Supplementary Section

Docking poses of the ligands with ATM

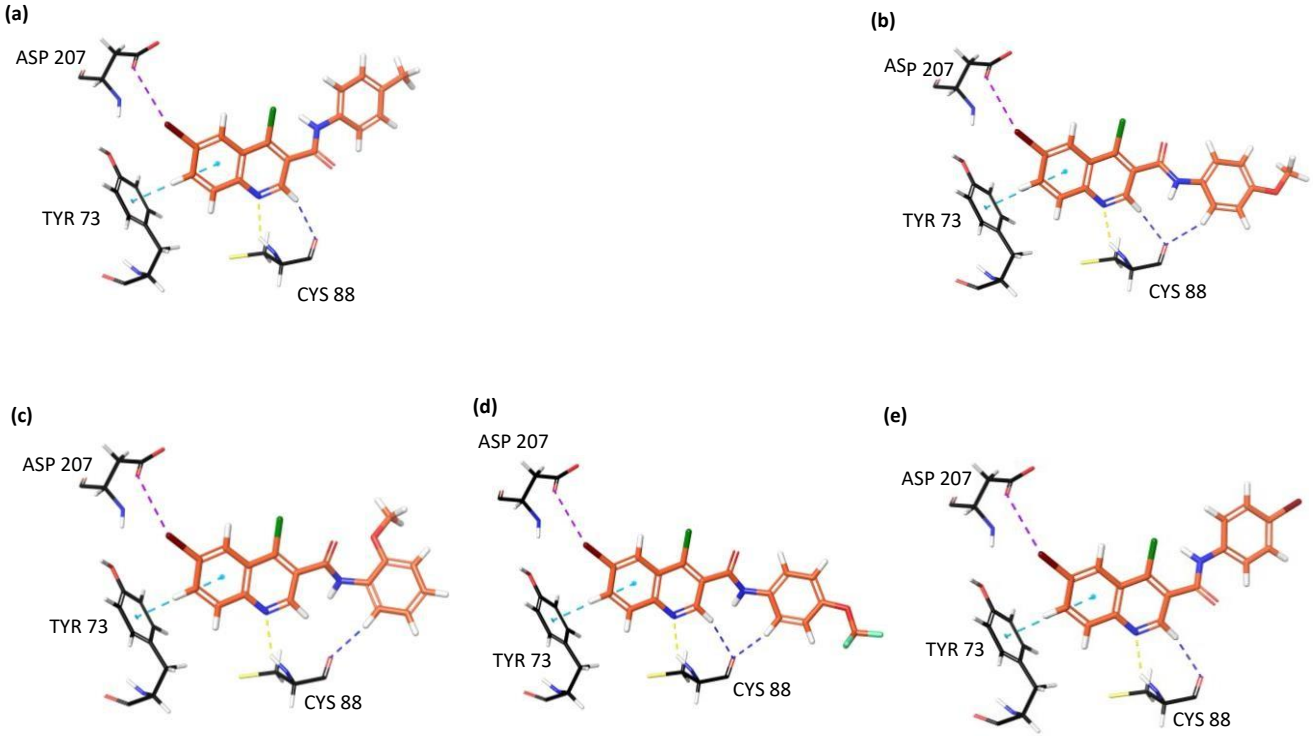


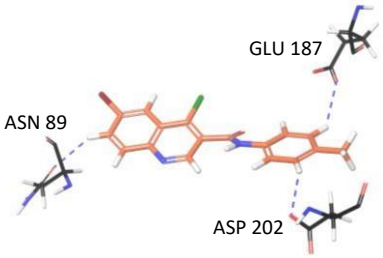
Figure S1. Interaction of the ligands with ATM (a) 6a (b) 6b (c) 6b' (d) 6d (e) 6e

Table S1. Summary of interactions of the ligands with ATM

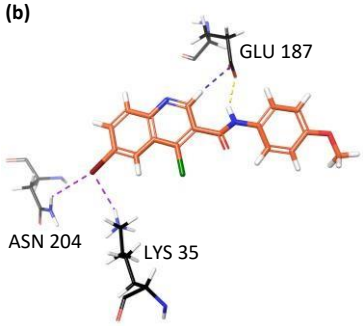
Ligand	Interacting Residues	Types of Interactions
6a	ASP 207, TYR 73, CYS 88	Halogen bonding, π-π stacking, hydrogen bonding, aromatic hydrogen bonding
6b		
6b'		
6d		
6e		

Docking poses of the ligands with ATR

(a)



(b)



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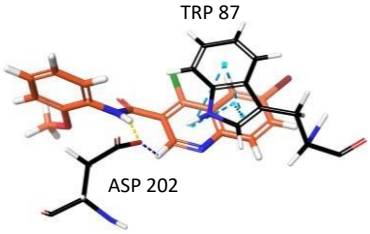

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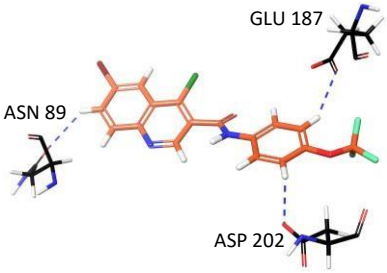


(e)

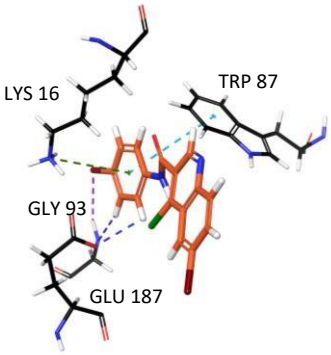


Figure S2. Interaction of the ligands with ATR (a) 6a (b) 6b (c) 6b’ (d) 6d (e) 6e

Table S2. Summary of interactions of the ligands with ATR

Ligand	Interacting residues	Type of interactions
6a	ASN 89, GLU 187, ASP 202	Aromatic hydrogen bonding
6b	LYS 35, ASN 204, GLU 187	Halogen bonding, hydrogen bonding
6b’	ASP 202, TRP 87	Hydrogen bonding, aromatic hydrogen bonding, π-π stacking
6d	ASN 89, GLU 187, ASP 202	Aromatic hydrogen bonding
6e	GLY 93, LYS 16, TRP 87, GLU 187	Halogen bonding, π-cation, π-π stacking, aromatic hydrogen bonding

Docking poses of the ligands with DNA-PKcs

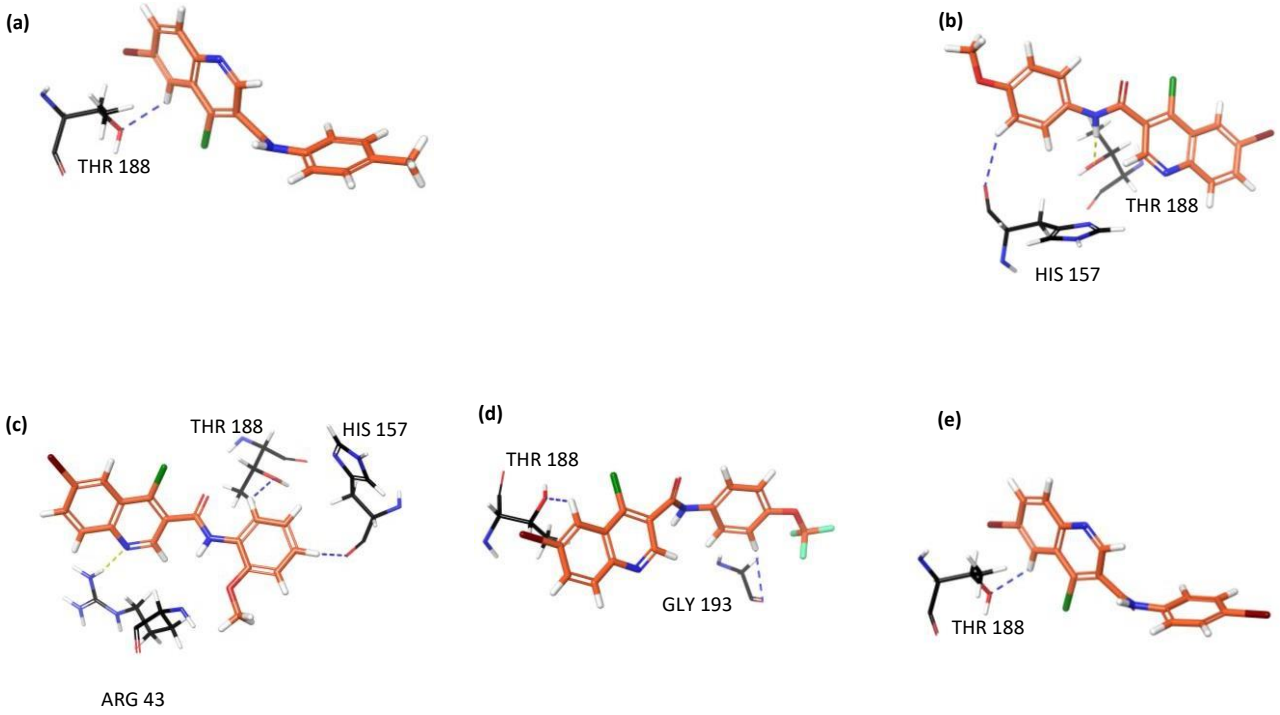


Figure S3. Interaction of the ligands with DNA-PKcs (a) 6a (b) 6b (c) 6b’ (d) 6d (e) 6e

Table S3. Summary of interactions of the ligands with DNA-PKcs

Ligand	Interacting residues	Type of interactions
6a	THR 188	Aromatic hydrogen bonding
6b	THR 188, HIS 157	Hydrogen bonding, aromatic hydrogen bonding
6b’	ARG 43, THR 188, HIS 157	Hydrogen bonding, aromatic hydrogen bonding
6d	THR 188, GLY 193	Aromatic hydrogen bonding
6e	THR 188	Aromatic hydrogen bonding

Docking poses of the ligands with mTOR

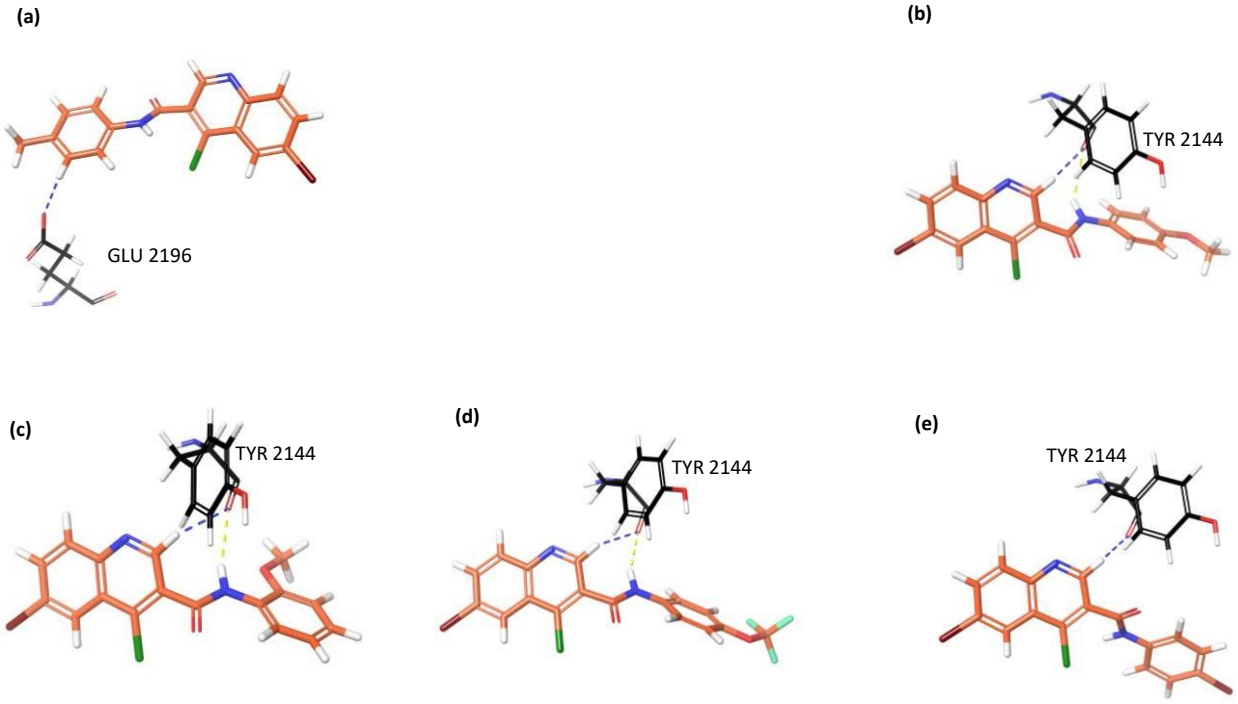


Figure S4. Interaction of the ligands with mTOR (a) 6a (b) 6b (c) 6b' (d) 6d € 6e

Table S4. Summary of interactions of the ligands with mTOR

Ligand	Interacting residues	Type of interactions
6a	GLU 2196	Aromatic hydrogen bonding
6b	TYR 2144	Aromatic hydrogen bonding, hydrogen bonding
6b'		Aromatic hydrogen bonding, hydrogen bonding
6d		Aromatic hydrogen bonding, hydrogen bonding
6e		Aromatic hydrogen bonding

Docking poses of the ligands with PI3Kγ

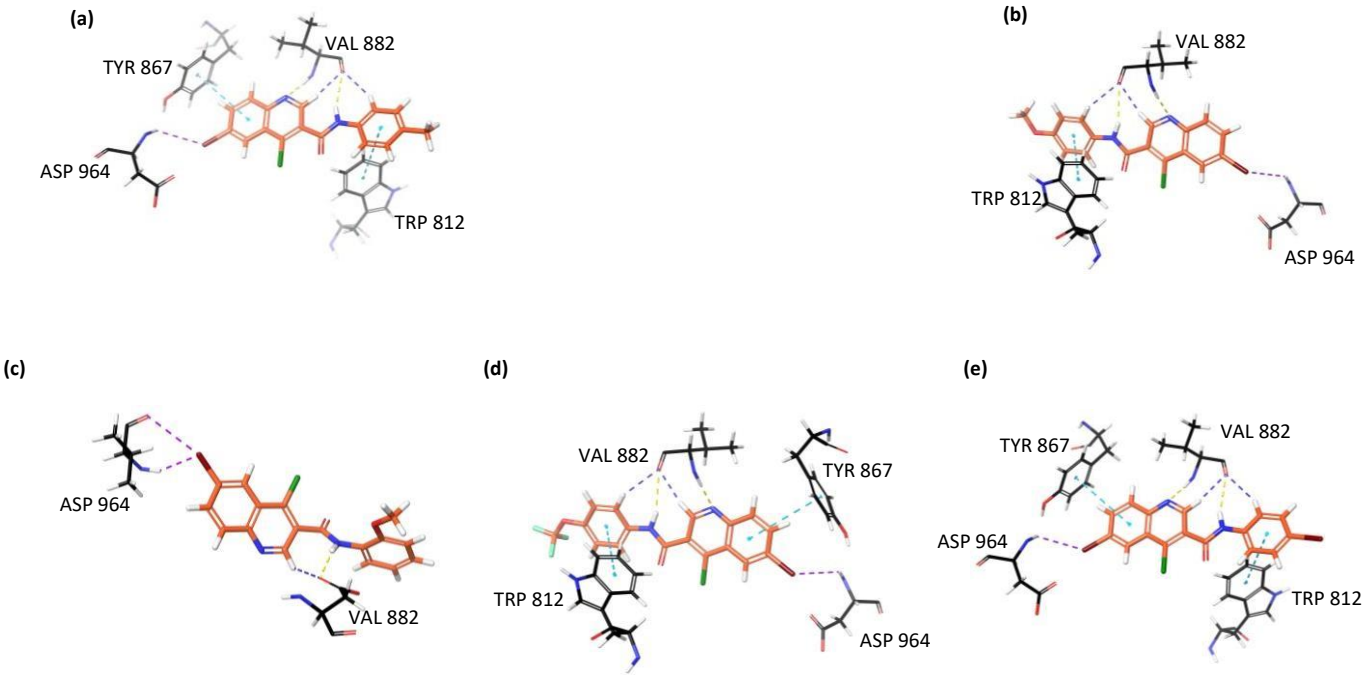


Figure S5. Interaction of the ligands with PI3Kγ (a) 6a (b) 6b (c) 6b' (d) 6d (e) 6e

Table S5. Summary of interactions of the ligands with PI3Kγ

Ligand	Interacting residues	Type of interactions
6a	ASP 964, TYR 867, VAL 882, TRP 812	Halogen bonding, π-π stacking, hydrogen bonding, aromatic hydrogen bonding
6b	ASP 964, VAL 882, TRP 812	Halogen bonding, hydrogen bonding, aromatic hydrogen bonding, π-π stacking
6b'	ASP 964, VAL 882	Halogen bonding, hydrogen bonding, aromatic hydrogen bonding
6d	ASP 964, TYR 867, VAL 882, TRP 812	Halogen bonding, π-π stacking, hydrogen bonding, aromatic hydrogen bonding
6e	ASP 964, TYR 867, VAL 882, TRP 812	Halogen bonding, π-π stacking, hydrogen bonding, aromatic hydrogen bonding

Table S6. Rewards and penalties for the ligand 6f against ATR, DNA-PKcs, and mTOR

Property	ATR (6f)	DNA-PKcs (6f)	mTOR (6f)
LipophilicEvdW	-3.04	-4.24	-3.90
PhobEnHB	0	0	0
HBond	0	0	0
Electro	0.05	0.07	-0.09
Penalties	0.18	0.29	1.01
ExposPenal	0	0.30	1.28

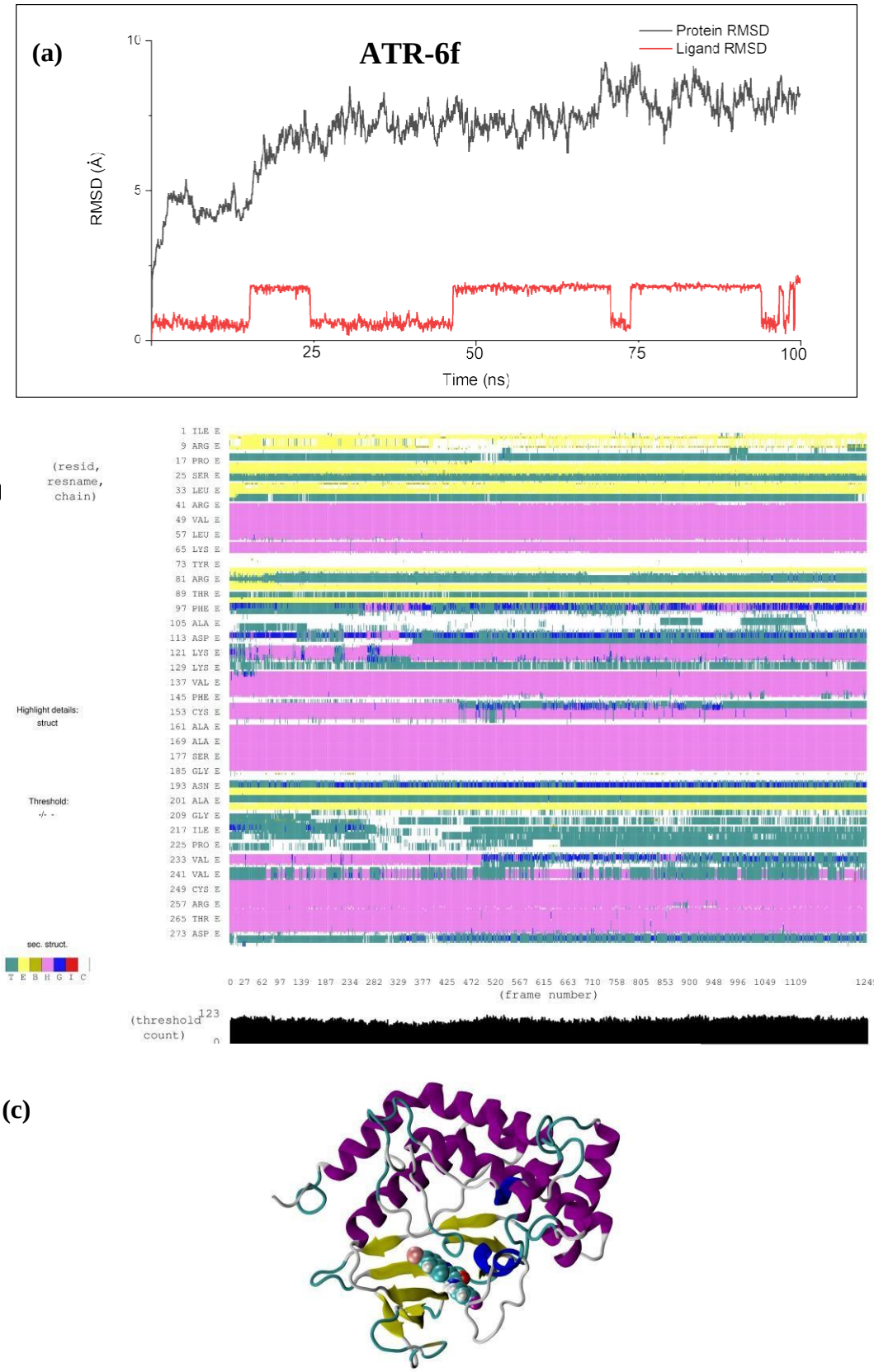


Figure S6. MD simulation analysis of 6f with the ATR (a) RMSD (b) Timeline analysis of Protein Secondary structure (c) Representative structure of ATR-6f complex (after 100 ns simulation).

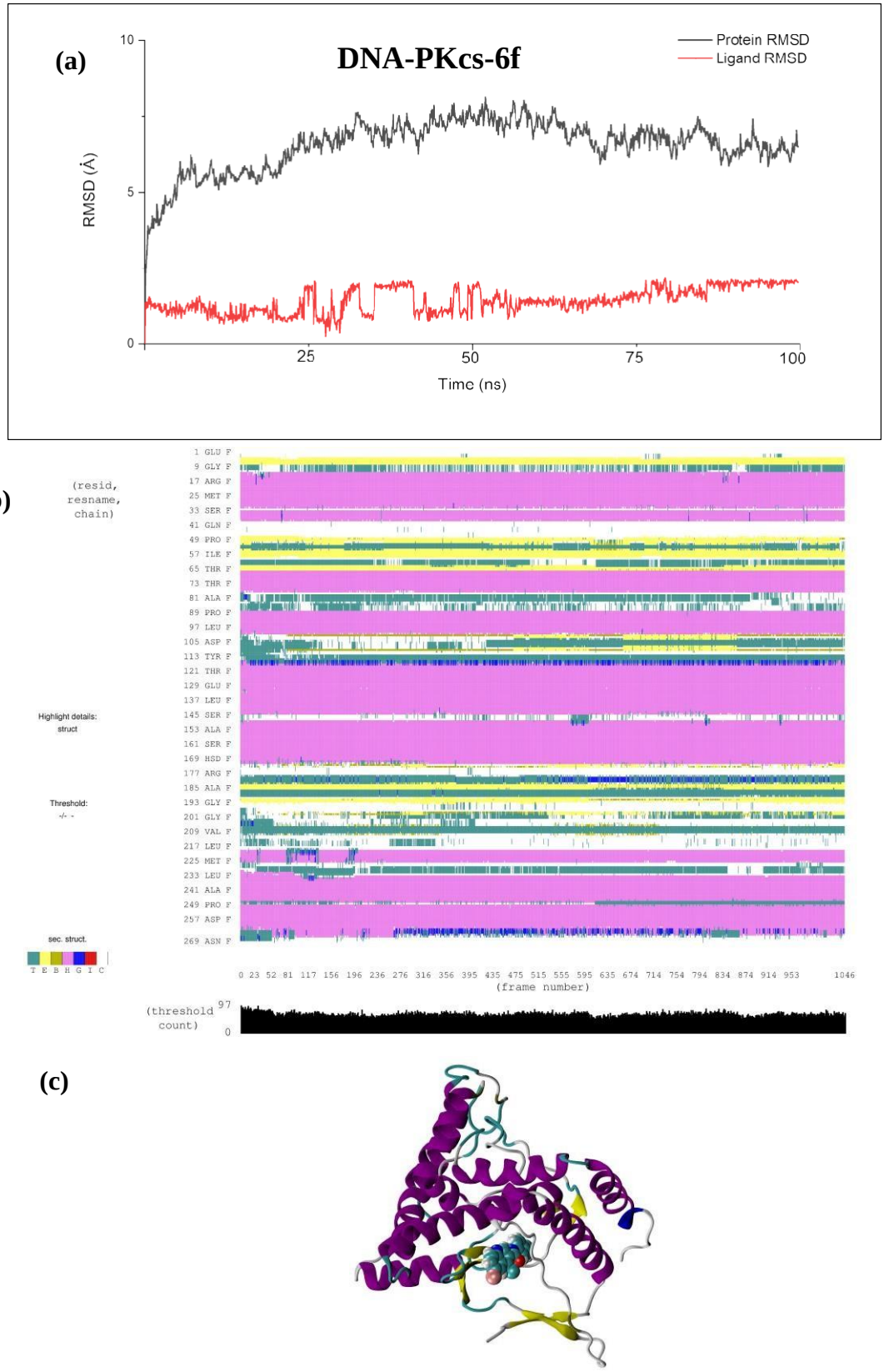
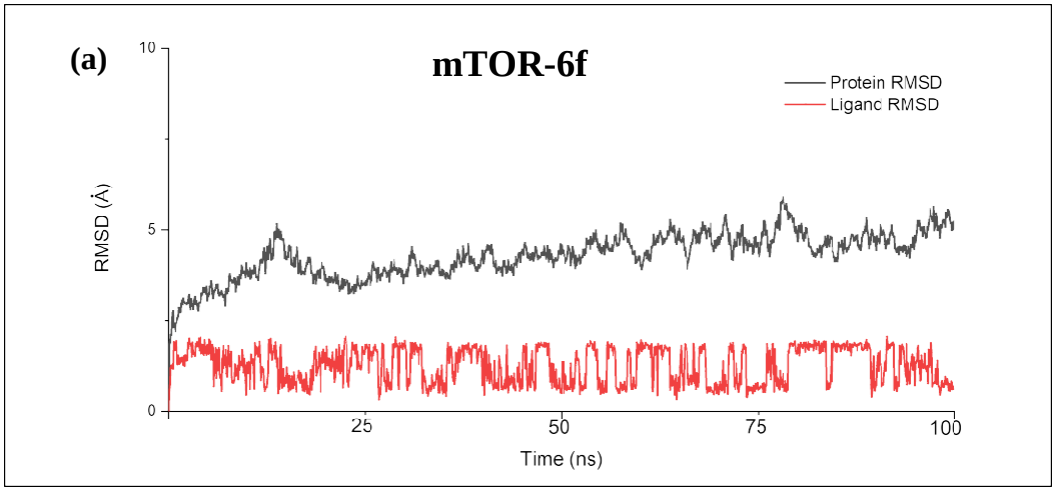
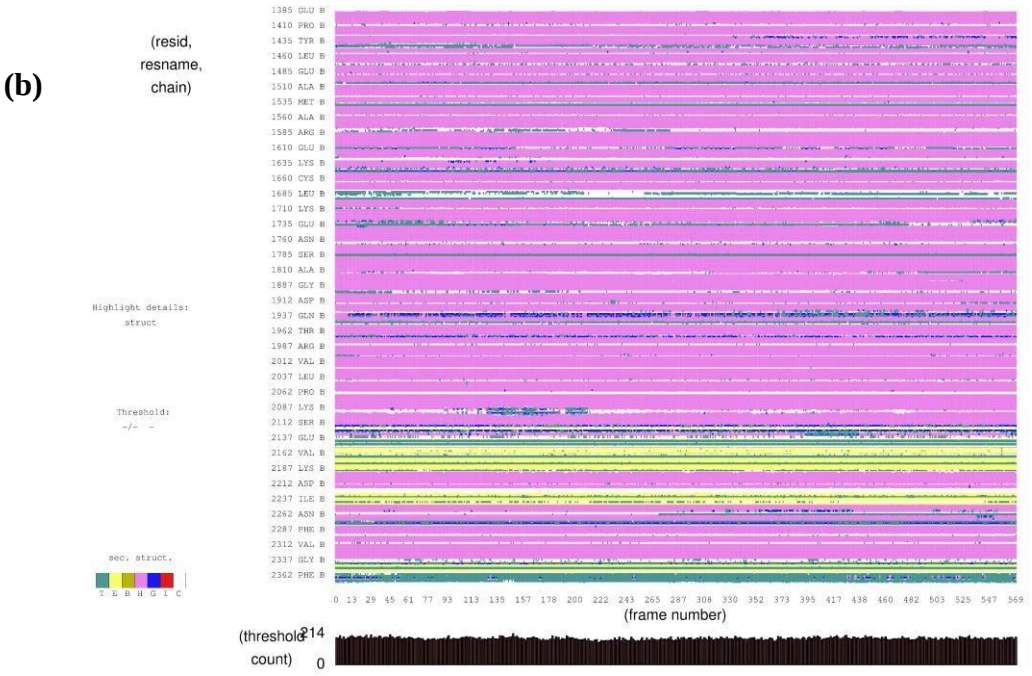


Figure S7. MD simulation analysis of 6f with the DNA-PKcs (a) RMSD (b) Timeline analysis of Protein Secondary structure (c) Representative structure of DNA-PKsc-6f complex (after 100 ns simulation).





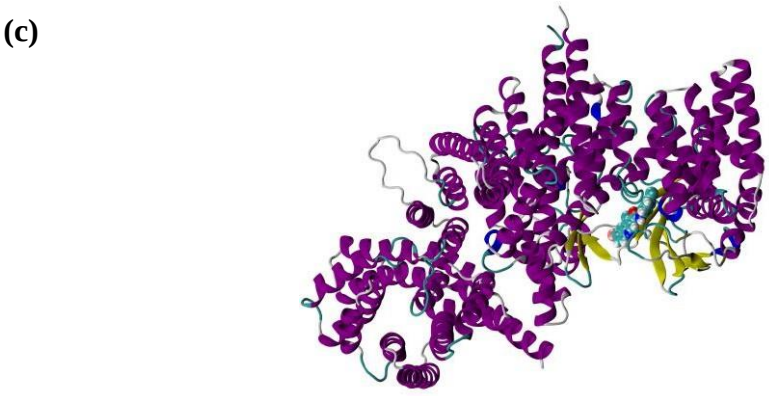


Figure S8. MD simulation analysis of 6f with the mTOR (a) RMSD (b) Timeline analysis of Protein Secondary structure (c) Representative structure of mTOR-6f complex (after 100 ns simulation).

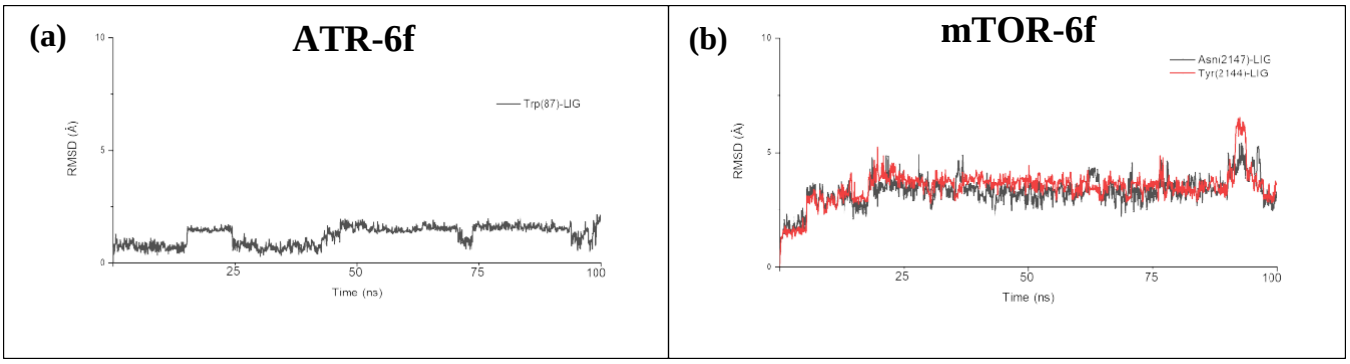


Figure S9. RMSD plot for binding site residues and ligand (6f) a) ATR-6f complex; RMSD plot for key binding residues and ligand (6f) b) mTOR-6f complex; RMSD plot for key binding residues and ligand (6f)