Identification of selective cyclin-dependent kinase 2 inhibitor from the library of pyrrolone-fused benzosuberene compounds: an in silico exploration

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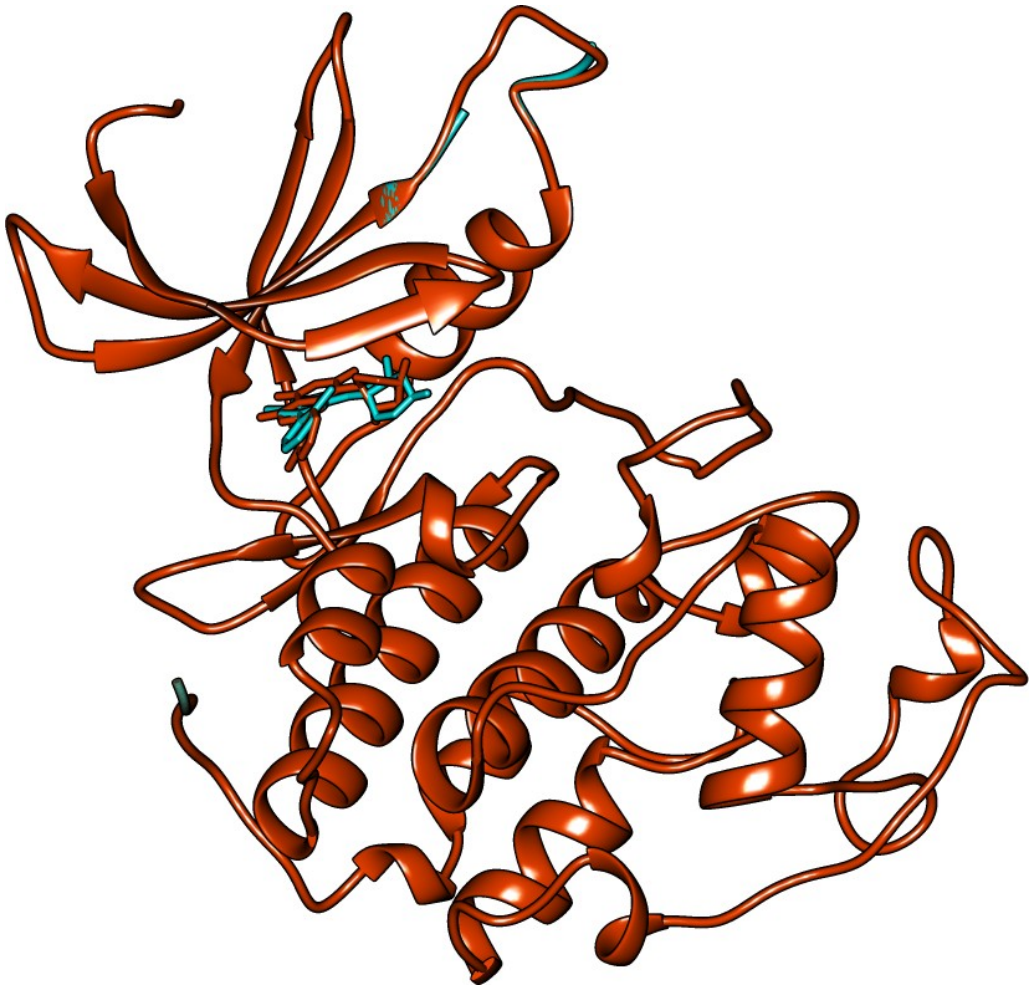


Figure S1. Superimposed protein 3-dimensional X-ray crystal structures. Color for experimental (cyan) and docked (dark red).

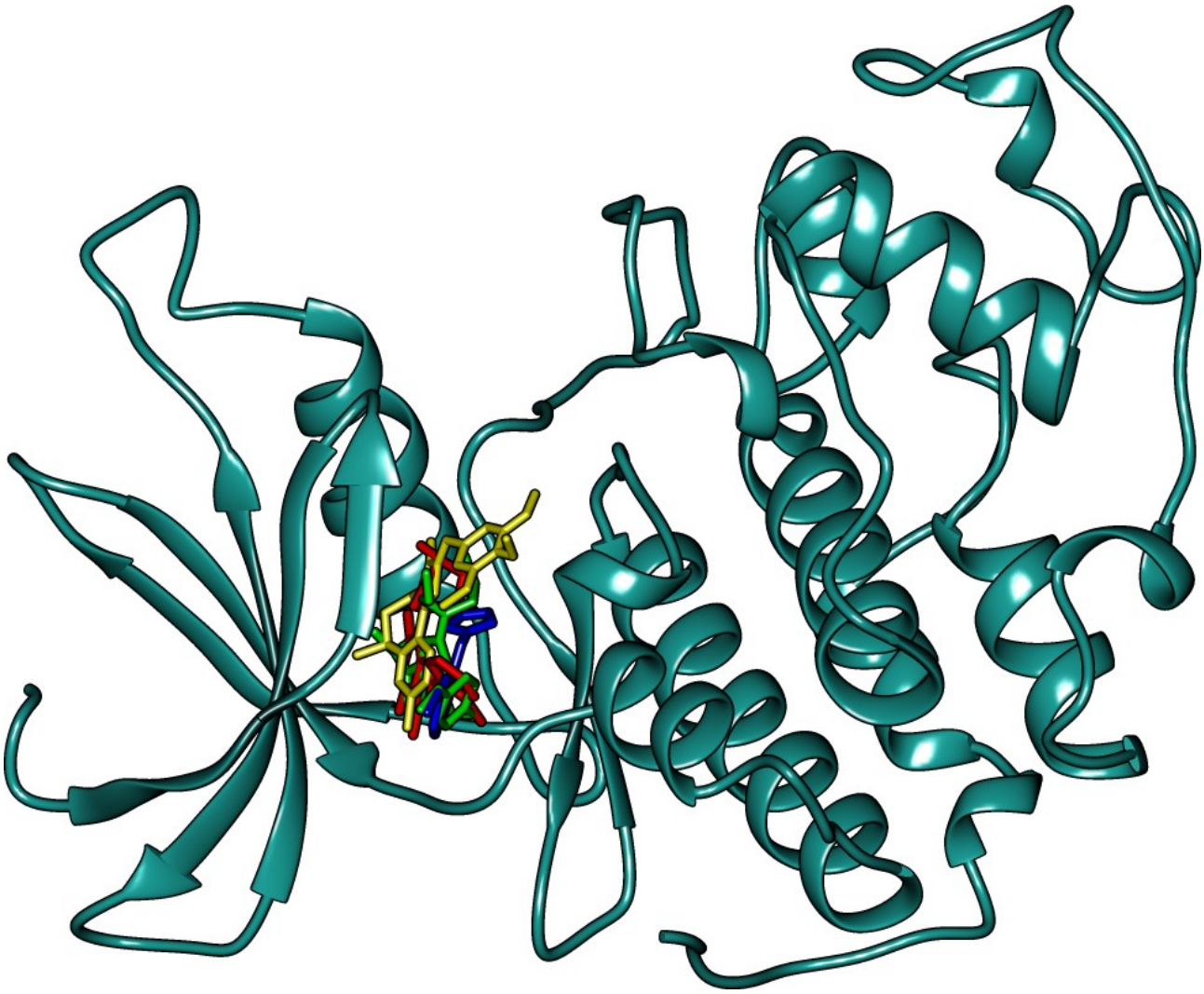


Figure S2: The superimposed complexes indicating the location of the selected and standard ligands in the active site of the CDK2. Color coding as follows: Ligand2 (yellow), CVT-313 (green), SU9516 (blue), and Flavopiridol (red).

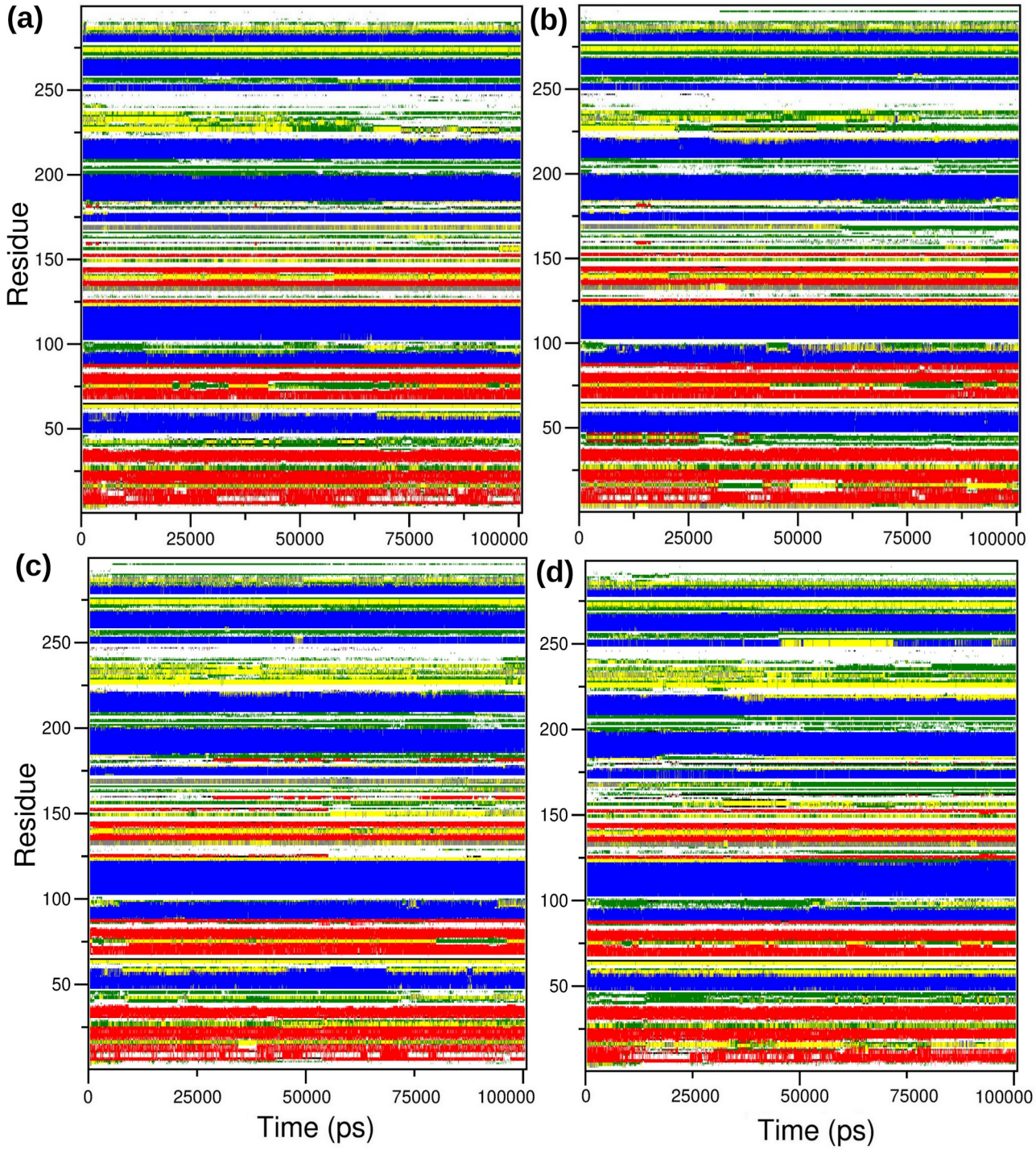
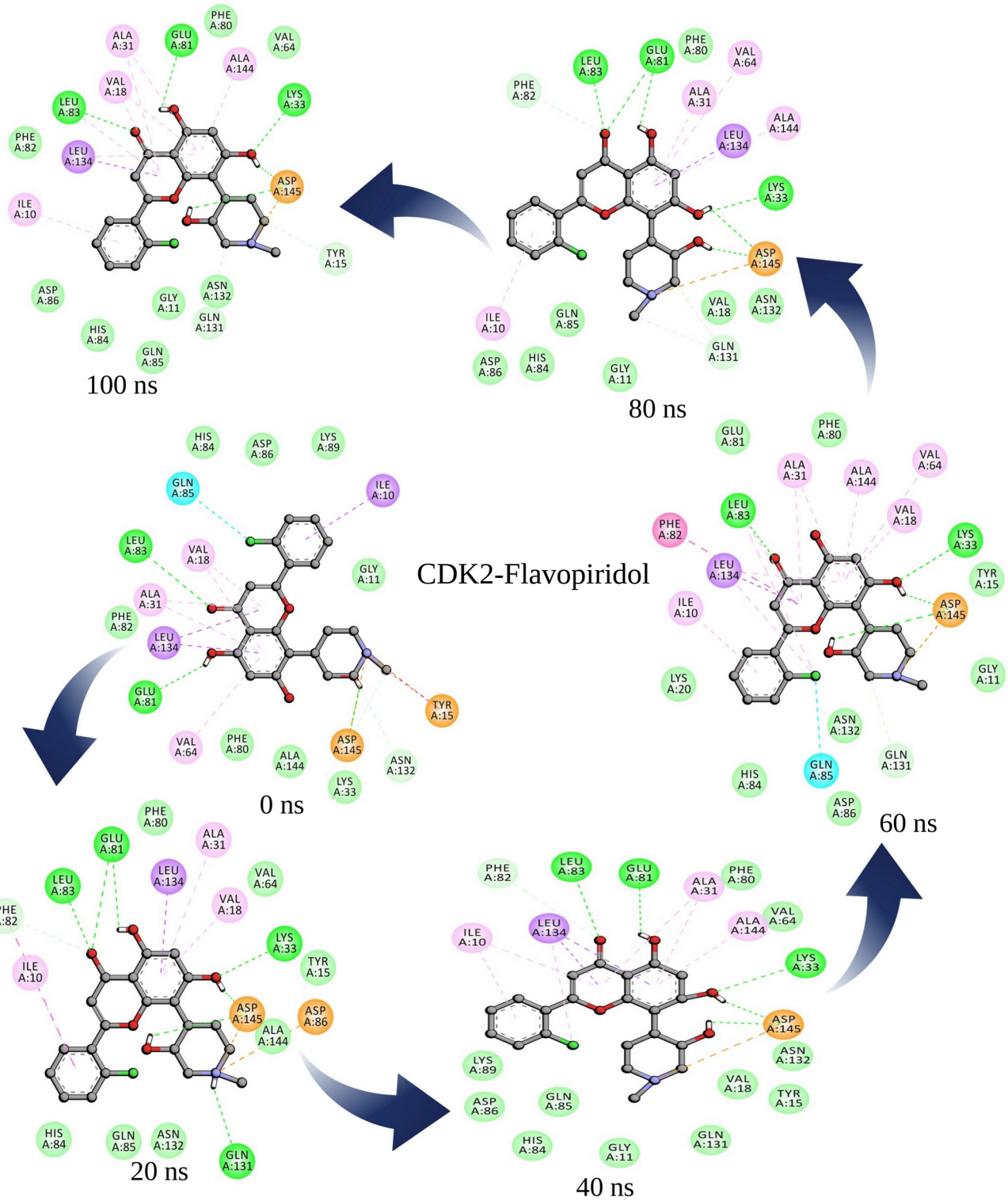
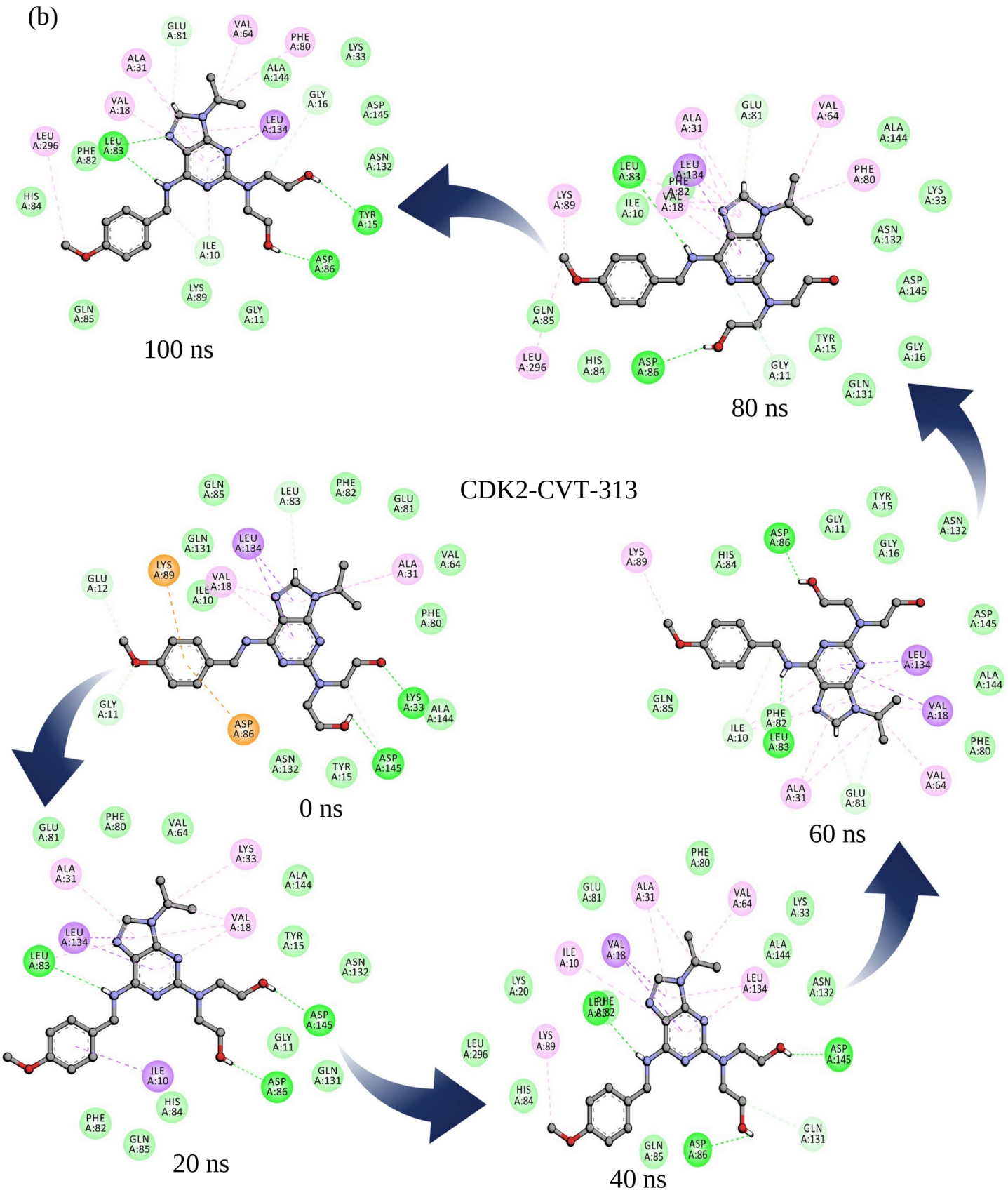


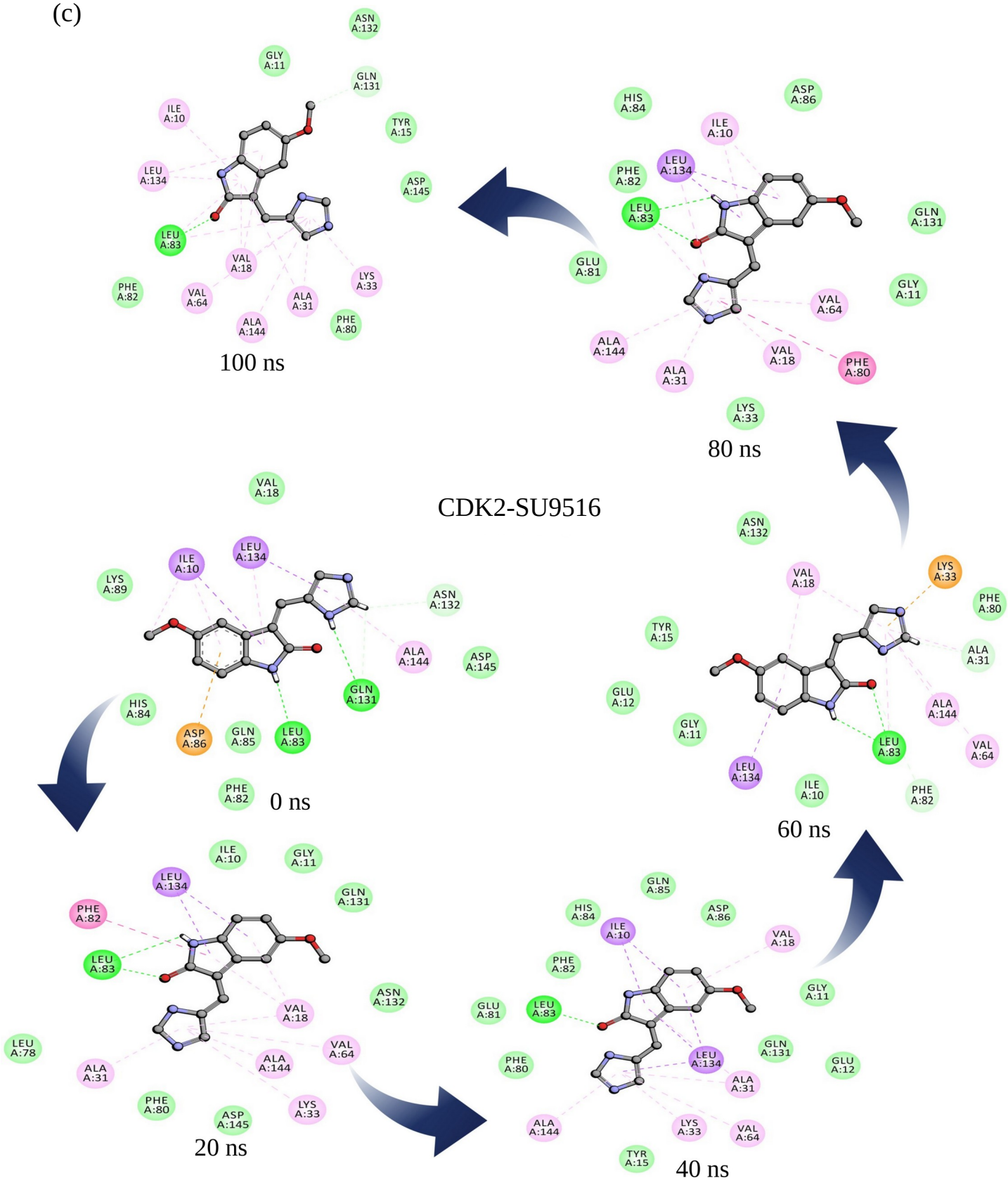
Figure S3. Time evolution of the secondary structural elements of CDK-2 complexes with (a) Flavopiridol (b) Ligand2, (c) SU9516 (d) CVT-313 at 300K (DSSP classification).

(a)




(b)
CDK2-CVT-313
100 ns
80 ns
60 ns
40 ns
20 ns
0 ns

(c)



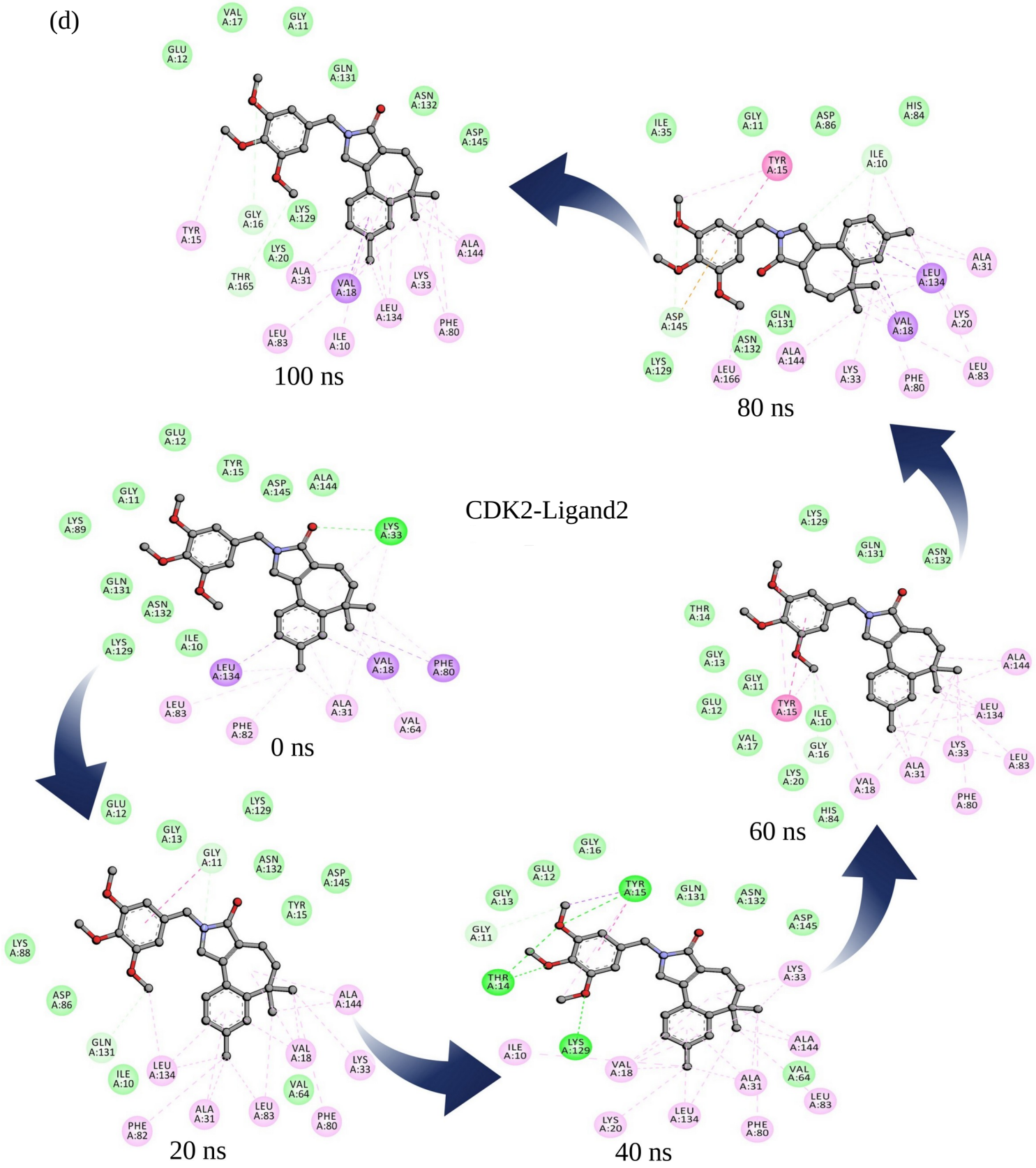


Figure S4: 2D plot showing interactions with residues of hinge, phosphate, solvent, ribose, and hydrophobic binding pockets at different time period of MD-simulations of the CDK2 visualized by Discovery studio.

Table S1: LE and Est. Affinity values for CDK1.

Molecules	LE	Estimated Affinity			
		pM	nM	μM	mM
Ligand-1	0.22				
Ligand-2	0.08				
Ligand-3	0.09				
Ligand-4	0.10				
Ligand-5	0.21				
Ligand-6	0.05				
Ligand-7	0.04				
Ligand-8	0.06				
Ligand-9	0.07				
Ligand-10	0.03				
Ligand-11	0.04				
Ligand-12	0.22				
Ligand-13	0.02				
Ligand-14	0.32				
Ligand-15	0.31				
Ligand-16	0.22				
Ligand-17	0.21				
Flavopiridol	0.02				
SU9516	0.31				
CVT-313	0.21				

Table S2: LE and Est. Affinity values for CDK2.

Molecules	LE	Estimated Affinity			
		pM	nM	µM	mM
Ligand-1	0.21				
Ligand-2	0.30				
Ligand-3	0.23				
Ligand-4	0.10				
Ligand-5	0.21				
Ligand-6	0.08				
Ligand-7	0.21				
Ligand-8	0.22				
Ligand-9	0.07				
Ligand-10	0.21				
Ligand-11	0.23				
Ligand-12	0.22				
Ligand-13	0.23				
Ligand-14	0.24				
Ligand-15	0.22				
Ligand-16	0.22				
Ligand-17	0.21				
Flavopiridol	0.11				
SU9516	0.22				
CVT-313	0.08				

Table S3: LE and Est. Affinity values for CDK9.

Molecules	LE	Estimated Affinity			
		pM	nM	µM	mM
Ligand-1	0.21				
Ligand-2	0.08				
Ligand-3	0.09				
Ligand-4	0.10				
Ligand-5	0.21				
Ligand-6	0.05				
Ligand-7	0.04				
Ligand-8	0.06				
Ligand-9	0.07				
Ligand-10	0.03				
Ligand-11	0.04				
Ligand-12	0.22				
Ligand-13	0.02				
Ligand-14	0.32				
Ligand-15	0.31				
Ligand-16	0.22				
Ligand-17	0.21				
Flavopiridol	0.02				
SU9516	0.31				
CVT-313	0.08				

Table S4. Region-wise distribution of residues in the active-site of CDKs.

CDKs	Hinge	Phosphate	Hydrophobic	Ribose	Solvent
CDK1	PHE80, GLU81, LEU83,VAL64, ALA145, ALA31	LYS33	VAL18, GLY11, ILE10	VAL18, ILE10, GLY11, GLN131, ALA144	ASP86, ILE10, GLN85, LYS89
CDK2	PHE80, GLU81, LEU83,VAL64, ALA145, ALA31	ASP145, LYS129, GLY13,LYS33	VAL18, GLY11, ILE10	VAL18, ILE10, GLY11, GLN131, ALA144	ASP86, ILE10, GLN85, LYS89
CDK9	CYS106, ASP104, PHE103	LYS48, ASP167	VAL79, ALA46	GLY26, ILE25	ILE25, ASP109