Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary material

Molecular Modeling Studies of Quinazolinone Derivatives as Novel PI3Kδ Selective Inhibitors

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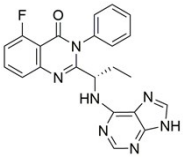
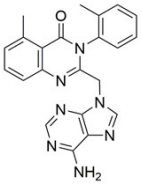
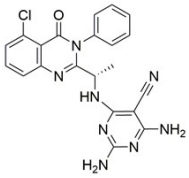
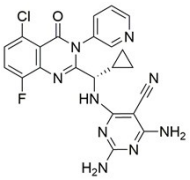
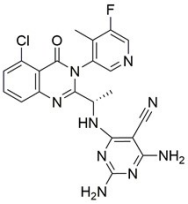
Table 1S. Analysis of critical amino acid residues for PI3Kδ complexes deposited in protein databank database

PDB	**4XE0**	**2X38**	**5I4U**	**5T8I**	**5T7F**
Resolution	2.43 Å	2.20 Å	2.37 Å	2.60 Å	2.60 Å
Ligand					
Released date	2015-02-04	2010-02-02	2017-02-22	2016-12-18	2016-12-18
Interception residue	LYS708	LYS708			
	THR750	THR750	THR750	THR750	THR750
	MET752	MET752	MET752	MET752	MET752
	PRO758	PRO758	PRO758	PRO758	PRO758
	TRP760	TRP760	TRP760	TRP760	TRP760
	ILE777	ILE777	ILE777	ILE777	ILE777
	TYR813	TYR813	TYR813	TYR813	TYR813
	ILE825	ILE825	ILE825	ILE825	ILE825
	CLU826	CLU826	CLU826	CLU826	CLU826
	VAL828	VAL828	VAL828	VAL828	VAL828
			LEU829	LEU829	LEU829
	SER831	SER831	SER831	SER831	SER831
	ASP832	ASP832	ASP832	ASP832	ASP832
	THR833	THR833	THR833	THR833	THR833
	ASN836	ASN836		ASN836	
	ASP897		ASP897	ASP897	ASP897
				ASN898	ASN898
	MET900	MET900	MET900	MET900	MET900
	ILE910	ILE910	ILE910	ILE910	ILE910
	ASP911	ASP911	ASP911	ASP911	ASP911

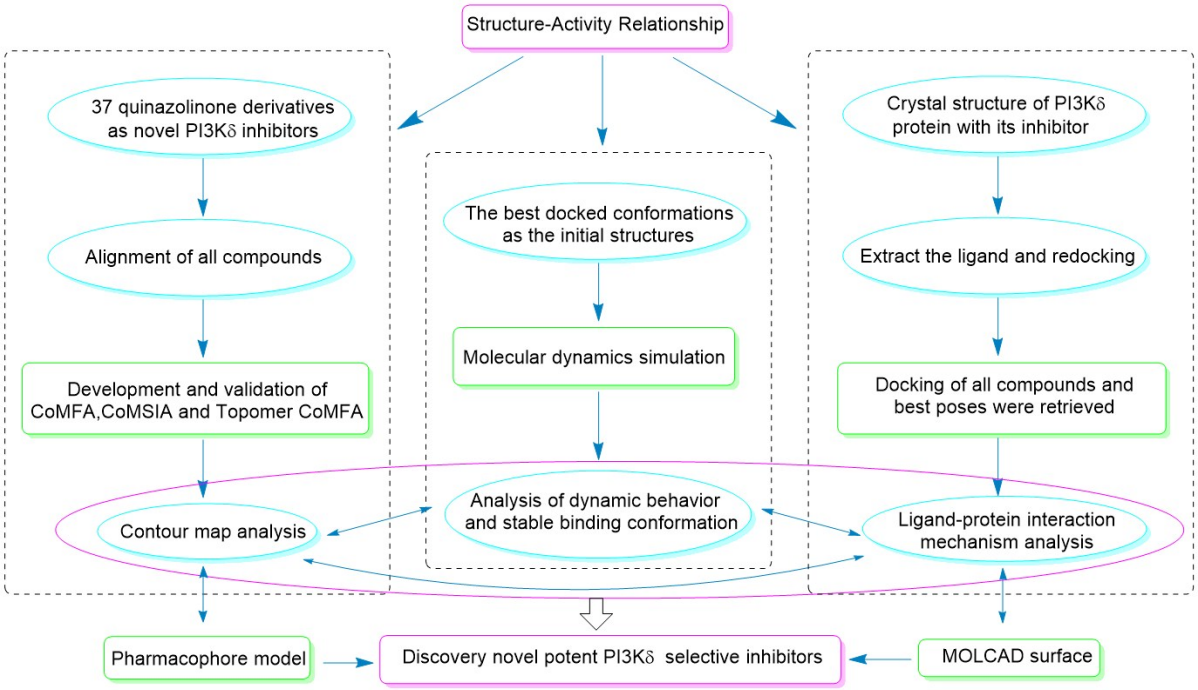


Fig. 1S Flowchart for the application of the 3D-QSAR model, Molecular docking studies, pharmacophore model and MD simulations.

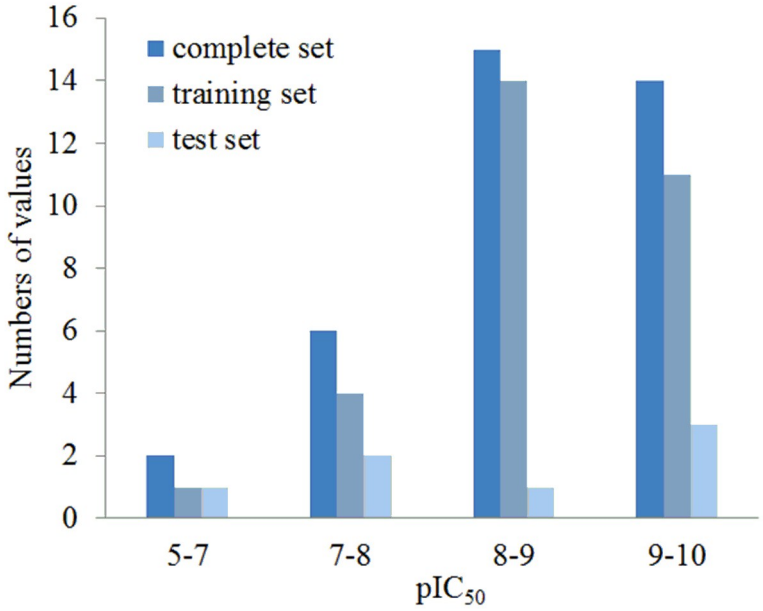


Fig. 2S Distribution of the inhibitory activity of all the compounds.

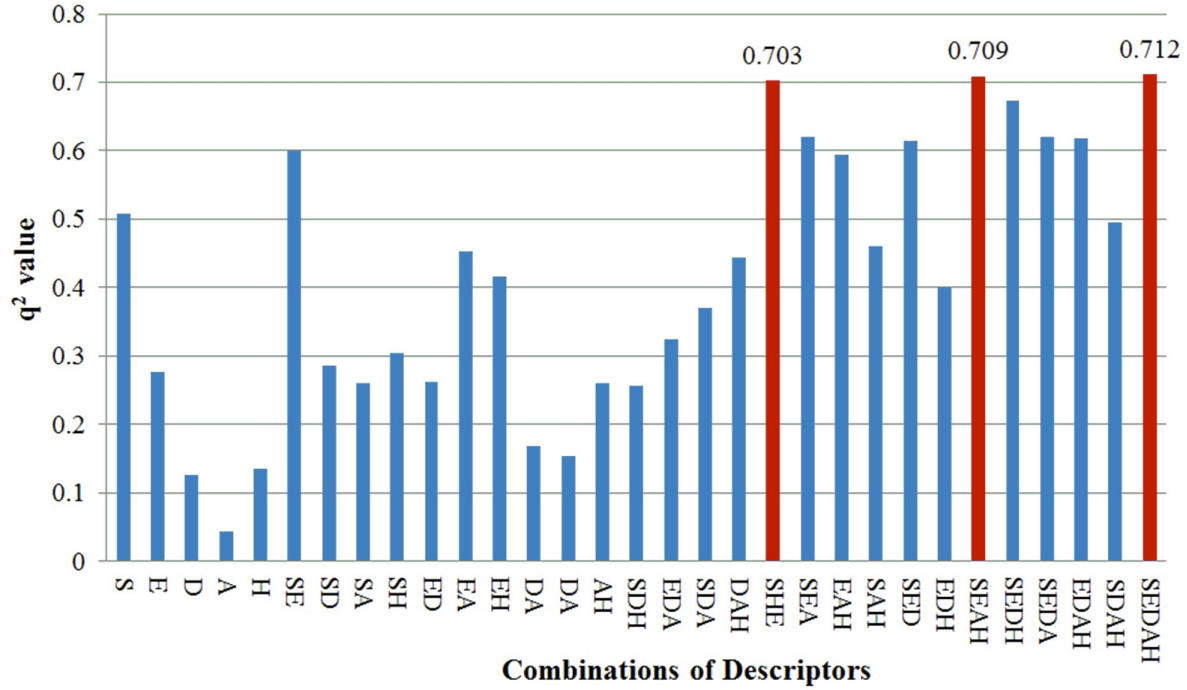


Fig. 3S Graph of the 31 possible CoMSIA descriptor combinations with their respective q^2 values.

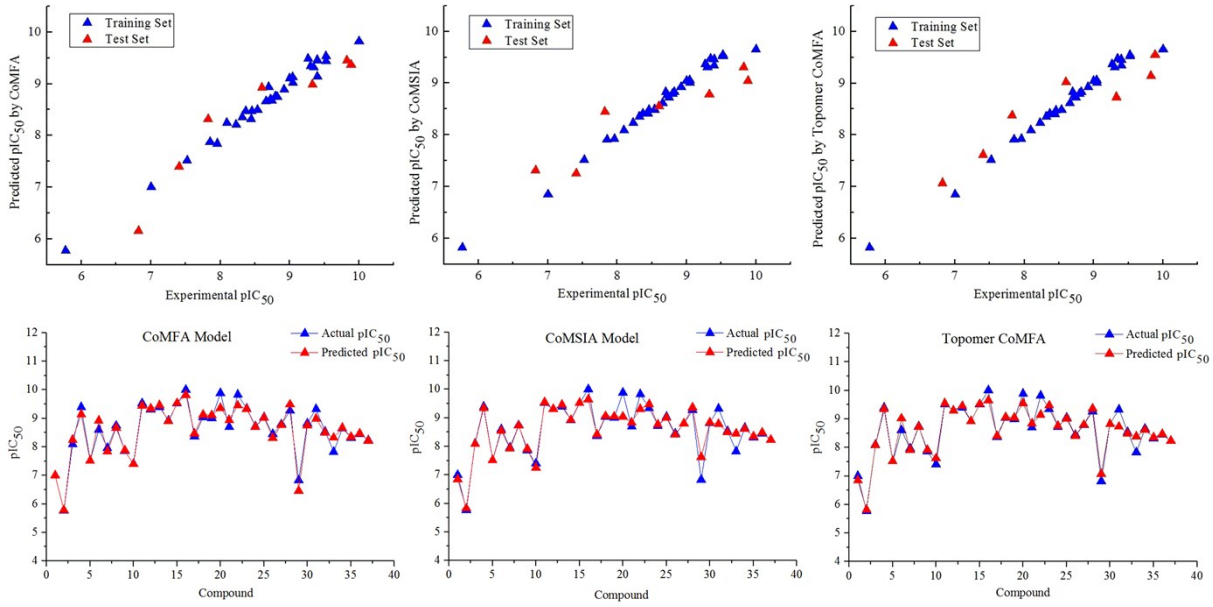


Fig. 4S The correlation plots of experimental and predicted pIC_{50} values for the total set in the CoMFA, CoMSIA and Topomer CoMFA models.

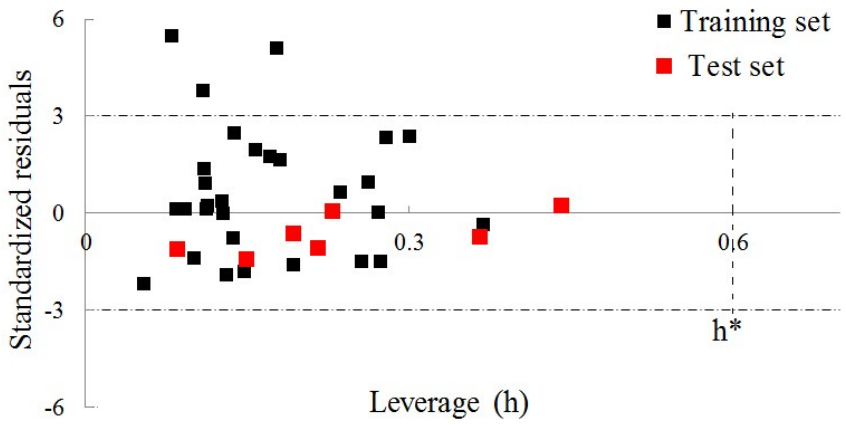


Fig. 5S William's plot (standardized residuals versus leverages) of CoMSIA model.

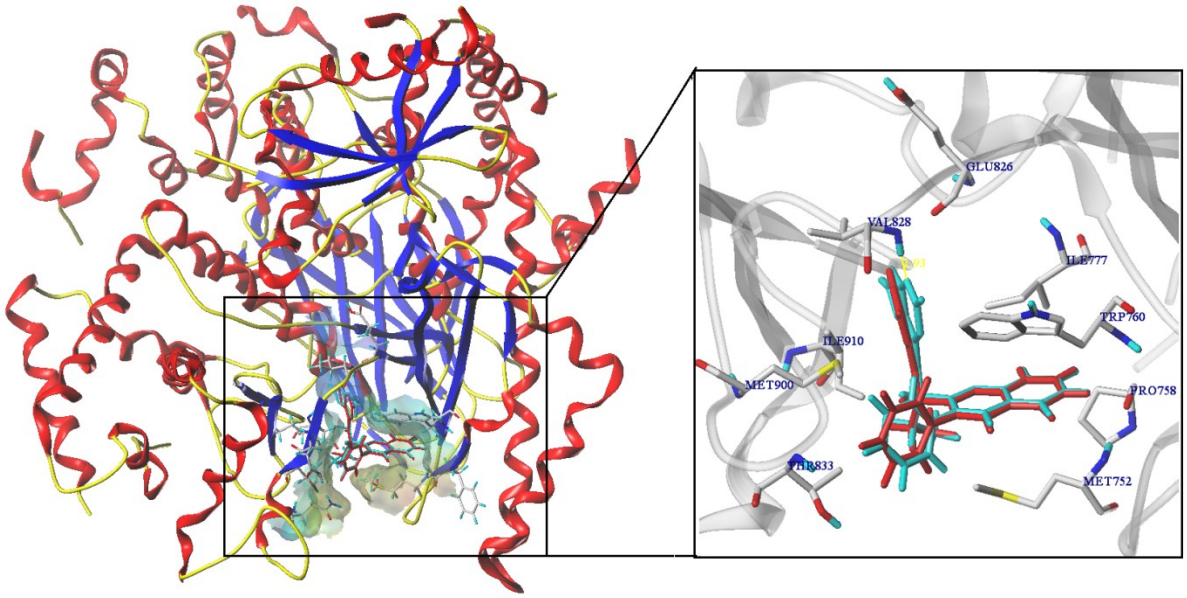


Fig. 6S Re-docking results of the original ligand in the binding site of PI3Kδ protein.

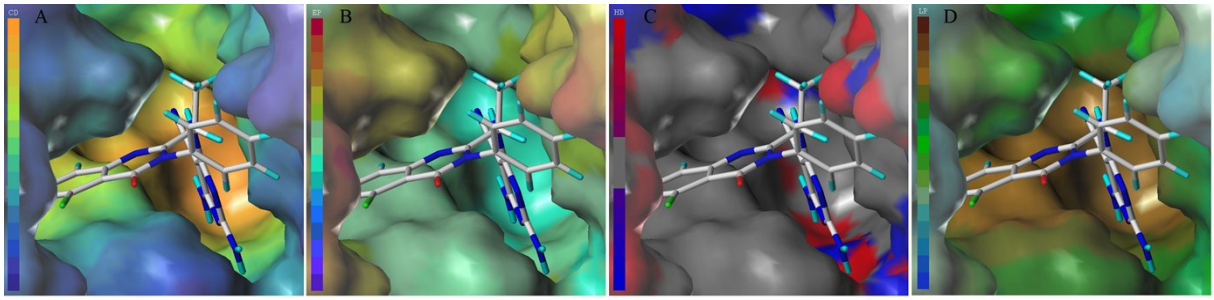


Fig. 7S Active site MOLCAD surface with the compound **16** representation Cavity Depth (A), Electrostatic potential (B), Hydrogen bonding ability (C) and Lipophilic Potential (D).

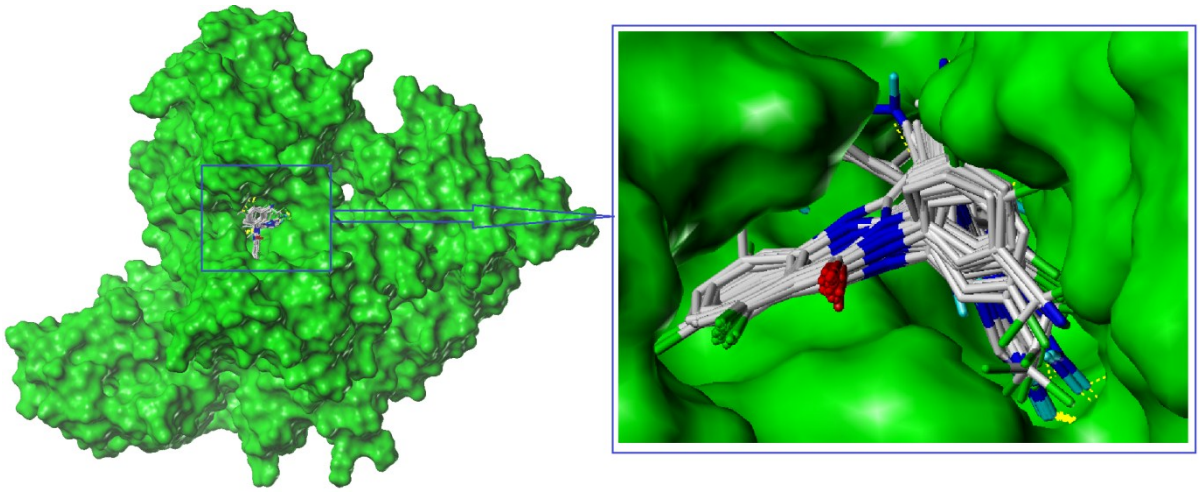


Fig. 8S Docking results of all the compounds in the study and surface of the binding site (4XE0).

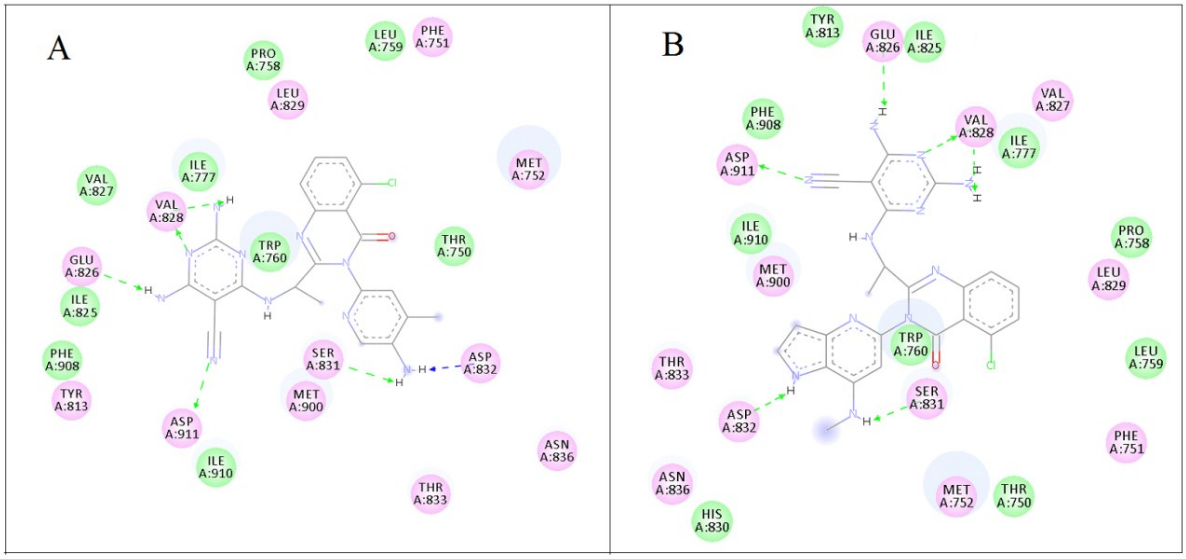


Fig. 9S 2D interaction map of newly designed compound **D04** (A) and **D06** (B) with PI3Kδ protein.

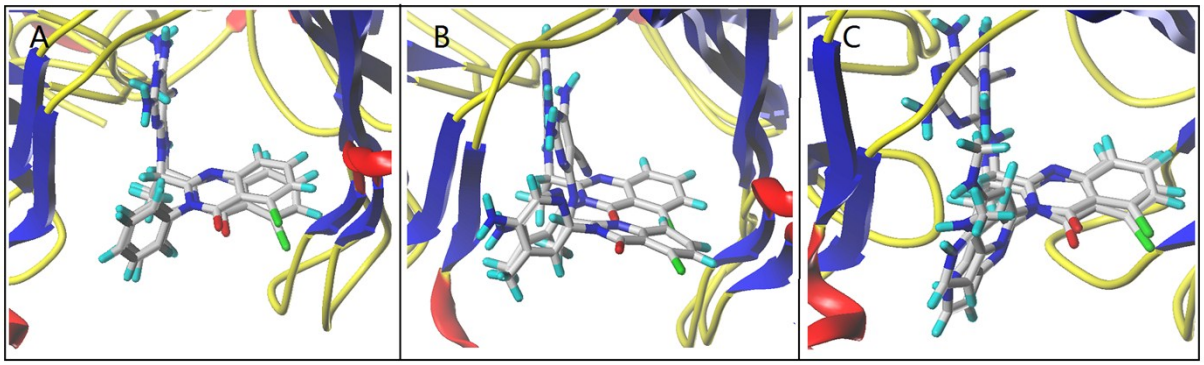


Fig. 10S Structural comparison between initial and representative snapshots from MD of compound **16** (A), **D04** (B) and **D06** (C).

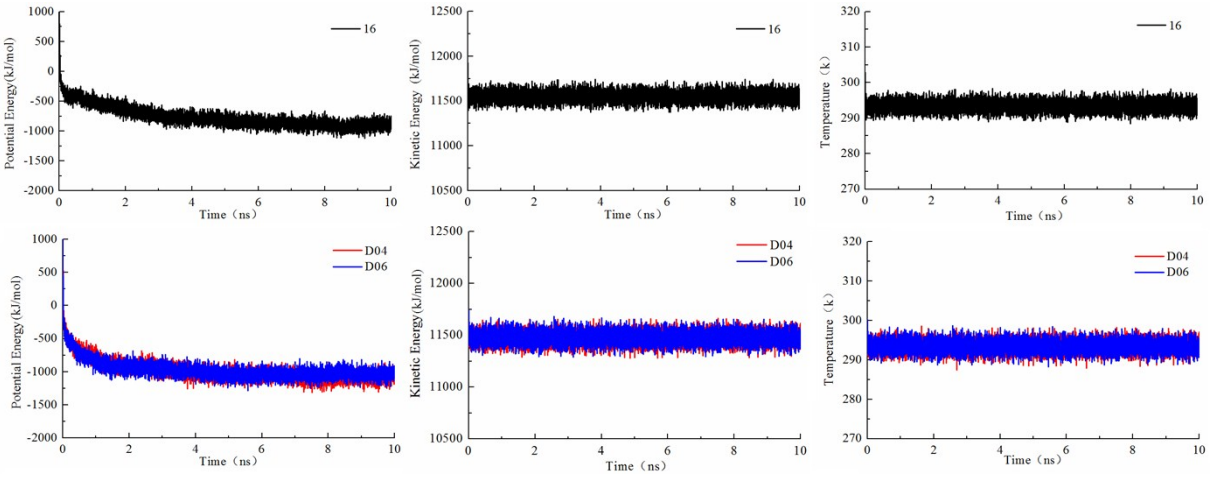


Fig. 11S Change in potential energy, kinetic energy and temperature of compound **16, D04** and **D06** with respect to simulation time.

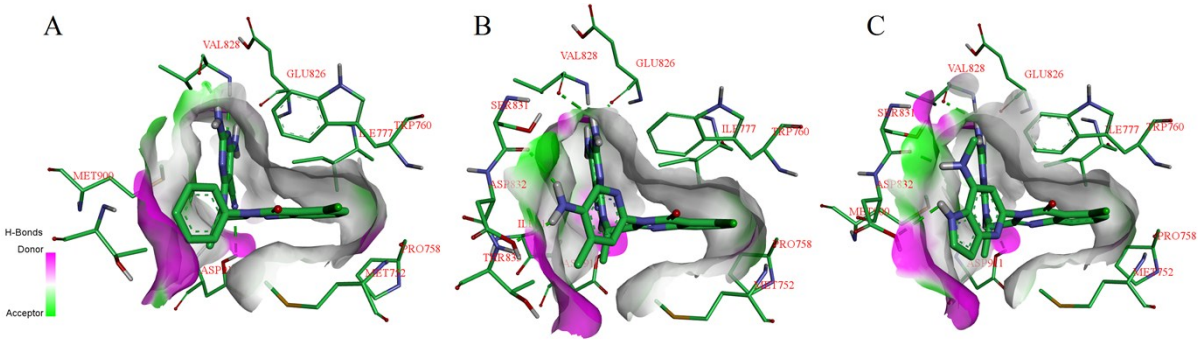


Fig. 12S The binding mode and H-bond surface determined via MD analysis: 4XE0-**16** (A), 4XE0-**D04** (B), 4XE0-**D06** (C).