Molecular simulation studies on the binding activity and selectivity of 3-Amino-phenyl-5-chloro-pyrimidine-2, 4-diamine derivatives in complexes with kinases *c*-Met and ALK

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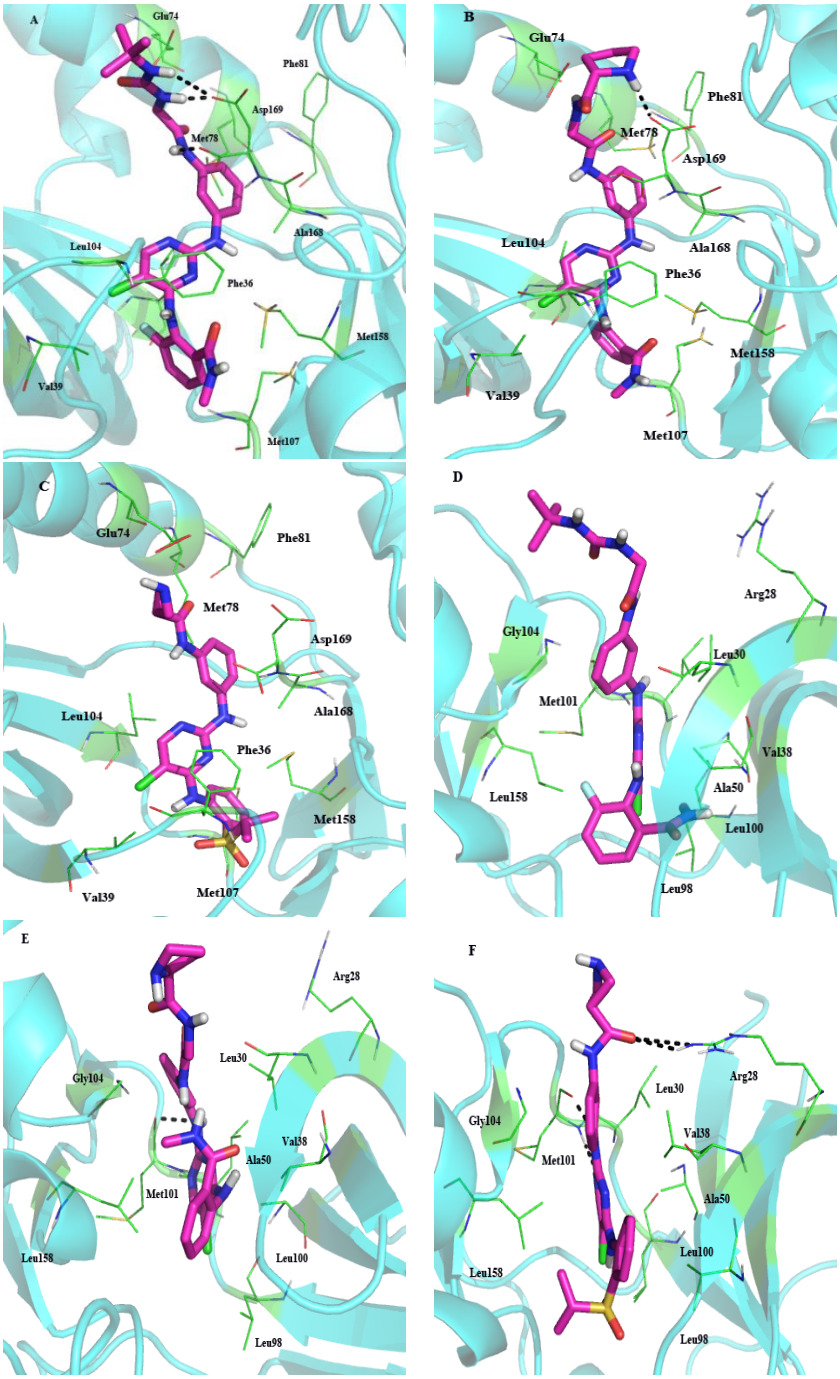

Figure S1. The initial structure for the MD simulation from docking result (A) Lig1-*c*-Met, (B) Lig2-*c*-Met, (C) Lig3-*c*-Met, (D) Lig1-ALK, (E) Lig2-ALK, (F) Lig3-ALK

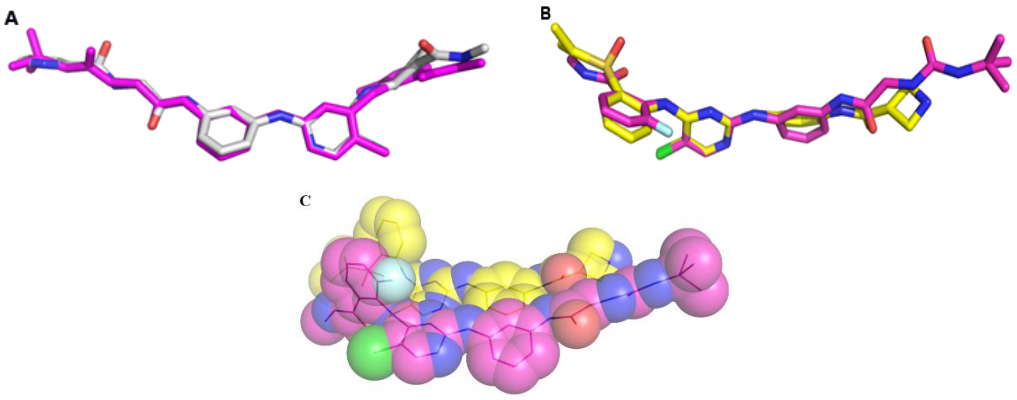

Figure S2. The structure comparison (A) Lig1 and Lig2, magenta: Lig1, gray: Lig2; (B) Lig1 and Lig3, magenta: Lig1, yellow: Lig3; (C) Spheres type of Lig1 and Lig3, magenta: Lig1, yellow: Lig3.

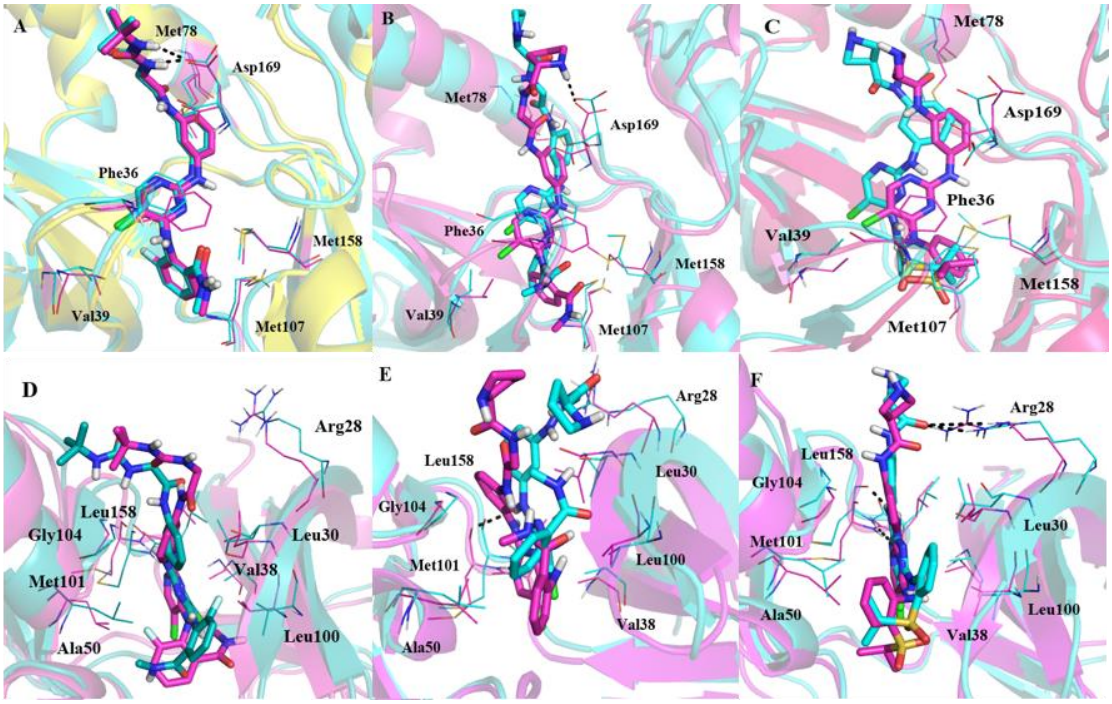

Figure S3. Structure comparison between initial (magenta) and representative snapshots from MD (cyan) of: (A) Lig1-*c*-Met; (B) Lig2-*c*-Met; (C) Lig3-*c*-Met; (D) Lig1-ALK; (E) Lig2-ALK; (F) Lig3-ALK. Line: binding pocket; stick: ligand

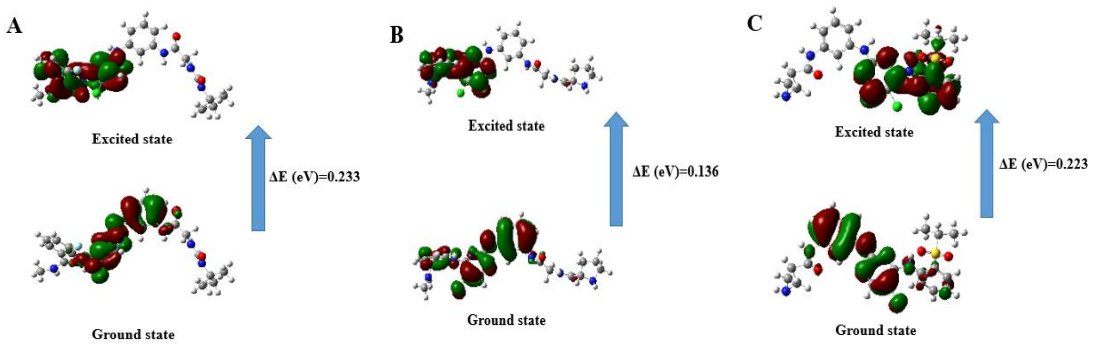

Figure S4. Molecular orbital for the HOMO-LUMO plot of (**A**) Lig1, (**B**) Lig2, (**C**) Lig3 with B3LYP/6-31G(d,p)

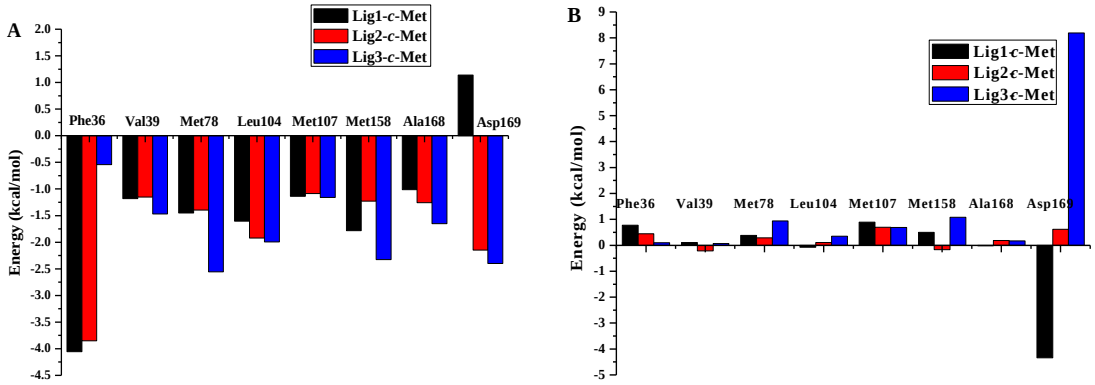

Figure S5. Comparison of per-residue energy decomposition for key residues for Lig1-*c*-Met, Lig2-*c*-Met and Lig3-*c*-Met systems. (A) the sums of vdW and nonpolar solvation energy ($\Delta G_{\text{vdW}} + \Delta G_{\text{nonpolar, sol}}$) of Lig1-*c*-Met, Lig2-*c*-Met and Lig3-*c*-Met; (B) the sums of electrostatic and polar solvation energy ($\Delta G_{\text{ele}} + \Delta G_{\text{ele, sol}}$) of Lig1-*c*-Met, Lig2-*c*-Met and Lig3-*c*-Met

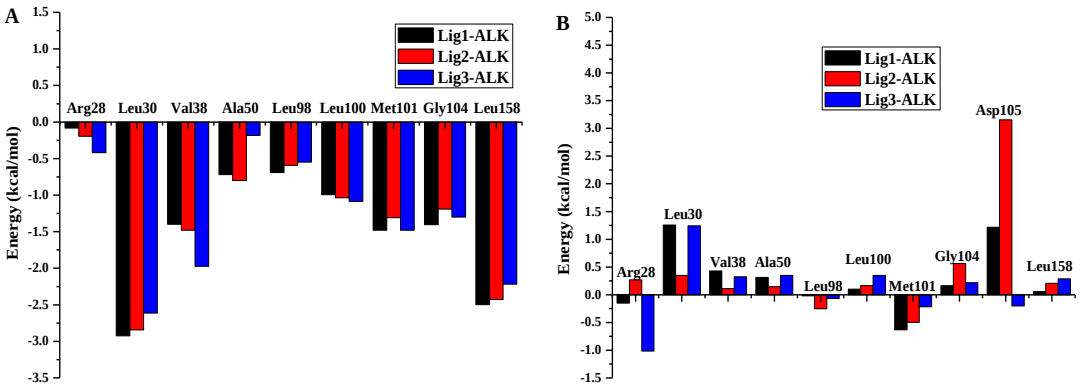

Figure S6. Comparison of per-residue energy decomposition for key residues for Lig1-ALK, Lig2-ALK and Lig3-ALK systems. (A) the sums of vdW and nonpolar solvation energy ($\Delta G_{\text{vdW}} + \Delta G_{\text{nonpolar, sol}}$) of Lig1-ALK, Lig2-ALK and Lig3-ALK; (B) the sums of electrostatic and polar solvation energy ($\Delta G_{\text{ele}} + \Delta G_{\text{ele, sol}}$) of Lig1-ALK, Lig2-ALK and Lig3-ALK

Table S1. Descriptors of quantum chemical based on DFT calculations used for MESP for compounds Lig1, Lig2 and Lig3

Quantum Descriptors	Lig1	Lig2	Lig3
E_{LUMO} (eV)	-0.069	-0.086	-0.072
E_{HOMO} (eV)	-0.302	-0.222	-0.295
Total dipole moment μ (D)	12.556	7.759	13.228