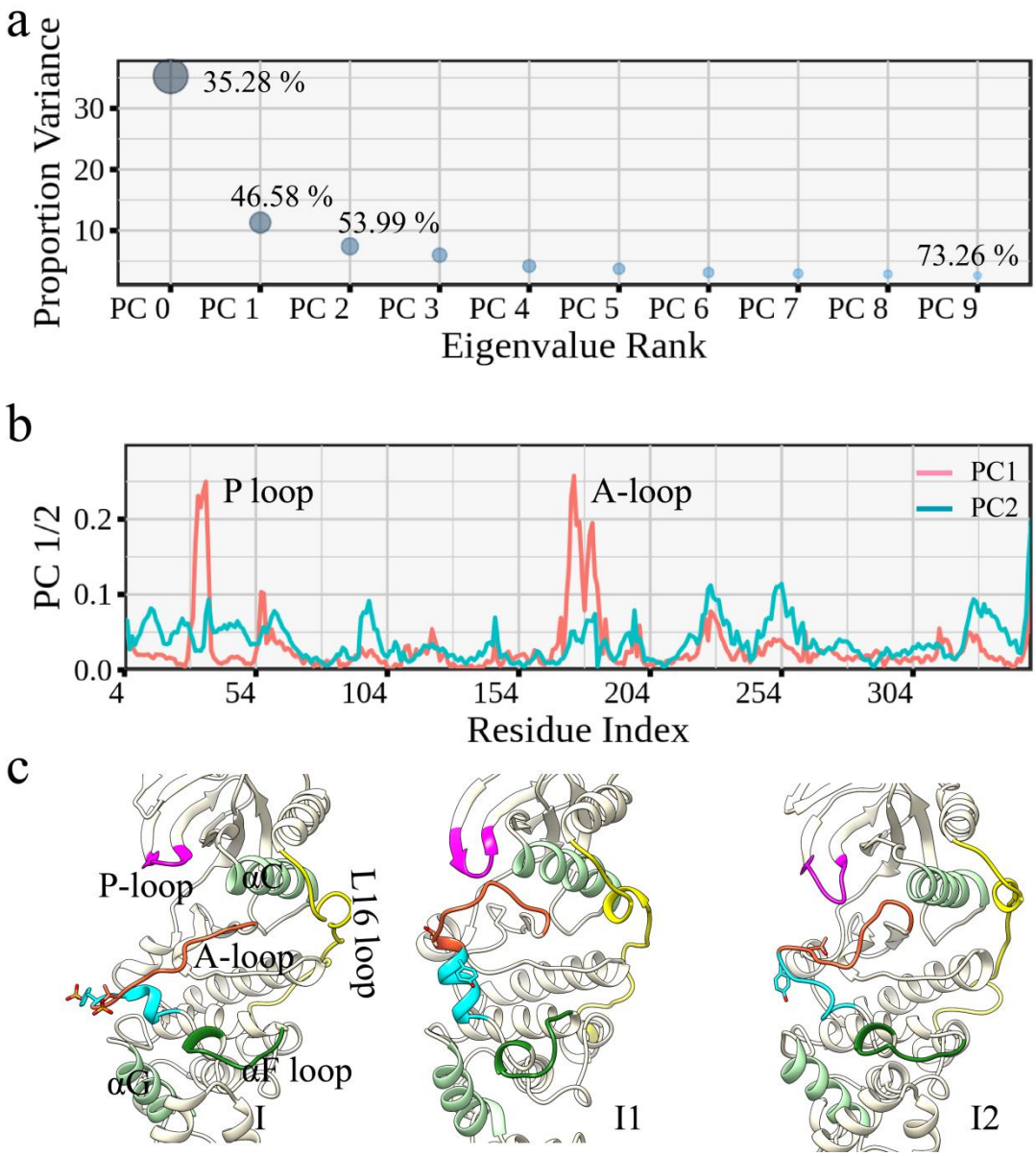

Fig. S1 (a) The 10 of the 684 PCs capture approximately 70% of the p38α motion in pp38α-TAB1 simulation. (b) The contribution of each residue to first two PCs is displayed. (c) Representative conformations of p38α in apo p38α simulation (I1), p38α-TAB1 simulation (I2), the pp38α-TAB1 simulation (I).

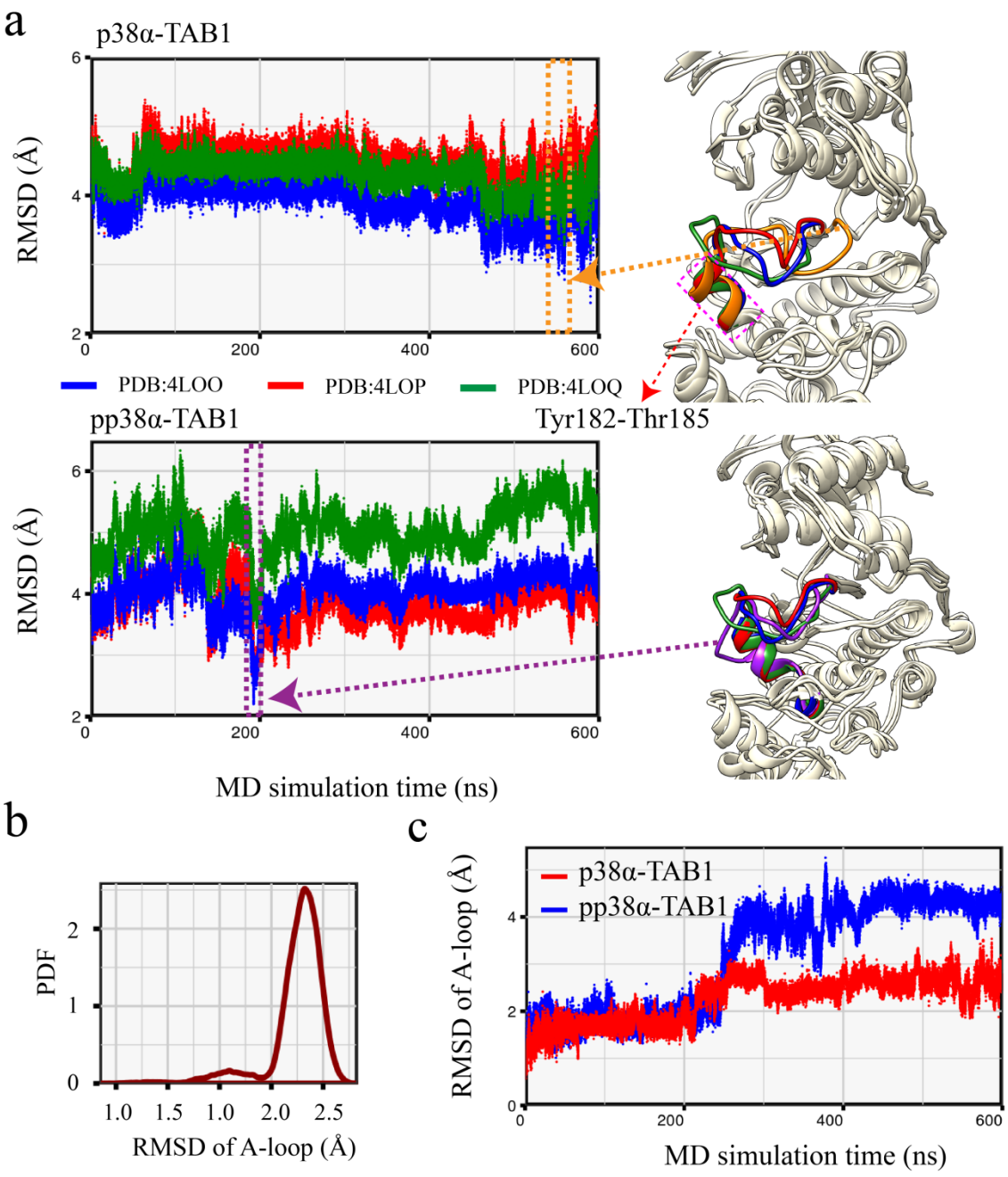

Fig. S2 (a) The root-mean-square deviation (RMSD) of p38α A-loop in p38α-TAB1 and pp38α-TAB1 simulations referenced to the crystal structure (PDB:4LOO, PDB:4LOP, PDB:4LOQ). The representative structures are given. (b) Probability distribution function (PDF) of the root-mean-square deviation (RMSD) of the A-loop in pp38α_{4LOO}-TAB1 simulations. (c) The RMSD of p38α A-loop in p38α-TAB1 and pp38α-TAB1 simulations referenced to the inactive p38α kinase.

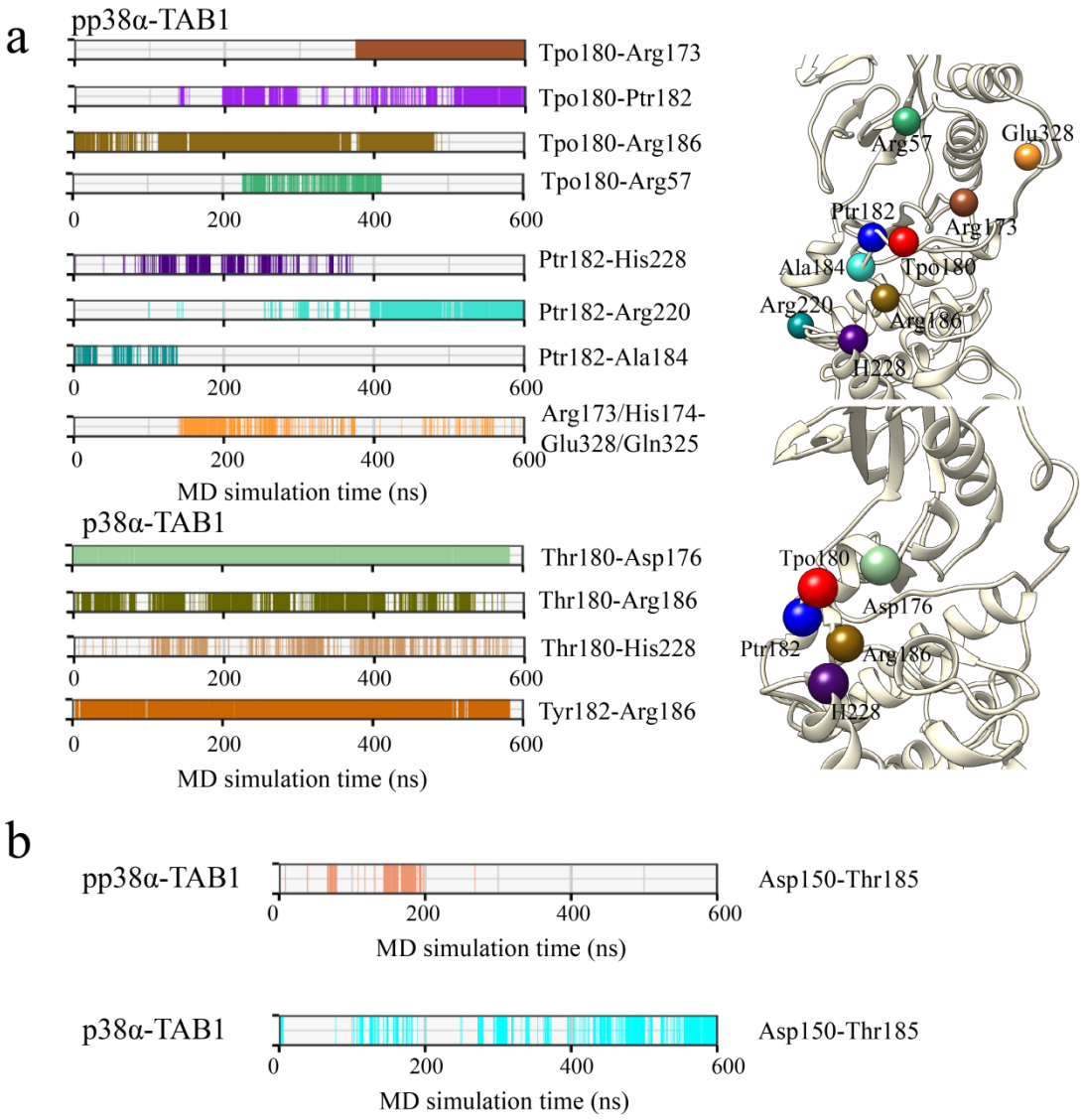

Fig. S3 (a) Hydrogen bond networks of Thr/Tpo180 and Tyr/Ptr182 in p38α-TAB1 and pp38α-TAB1 simulations. (b) The hydrogen bond between Asp150 and Thr185 during simulation of p38α-TAB1 and pp38α-TAB1 systems.

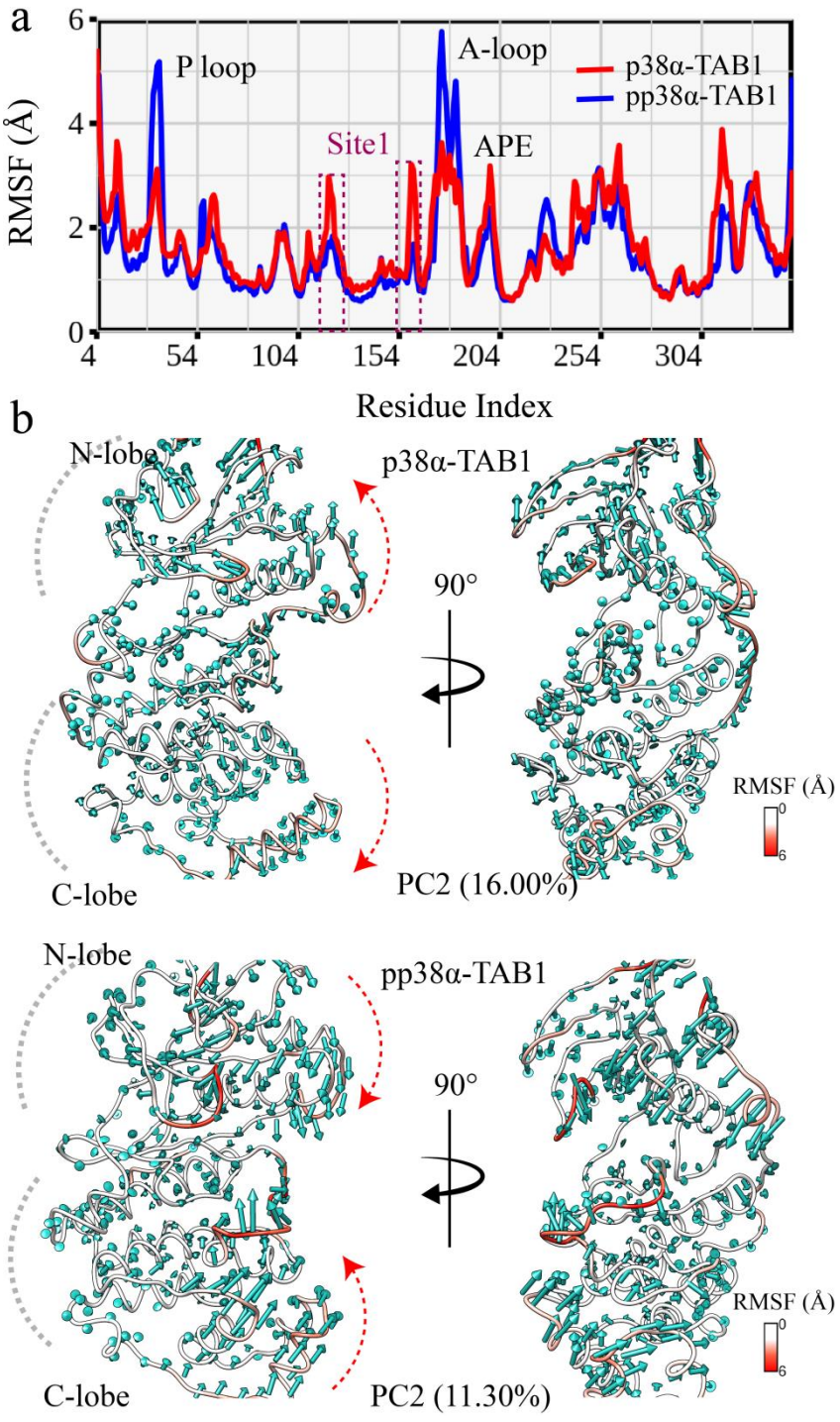

Fig. S4 (a) The root-mean-square fluctuation (RMSF) per residue for p38α in p38α-TAB1 and pp38α-TAB1simulations. (b) Vector field representations of the second principal component (PC) obtained from p38α of p38α-TAB1 simulation and pp38α-TAB1 simulation. The colors of residues are in accordance with the RMSFs values (units in Å).

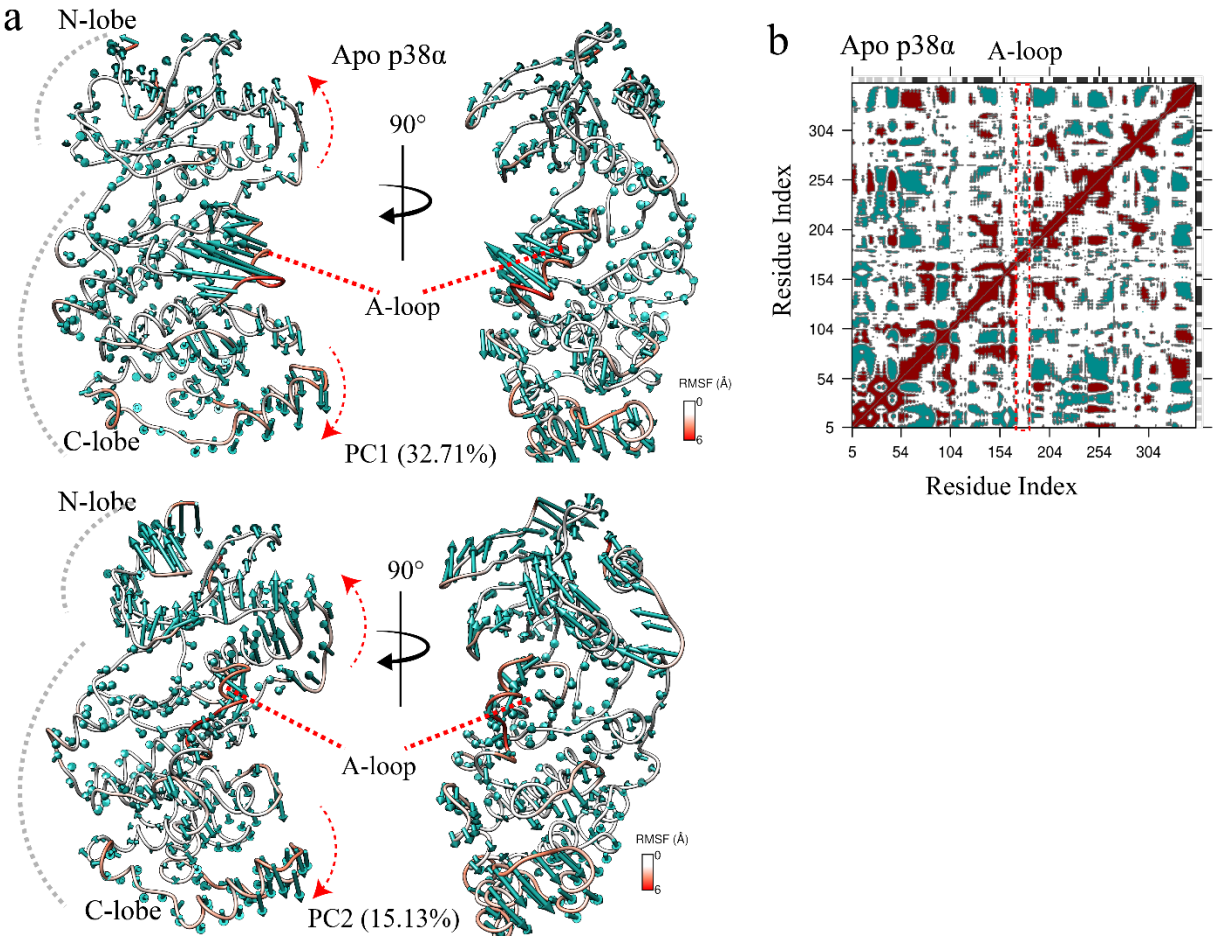

Fig. S5 (a) Dynamic cross-correlation maps for p38α kinase in apo p38α simulation. Correlation values range from −1 to +1, with positive values (dark red) indicating that two residues are correlated and negative values (light sea blue) indicating that they are anti-correlated. (b) Vector field representations of the first two principal components (PCs) obtained from apo p38α simulation. The colors of the residues indicate the root-mean-square fluctuation (RMSF) values (units in Å).

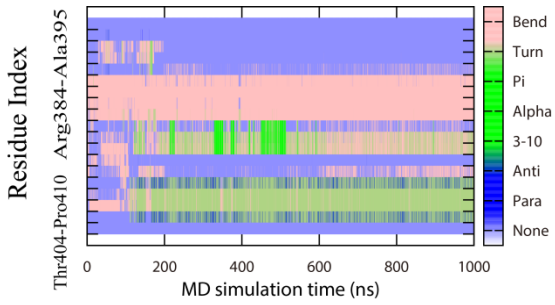

Fig. S6 The time evolution of secondary structures (structures defined using the dictionary of the secondary structure of proteins (DSSP)) of the disordered fragment of TAB1 during pp38α-TAB1 simulation.

The key structural of p38α differences between active and inactive states are the changes in the unfolding of the A-loop. The A-loop RMSD value of the sampling structures in our simulation is ~4.5 Å compared to inactive state. The following figures show the difference among the intermediate states sampling in our simulation, inactive state, and active state.

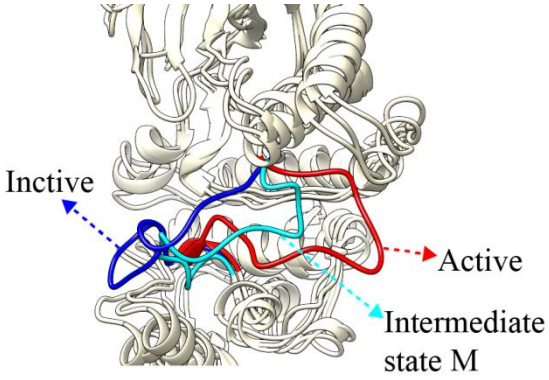

Fig. S7 Superposition of the three p38α structures, including the inactive state (A-loop in blue), active state (A-loop in red), and the intermediate state M (A-loop in cyan).

We extend the simulation time of the apo p38α, p38α-TAB1, pp38α-TAB1 and pp38α-TAB1 systems to 1000 ns. The RMSD of the three systems was recalculated and shown in the following figure. The RMSD values reached a plateau with minor variations after ~400 ns. Such motion suggests that the 600 ns simulation is sufficient for obtaining the stability of each system.

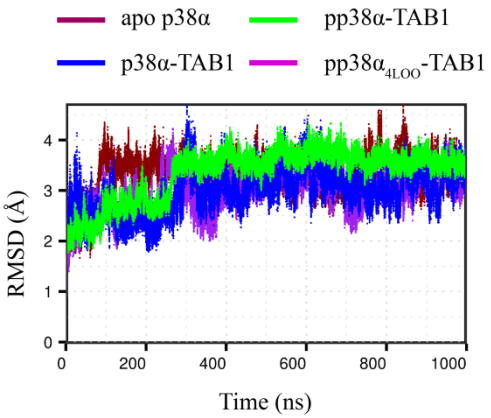

Fig. S8 The root-mean-square deviation (RMSD) of backbone atom of the apo p38α, p38α-TAB1, pp38α-TAB1 and pp38α-TAB1 simulations over the 1000 ns MD trajectories.