Supplementary Information

Design and Investigation of Binding Interactions of Novel Peptide Conjugates of Purine and Pyrimidine Derivatives with EGFR and its MutantT790M/L858R– An *in silico* and Laboratory Study

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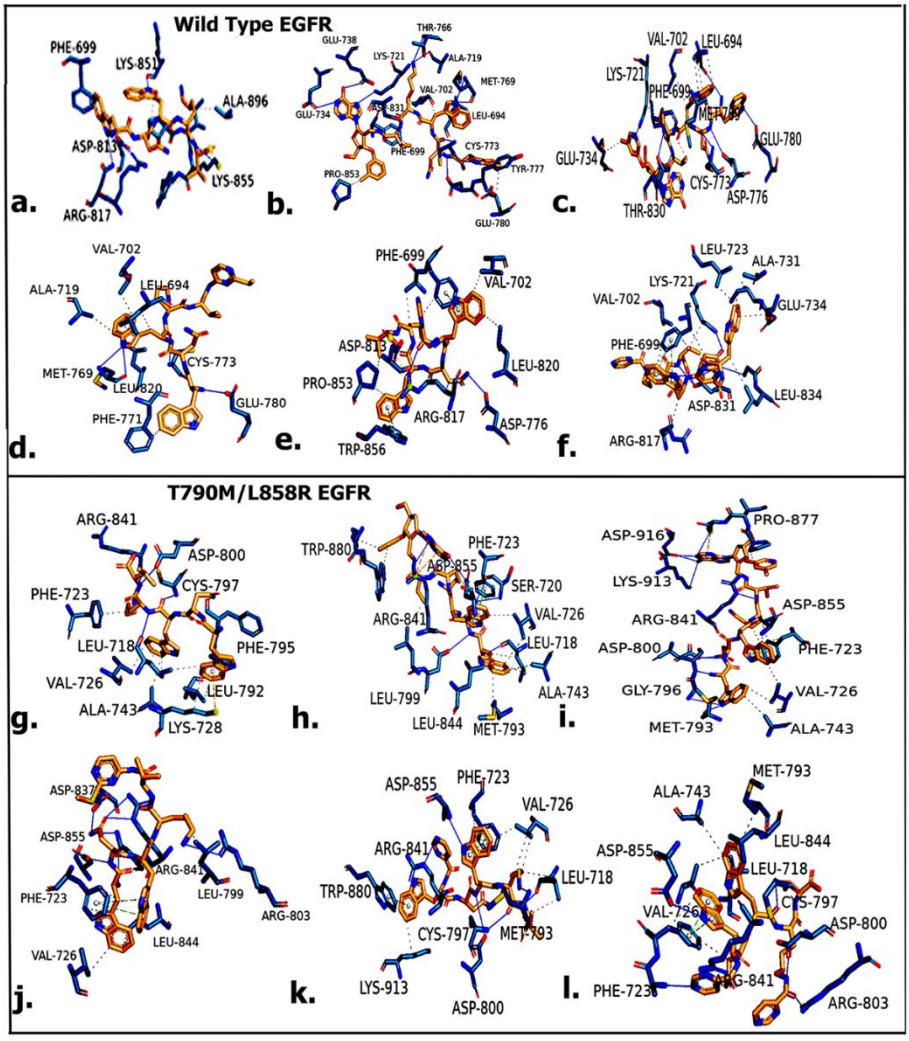

Figure S1. Comparison of protein-ligand interactions obtained using PLIP. Top: Wild Type EGFR (a) WNWKV; (b) WNWKV-CPU; (c) WNWKV-NPU; (d) WNWKV-MPY; (e) WNWKV-PYC; (f) WNWKV-$(PYC)_2$. Bottom: Double Mutant T790M/L858R. (g) WNWKV; (h) WNWKV-CPU; (i) WNWKV-NPU; (j) WNWKV-MPY; (k) WNWKV-PYC; (l) WNWKV-$(PYC)_2$. Yellow indicates ligands while blue segmentsare indicative of the receptor.

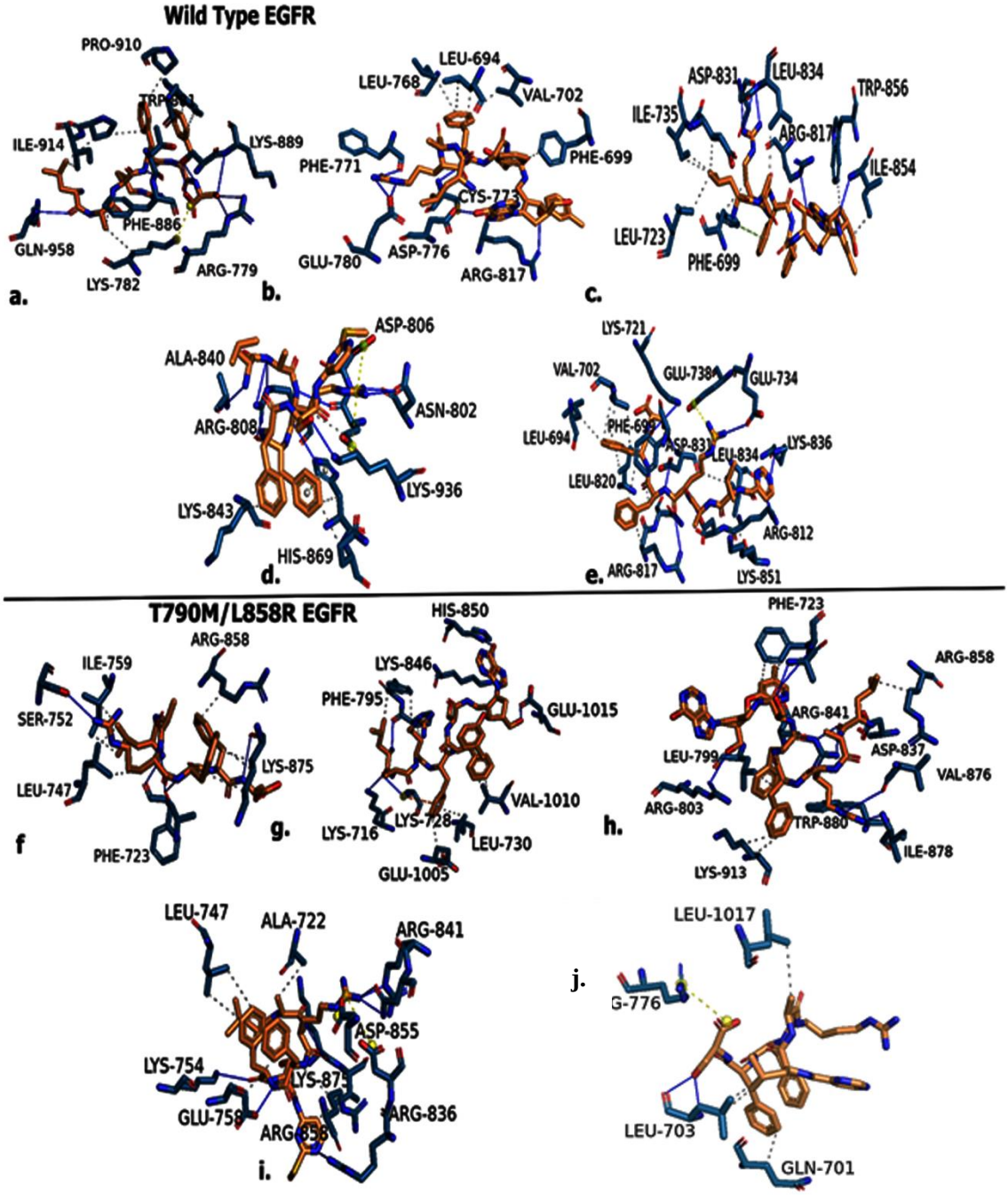

Figure S2. Comparison of protein-ligand interactions obtained using PLIP. Top: Wild Type EGFR (a) LARFFS; (b) LARFFS-CPU; (c) LARFFS-NPU; (d) LARFFS-MPY; (e) LARFFS-PYC; Bottom: Double Mutant T790M/L858R. (f) LARFFS; (g) LARFFS-CPU; (h) LARFFS-NPU; (i) LARFFS-MPY; (j) LARFFS-PYC.

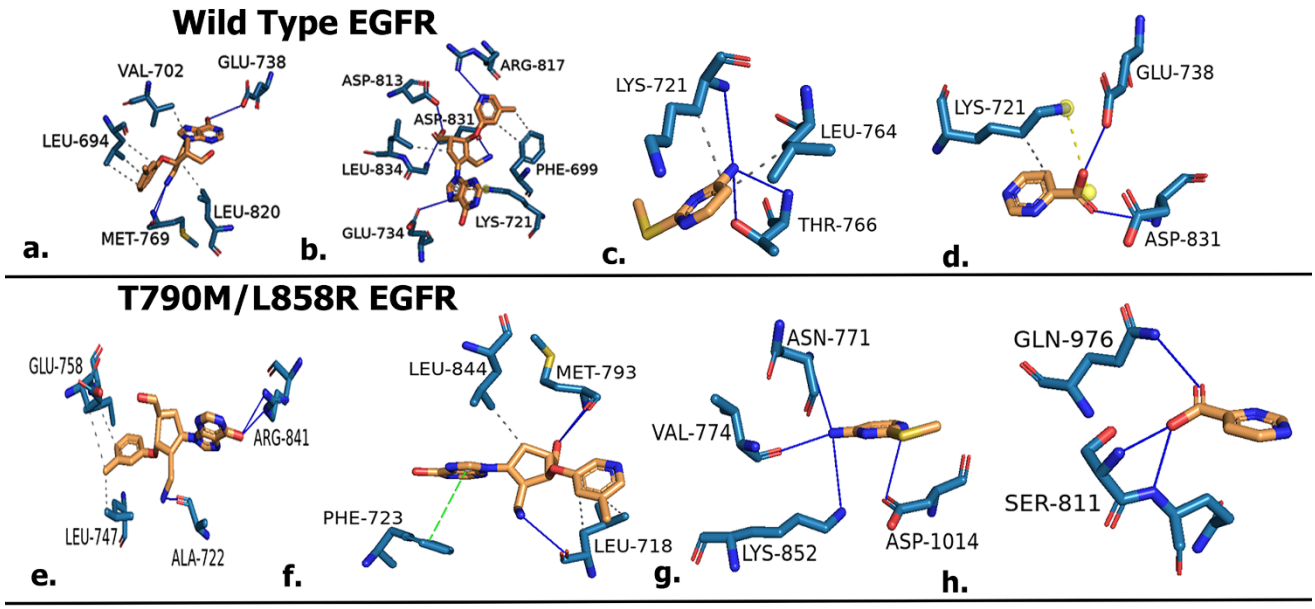

Figure S3. Protein-ligand Interactions after molecular docking with wild type EGFR receptor (Top) (a) CPU, (b) NPU, (c) MPY and (d) PYC; Bottom figures show interactions with EGFR T790M/L858R. (e) CPU; (f) NPU; (g) MPY and (h) PYC.

Table S1. Binding interactions of unconjugated compounds with wild-type EGFR

CPU	GLU738 MET769 MET769	3.37 2.47 3.56	LEU694 LEU694 LEU694 VAL702 LEU820	3.36 3.92 3.63 3.40 3.69	N/A	N/A	N/A	N/A	N/A
NPU	GLU734 ASP813 ARG817 ASP831 GLY833	3.21 2.33 2.39 2.46 2.93	PHE699 PHE699 LEU835	3.75 3.66 3.56	N/A	N/A	LYS721	5.03	N/A
MPY	LYS721 THR766 THR766	3.16 3.09 2.43	LYS721 LEU764	3.68 3.46	N/A	N/A	N/A	N/A	N/A
PYC	GLU738 ASP831	2.25 2.39	LYS721	3.77	LYS721	4.19	N/A	N/A	N/A

Table S2. Binding interactions of unconjugated compounds with EGFR [L858R/ T790M]

CPU	ALA722 ARG841 ARG841	2.14 2.55 2.41	LEU747 GLU758 ILE759	3.76 3.75 3.79	N/A	N/A	N/A	N/A	N/A
NPU	LEU718 MET793 MET793	2.42 2.03 2.59	LEU718 LEU718 LEU844	3.88 3.70 3.71	N/A	N/A	N/A	N/A	PHE723
MPY	ASN771 VAL774 LYS852 ASP1014	3.14 2.28 3.04 3.15	N/A	N/A	N/A	N/A	N/A	N/A	N/A
PYC	SER811 GLN812 GLN976	2.69 1.95 2.14	N/A	N/A	N/A	N/A	N/A	N/A	N/A

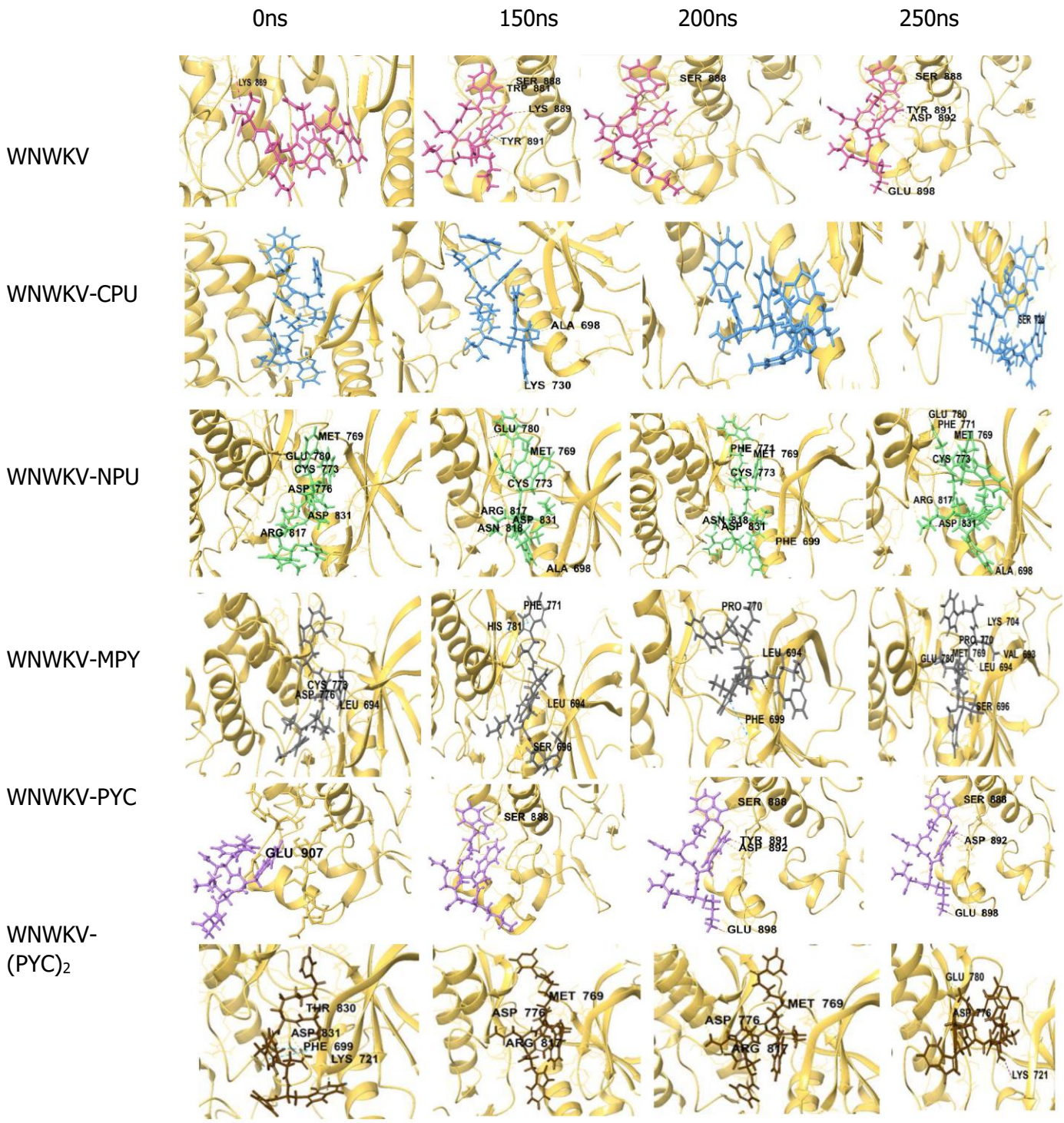

Figure S4. Trajectory images over 250 ns simulation of WNWKV and its conjugates with the kinase domain of the wild type EGFR receptor.

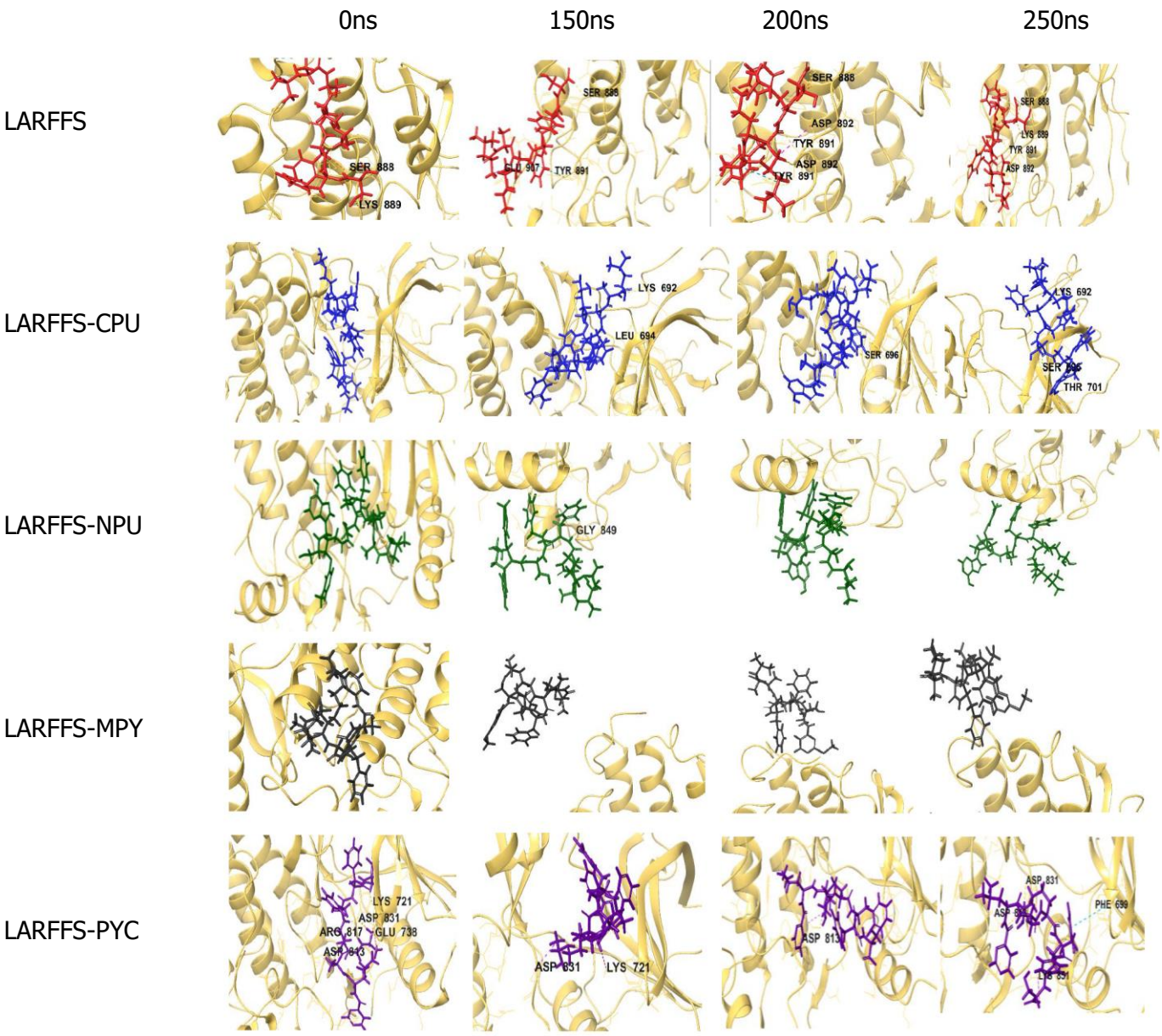

Figure S5. Trajectory images over 250 ns simulation of LARFFS and its conjugates with the kinase domain of the wild type EGFR receptor.

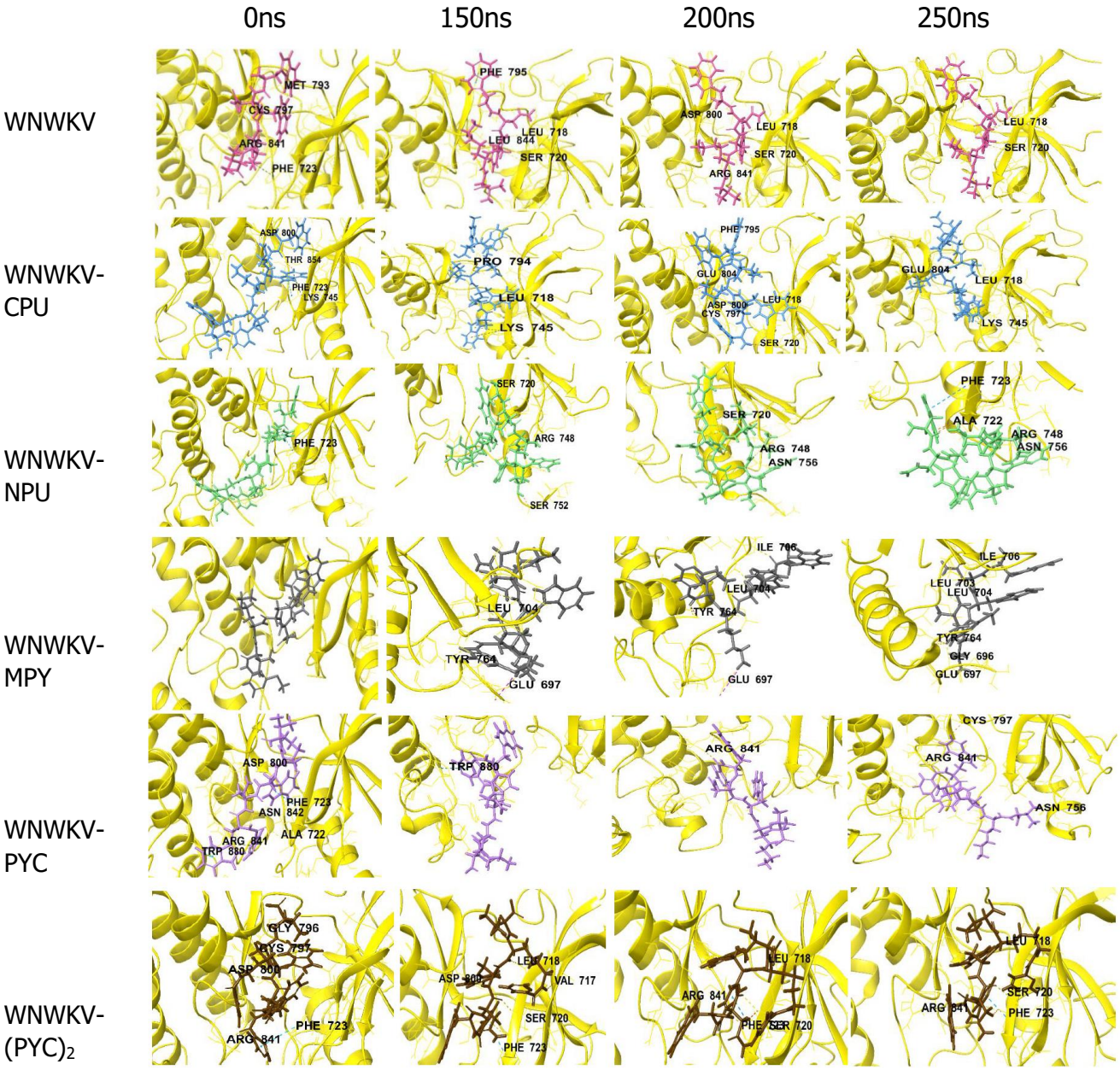

Figure S6. Trajectory images over 250 ns simulation of WNWKV and its designed conjugates with the kinase domain of the T790M/L858R double mutant EGF receptor.

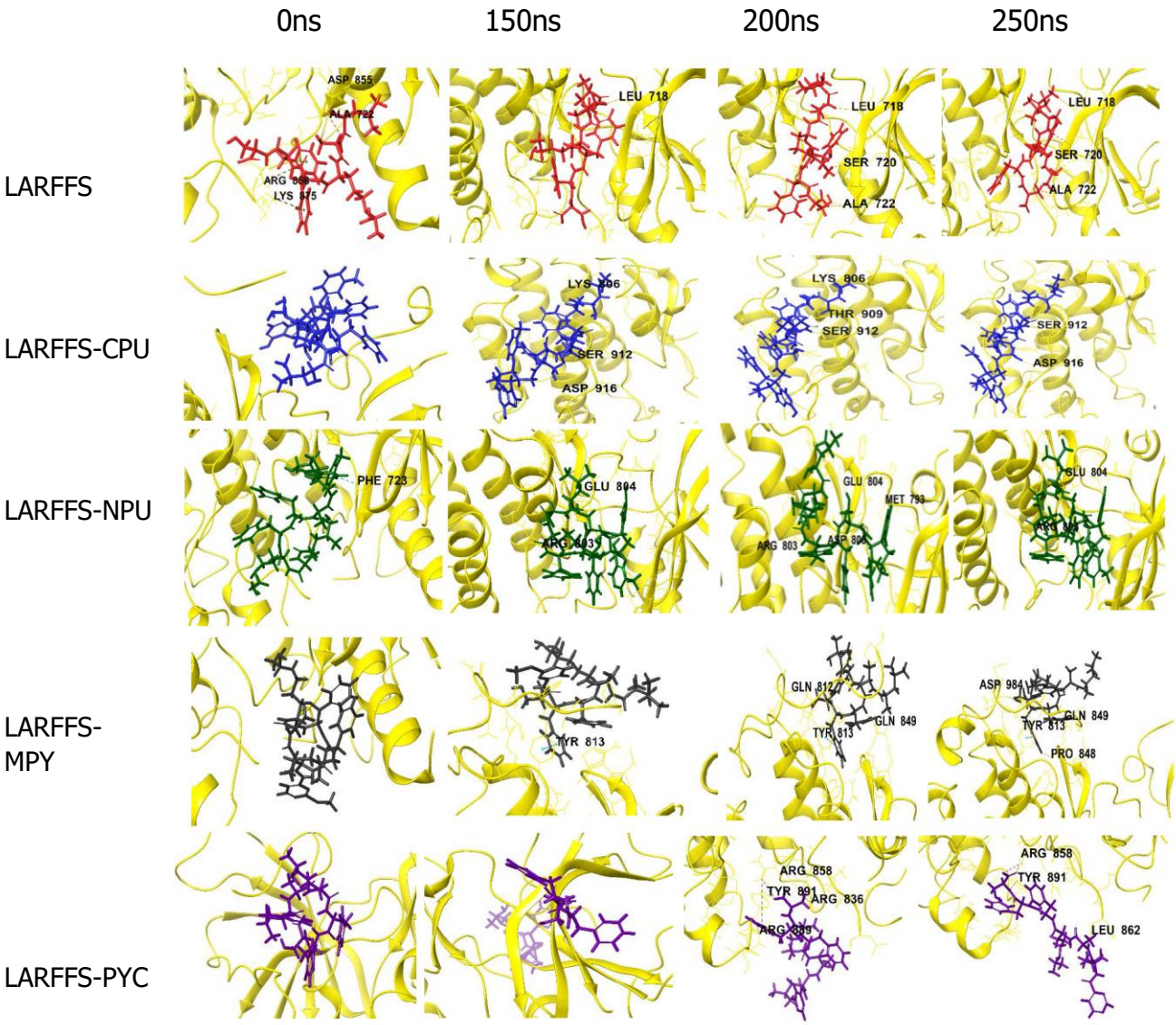

Figure S7. Trajectory images over 250 ns simulation of LARFFS and its designed conjugates with the kinase domain of the T790M/L858R double mutant EGF receptor.

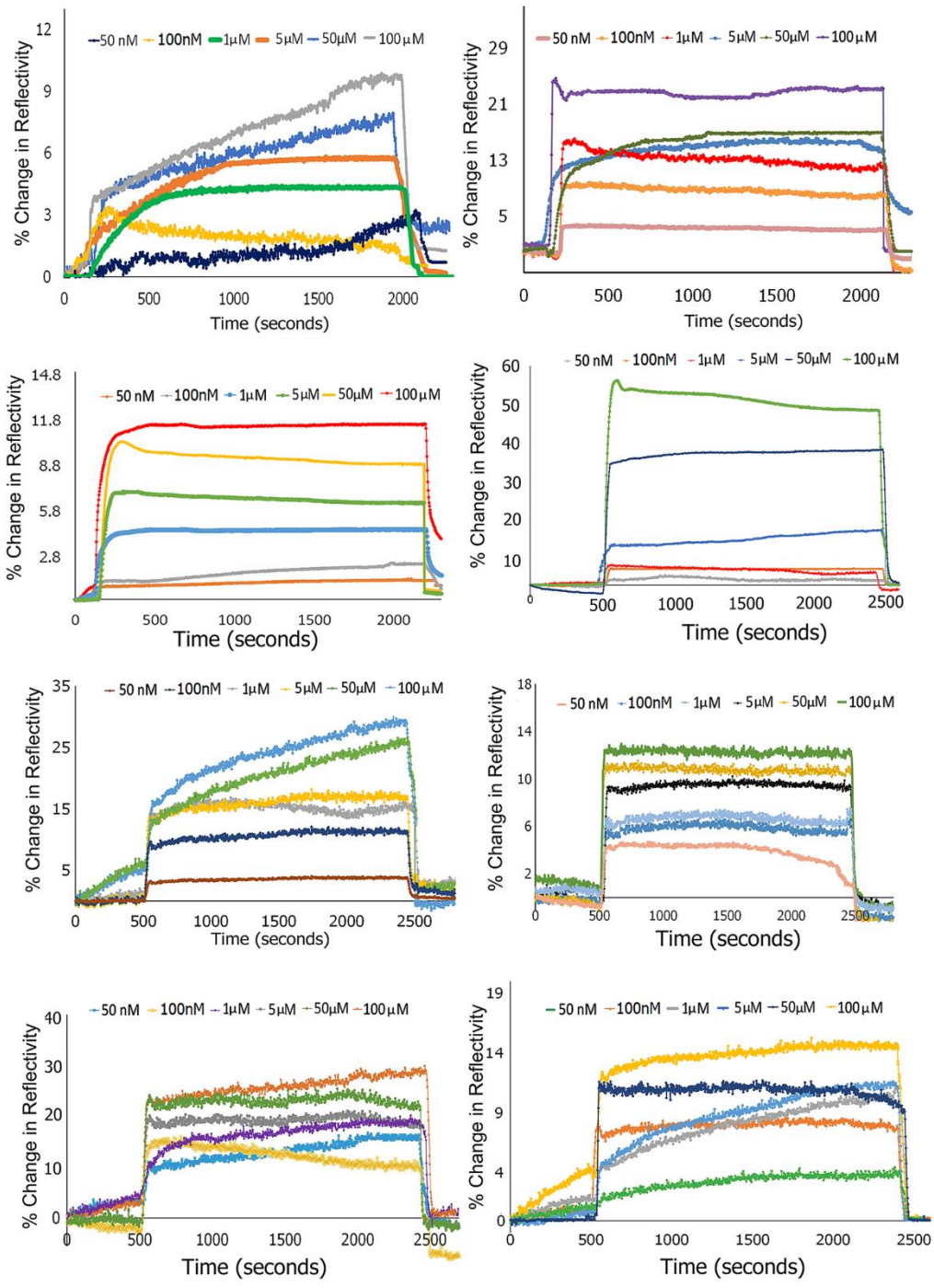

Figure S8. SPR sensograms obtained for binding with Wild Type EGFR (left hand side) and T790M/L858R EGFR (right hand side). Top through bottom: WNWKV; WNWKV-$(PYC)_2$; LARFFS and LARFFS-PYC.

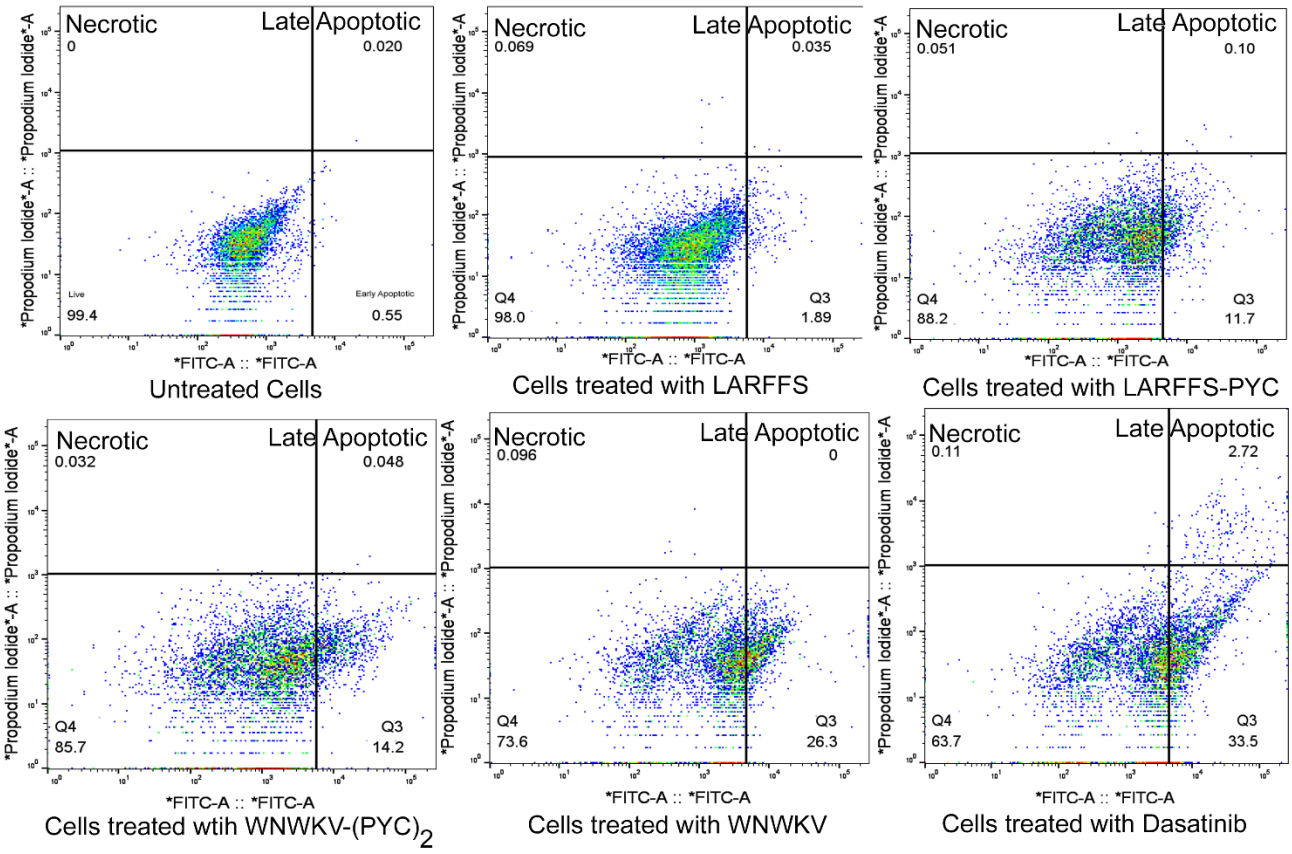

Figure S9. Annexin V/propidium iodide apoptosis studies using flow cytometry results showing effects of various constructs on primary lung fibroblasts after treatment over a 24 hour incubation period. The concentration of each of the constructs *5 μM*.