SUPPLEMENTARY INFORMATION

Deciphering mechanisms of acquired T790M mutation after EGFR inhibitors for NSCLC by computational simulations

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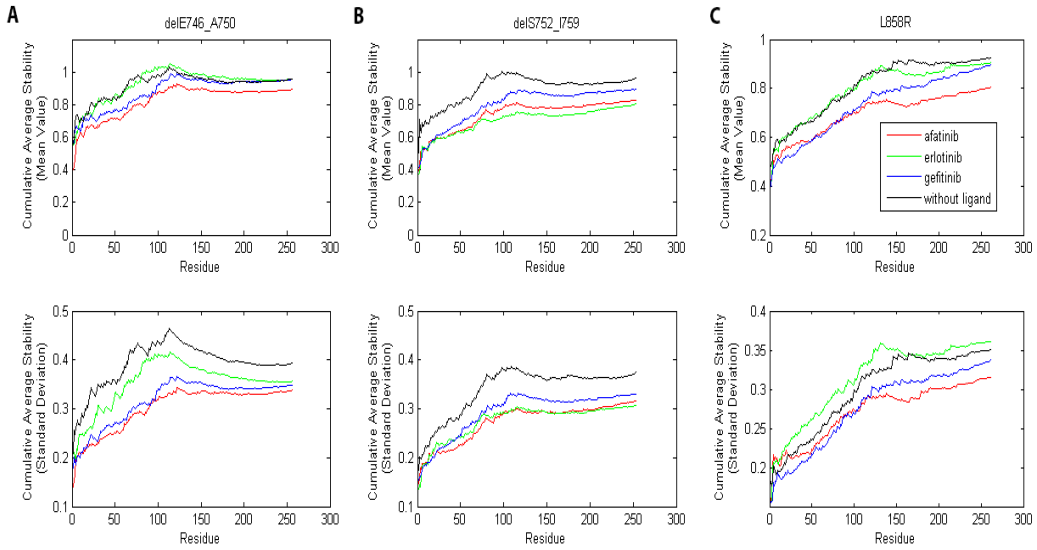
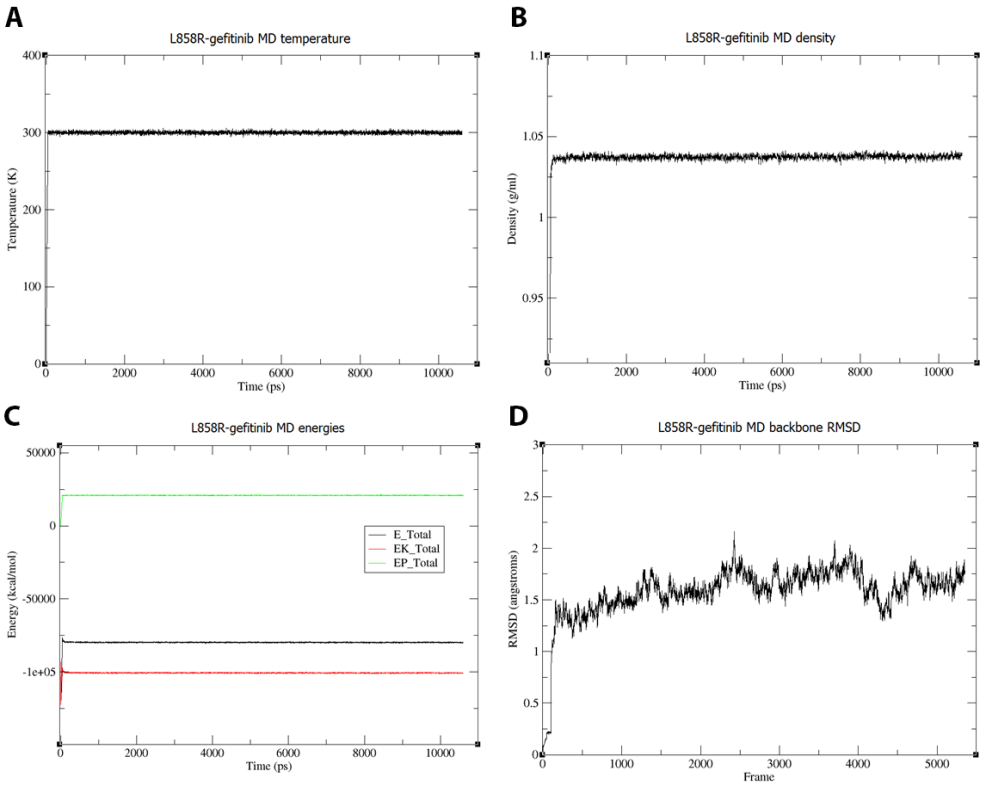
SUPPLEMENTARY FIGURES:



Supplementary Fig. S1. Comparison of the cumulative average stability between EGFR mutant-TKI complexes and EGFR mutants without ligand. The cumulative average stability for residue index k corresponded to the average stability of the first k residues closest to the residue T790. It was shown that, EGFR mutants without ligand (black) had a lower stability (larger values in the figures) than EGFR mutant-TKI complexes in most cases. This implied that combination with a ligand could increase the stability of the EGFR mutant. One exception was that the stability (standard deviation) of the L858R-erlotinib complex was lower than that of L858R. The reason might be that the stability of L858R was very high relative to delE746_A750 and delS752_I759 (Figure 4) and in this case the effect of the ligand (erlotinib) might not always work for L858R. It was also observed that EGFR mutant-afatinib complexes (red) demonstrated the highest stability in most cases. This is because that afatinib covalently binds to EGFR mutants, which could make EGFR mutant-TKI complexes more stable.



Supplementary Fig. S2. The (A) temperature, (B) density, (C) energy and (D) backbone RMSD of the L858R-gefitinib complex as functions of time. It was observed that the system finally achieved a stable state after a series of equilibration operations.