Supplementary materials:

1) Figures

Figure S1. 2D docking poses of compounds (A) MOR (B) TML (C) TMQ (D) galantamine in-to the galantamine binding site in choline esterase PDB: 1DX6.

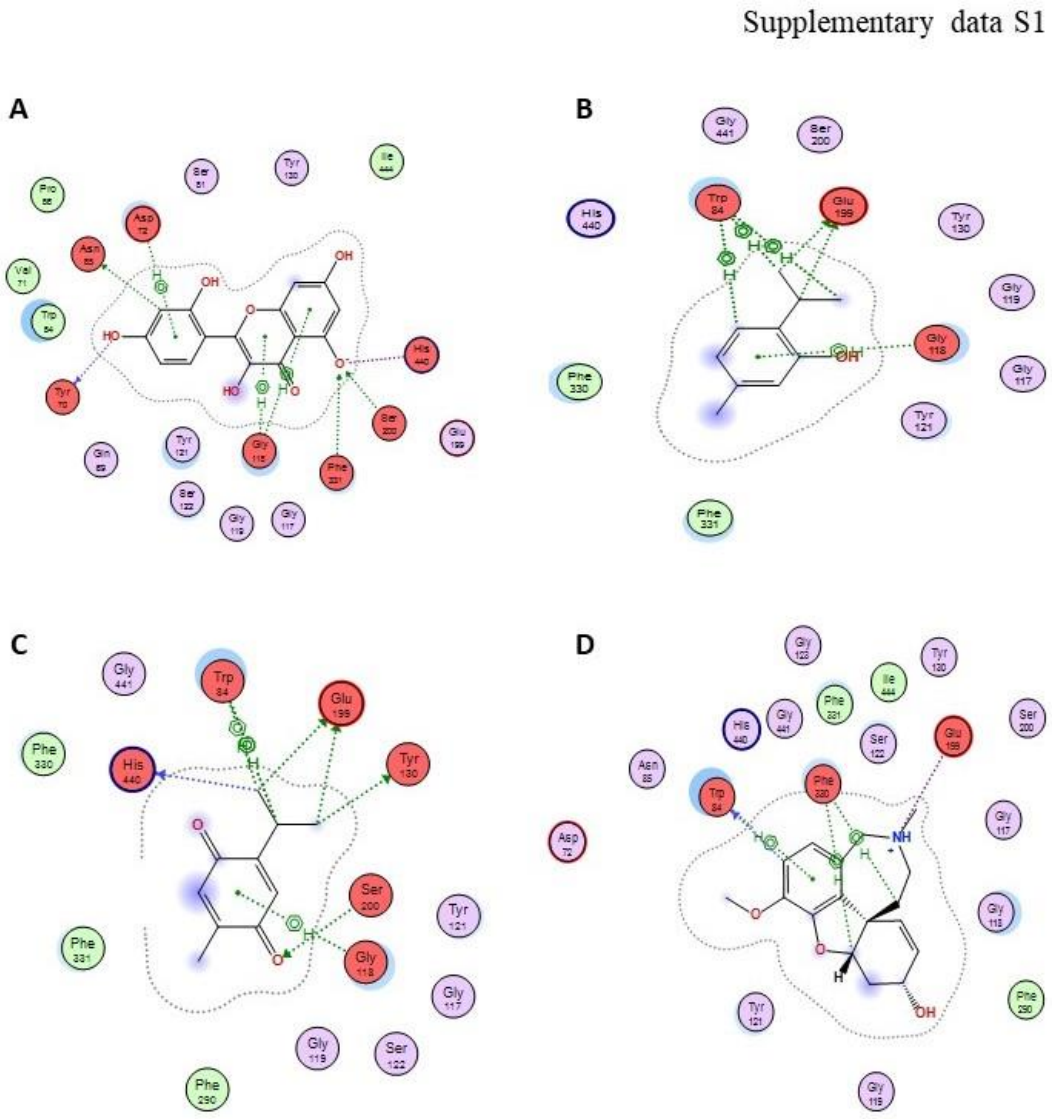


Figure S2. 2D docking poses of compounds (A) MOR (B) TML (C) TMQ (D) the ligand 3O0 into the 3O0 binding site in CDK5 PDB: 3O0G

Supplementary data S2

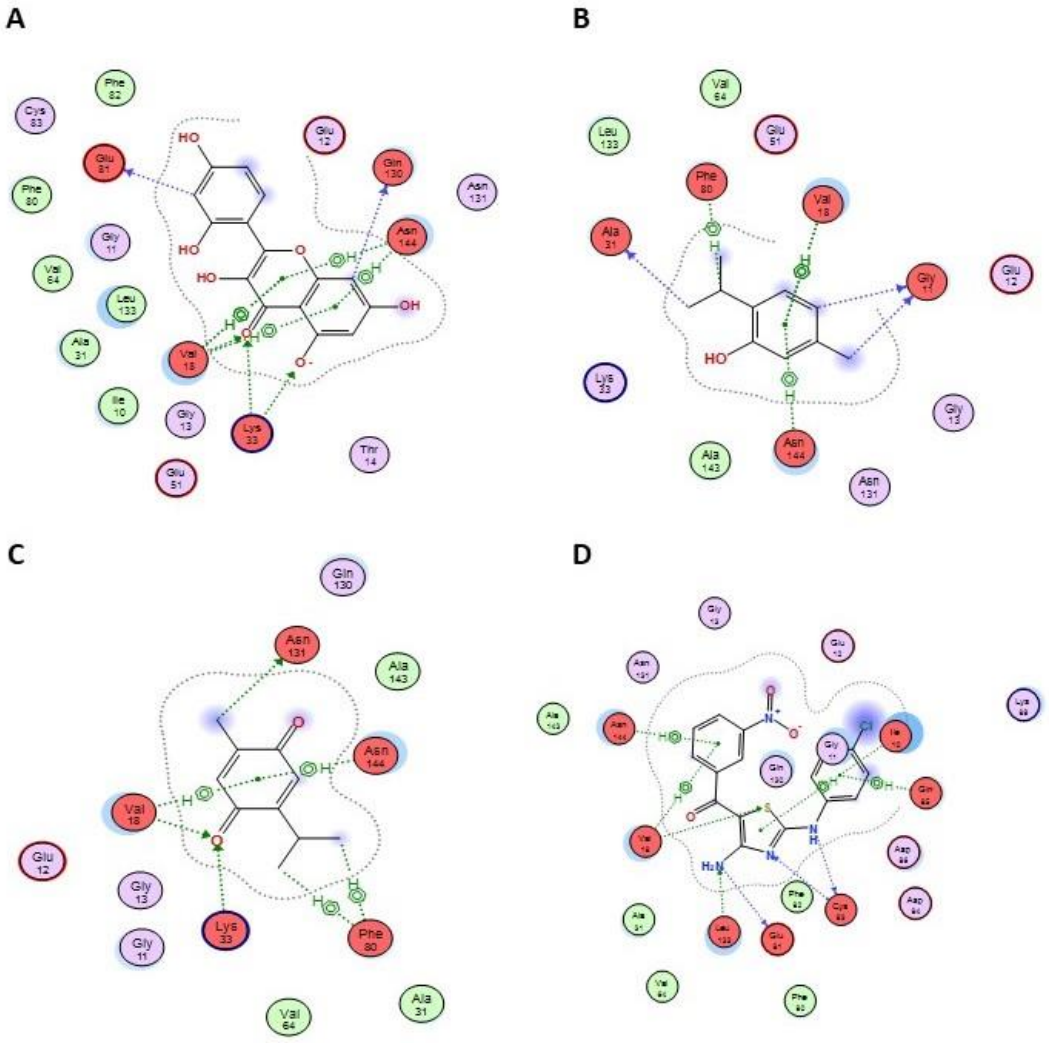


Figure S3. 2D docking poses of compounds (A) MOR (B) TML (C) TMQ (D) ligand 66F into the 66F binding site in BACE 1: 7D2V.

Supplementary data S3

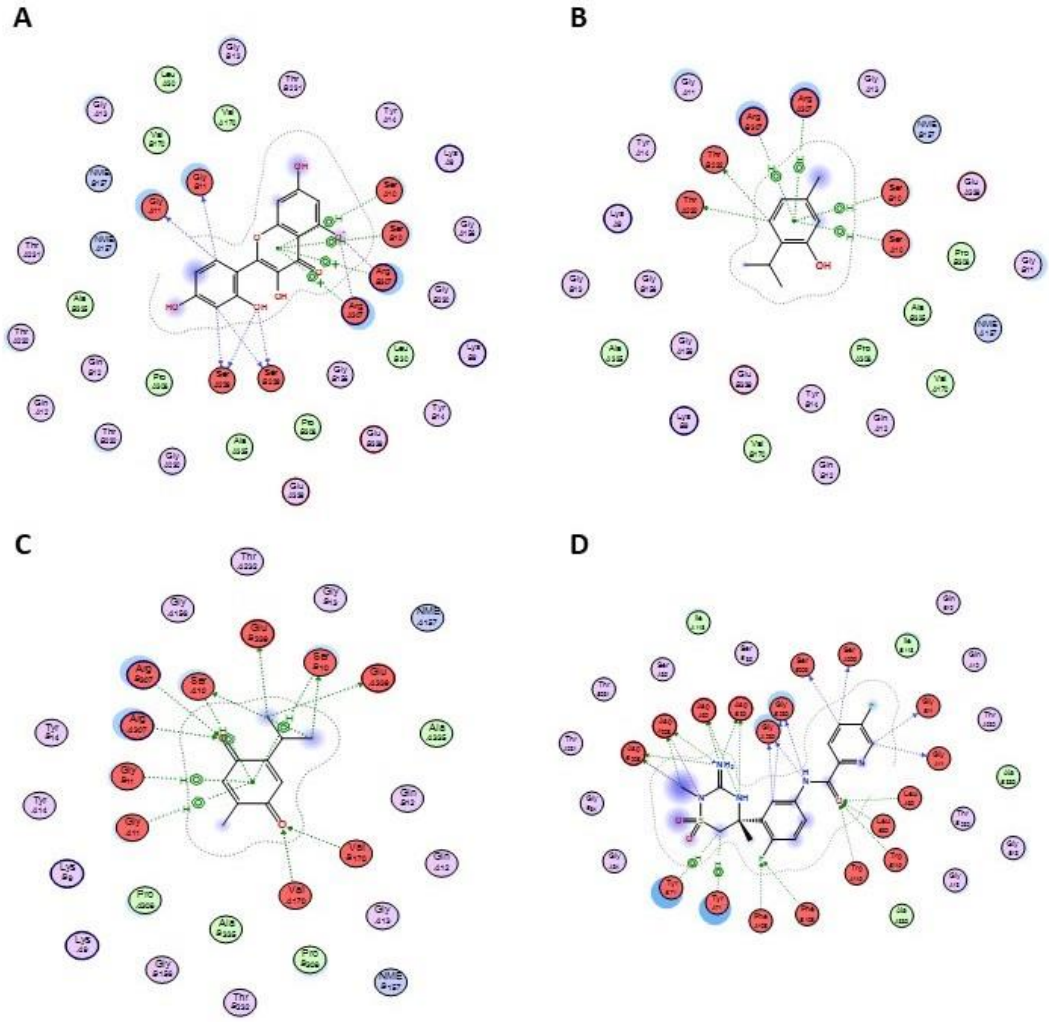


Figure S4. 2D docking of compounds (A) MOR (B) TML (C) TMQ (D) the ligand 65A into the 65A binding site in the glycogen synthase kinase 3 PDB: 5HLP.

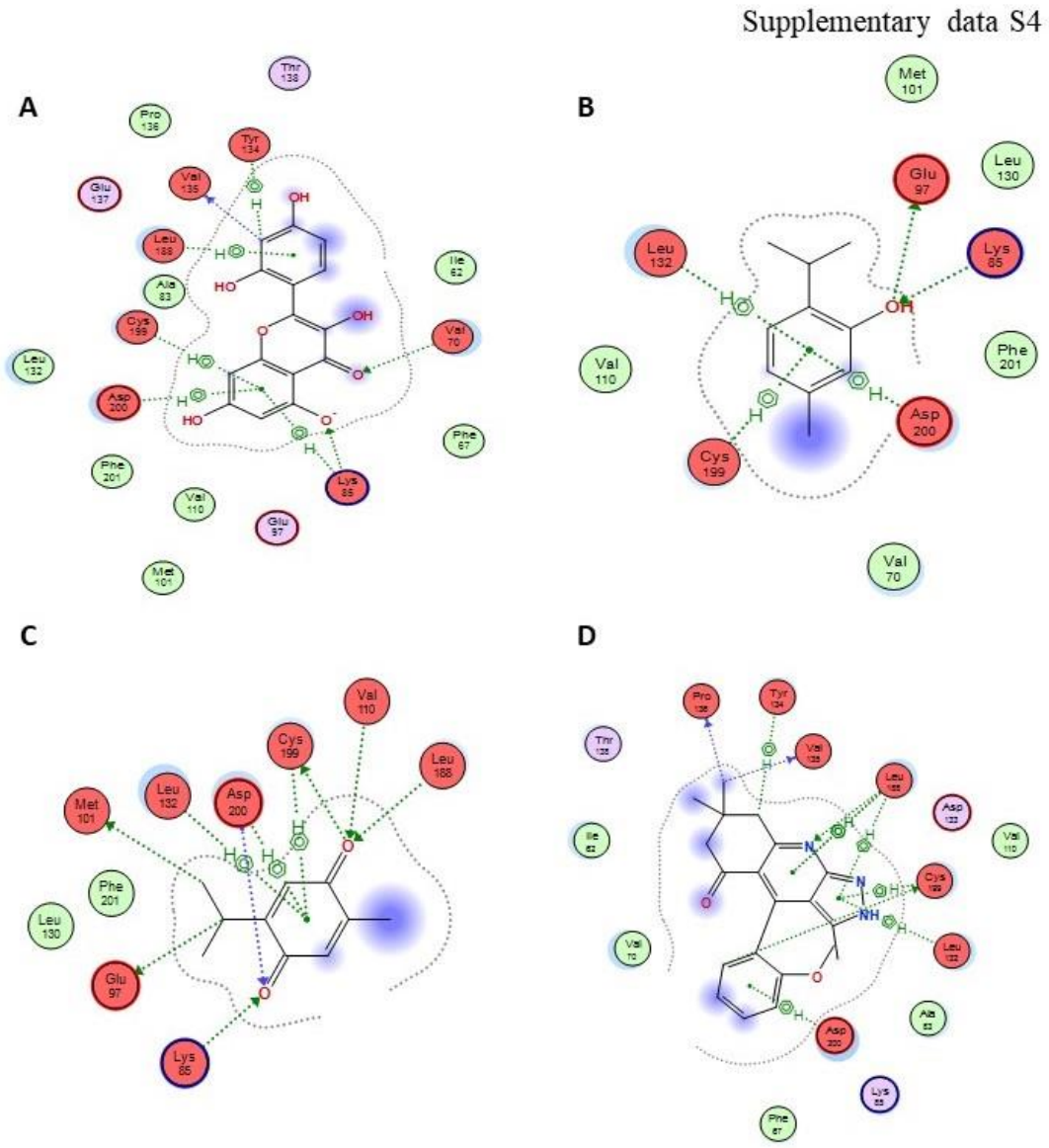


Figure S5. 2D docking of compounds (A) MOR (B) TML (C) TMQ (D) the ligand D8N into the D8N binding site in Keap1/5 complex (PDB ID 6FFM).

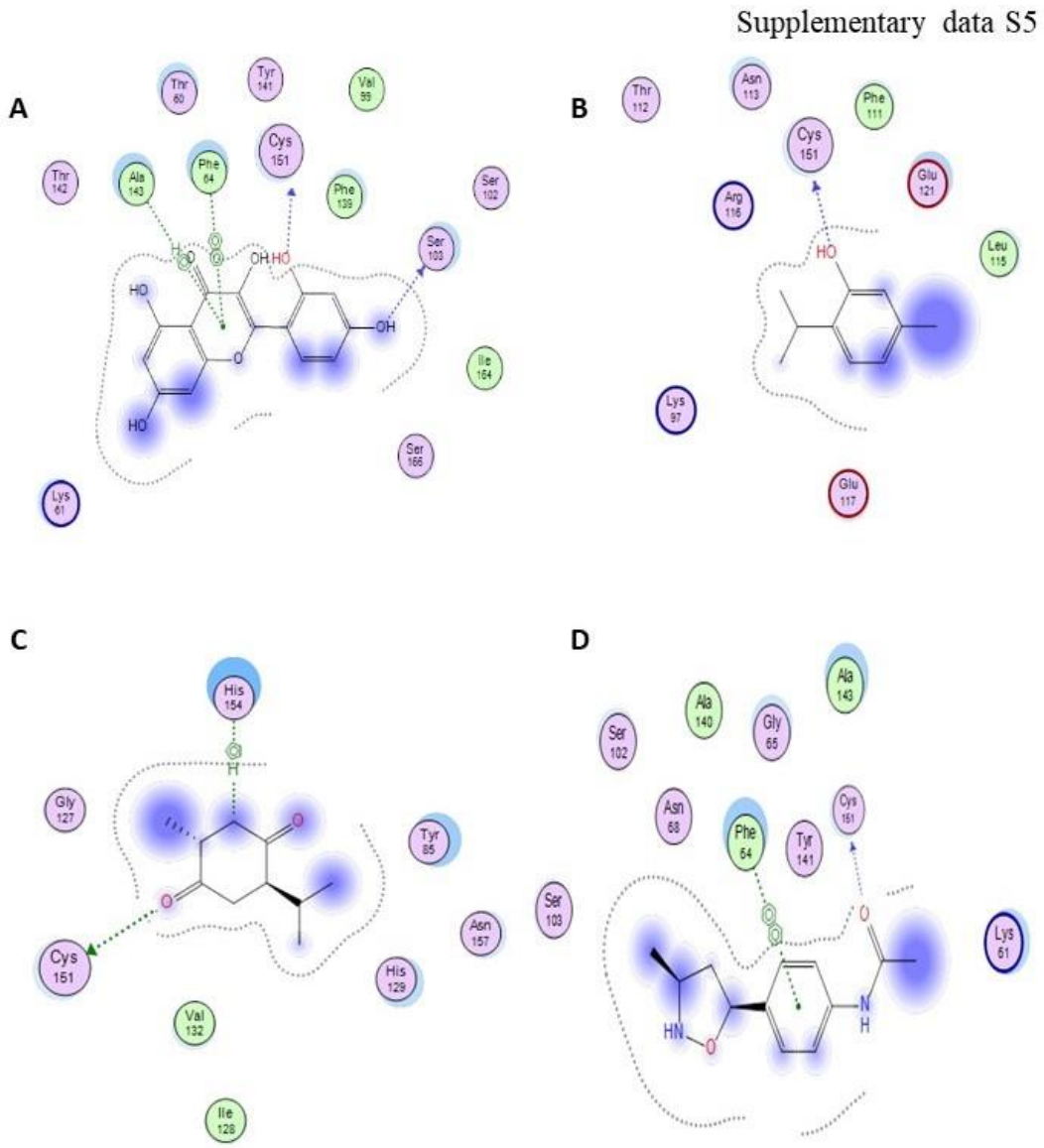


Figure S6. 3D docking poses of compounds (A) MOR (B) TML (C) TMQ (D) galantamine into the galantamine binding site in choline esterase PDB: 1DX6.

Supplementary data S6

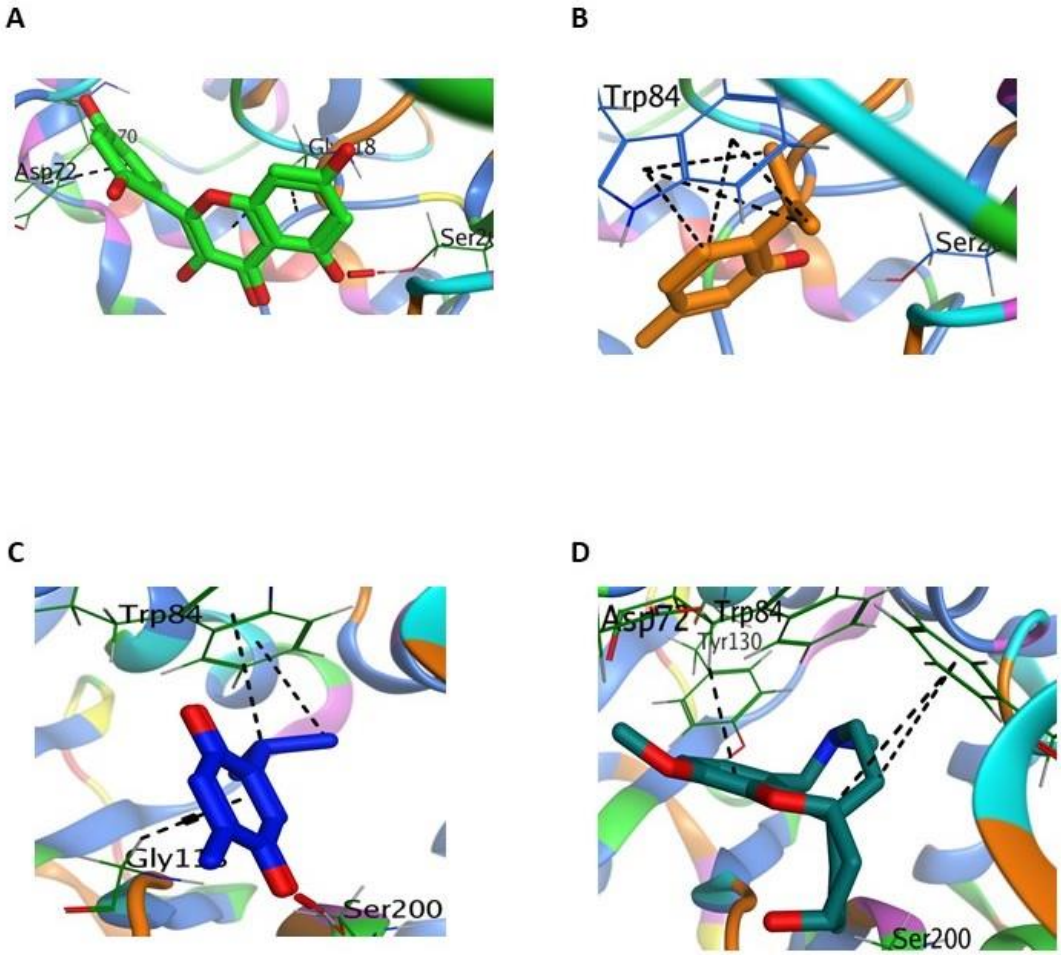


Figure S7. 3D docking poses of compounds (A) MOR (B) TML (C) TMQ (D) the ligand 3O0 into the 3O0 binding site in CDK5 PDB: 3O0G.

Supplementary data S7

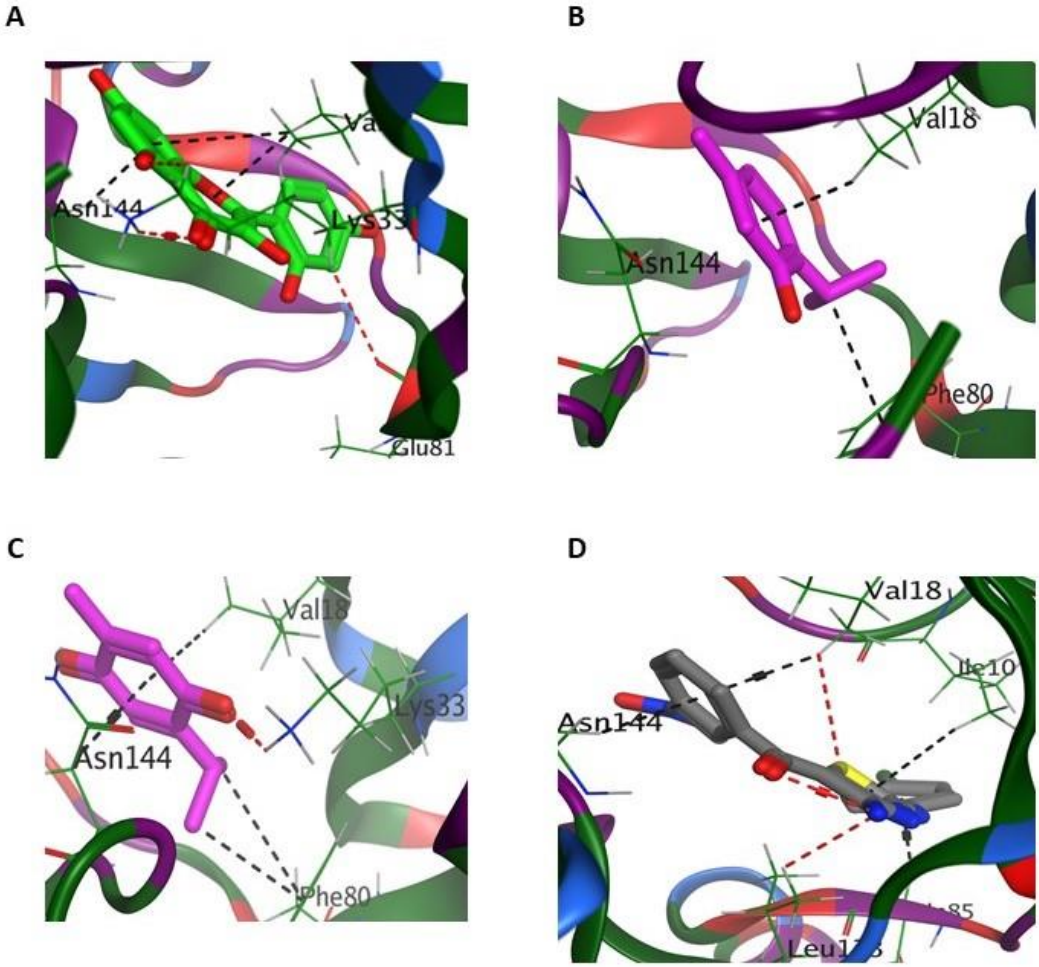


Figure S8. 3D docking poses of compounds (A) MOR (B) TML (C) TMQ (D) ligand 66F into the 66F binding site in BACE 1: 7D2V.

Supplementary data S8

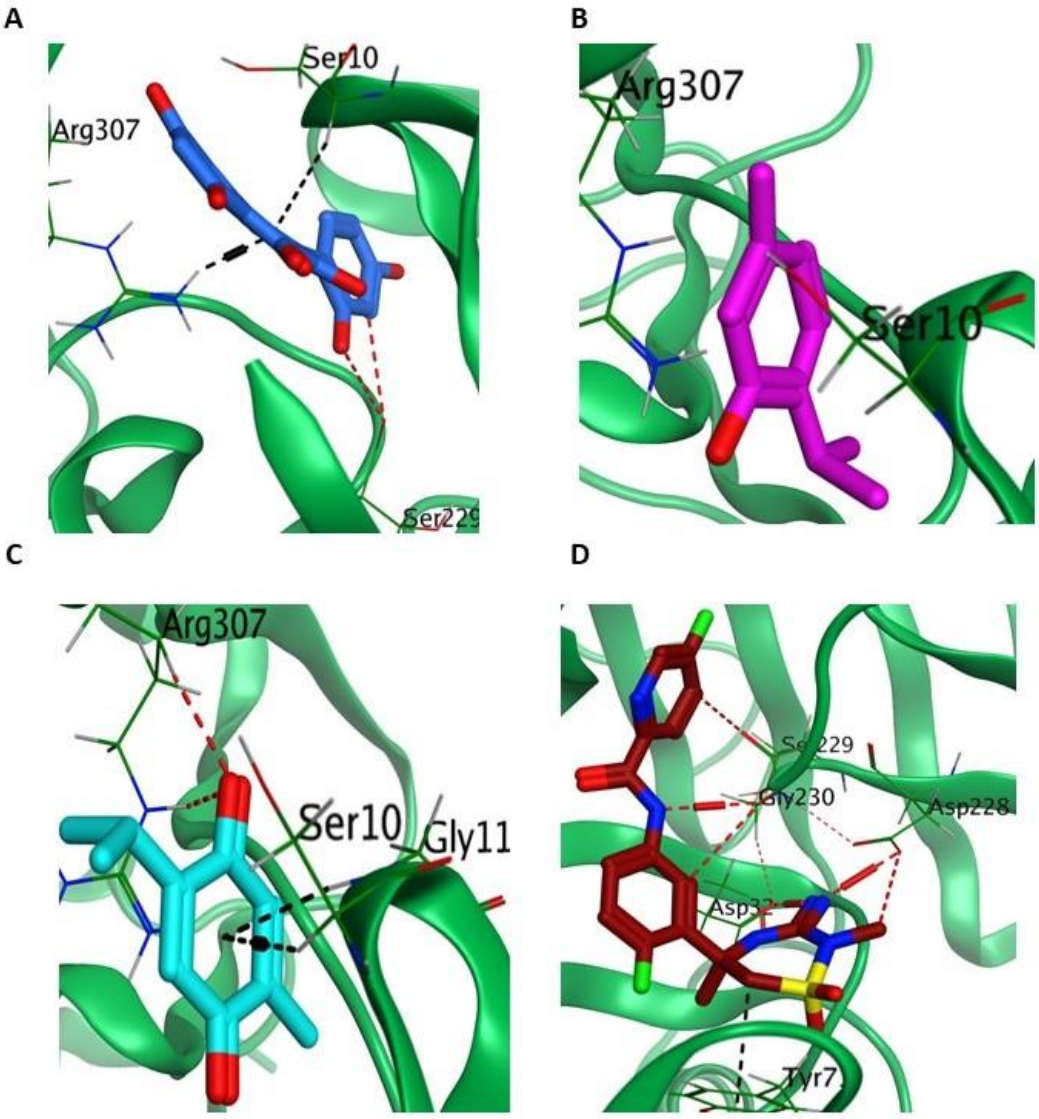


Figure S9. 3D docking of compounds (A) MOR (B) TML (C) TMQ (D) the ligand 65A into the 65A binding site in the glycogen synthase kinase 3 PDB: 5HLP.

Supplementary data S9

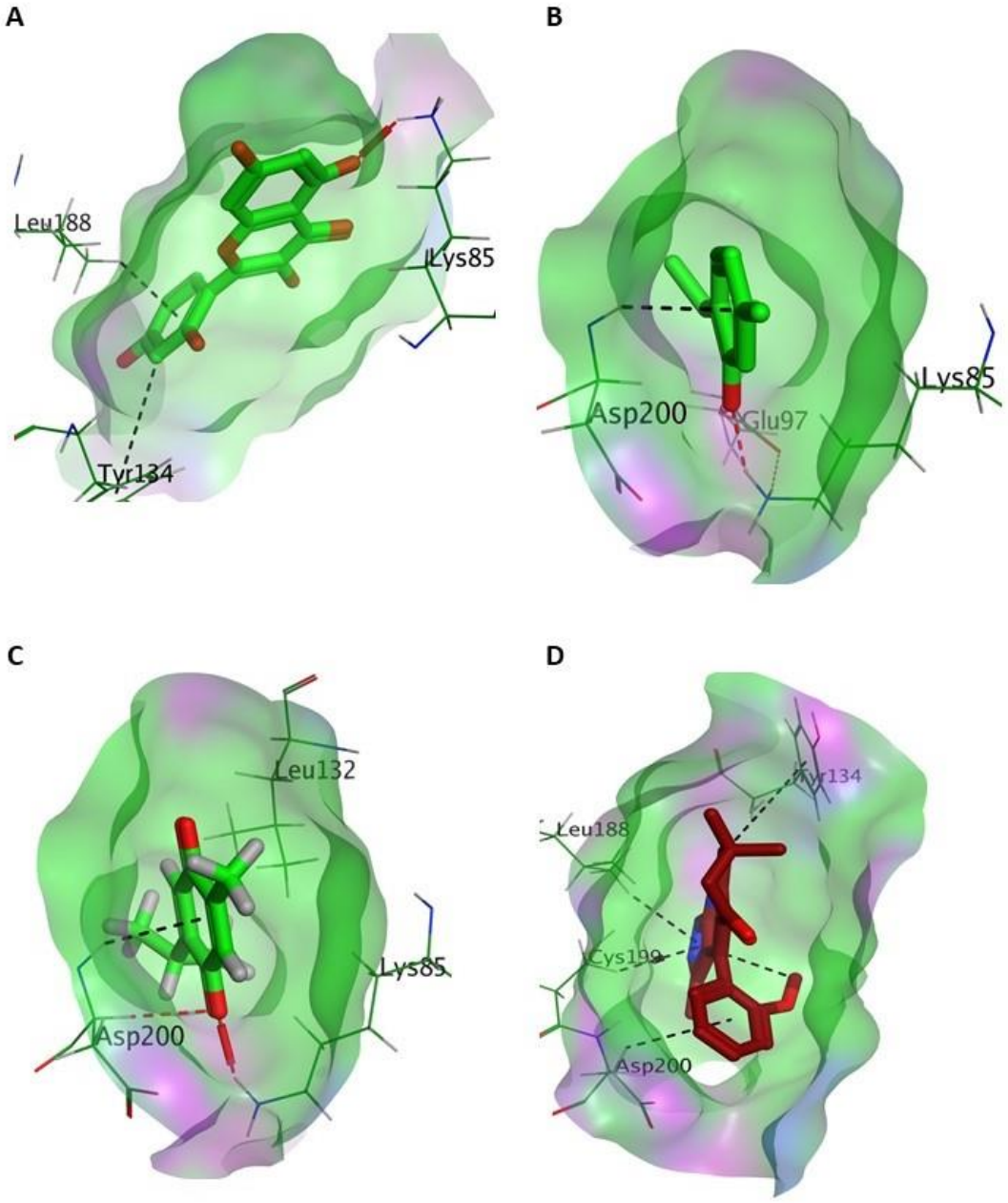
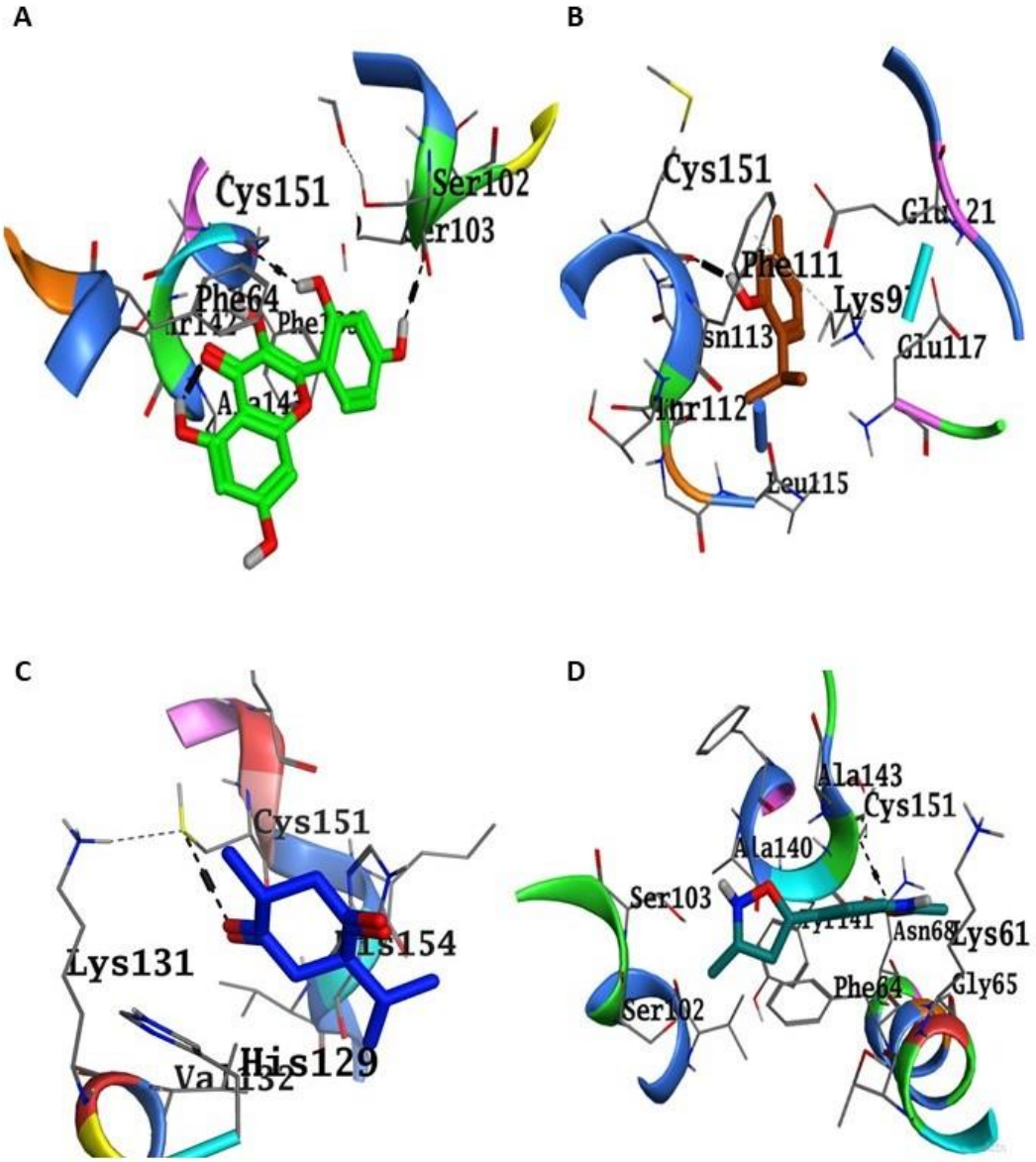


Figure S10. 3D docking of compounds (A) MOR (B) TML (C) TMQ (D) the ligand D8N into the D8N binding site in Keap1/5 complex (PDB ID 6FFM).

Supplementary data S10



2) Tables

Table. S1. Receptor interaction of compounds A-C and galantamine into the galantamine binding site in the choline esterase PDB: 1DX6.

Compound	S	E_conf	rmsd_refine	Receptor
	dG Kcal/mole	**Kcal/mole**		**Amino acid/Type of bonding/Distance (Å) / Binding Energy (Kcal/mole)**
1	-6.4961	-71.3709	1.7066	TYR 70/ H-donor/3.03/-2.5 ASN 85/H-donor/3.32/-0.1 SER 200/H-acceptor/2.76/-3.2 PHE 331/H-acceptor/4.11/-0.1 HIS 440/Ionic/3.08/-4.0 ASP 72/pi-H/3.74/-0.2 GLY 118/pi-H /3.75/-0.4 GLY 118/pi-H/ 4.17/ -0.4
2	-4.8590	-21.0856	1.8786	GLU 199/H-donor/3.31/-0.1 GLU 199/H-donor/3.73/-0.1 TRP 84/H-pi/3.78/-0.4 TRP 84/H-pi/ 4.67/-0.3 TRP 84/H-pi/4.11/-0.1 TRP 84/H-pi/4.67/-0.2 TRP 84/H-pi /4.81/-0.2 TRP 84/H-pi/4.21/-0.3 GLY 118/pi-H/4.77/-0.1
3	-5.3373	1.4910	1.6847	TYR 130/H-donor/3.64/-0.1 GLU 199/H-donor/3.56/-0.1 GLU 199/H-donor/3.55/-0.1 HIS 440/H-donor/3.68/-0.1 SER 200/H-acceptor/2.83/-2.0 TRP 84/H-pi/3.77/-0.1 TRP 84/H-pi/4.27/-0.2

				TRP 84/H-pi/3.87/-0.3 GLY 118/pi-H/3.60/-0.8
Galantamine	-7.1875	21.0709	1.4719	TRP 84/H-donor/3.39/-0.1 GLU 199/Ionic/3.91/-0.7 PHE 330/H-pi/4.75/-0.2 PHE 330/H-pi/4.62/-0.2 TRP 84/pi-H/3.86/-0.2

Table. S2. Receptor interaction of compounds 1-3 and the ligand 3O0 into the 3O0 binding site in the Cdk5 PDB: 3O0G.

Compound	S dG Kcal/mole	E_conf Kcal/mole	rmsd_refine	Receptor Amino acid/Type of bonding/Distance (Å) / Binding Energy (Kcal/mole)
1	-6.5722	-77.1360	1.5296	GLN 130/4.00/-0.1 GLU 81/H-donor/3.65/-0.2 LYS 33/H-acceptor/3.16/-0.2 VAL 18/H-acceptor/3.90/-0.1 LYS 33/H-acceptor/3.61/-1.0 LYS 33/Ionic/2.91/-5.1 VAL 18/pi-H/3.96/-0.1 VAL 18/pi-H/4.08/-0.5 VAL 18/pi-H/4.75/-0.2 ASN 144/pi-H/4.34/-0.1 ASN 144/pi-H/3.49/-0.3
2	-5.4249	-20.2428	0.8701	ALA 31/H-donor/4.12/-0.1 GLY 11/H-donor/3.47/-0.1 GLY 11/H-donor/3.62/-0.1 PHE 80/H-pi/3.68/-0.5 VAL 18/pi-H/3.63/-0.5 VAL 18/pi-H/4.27/-0.1 ASN 144/pi-H/3.97/-0.1
3	-5.3995	1.5897	1.6084	ASN 131/H-donor/3.65/-0.1 VAL 18/H-acceptor/3.51/-0.1 LYS 33/H-acceptor/3.08/-1.5 PHE 80/H-pi/4.36/-0.3 PHE 80/H-pi/3.66/-0.5 VAL 18/pi-H/4.33/-0.5 ASN 144/pi-H/3.63/-0.7

Ligand	-7.7325	-28.5348	1.8423	CYS 83/H-donor/3.14/-2.0 CYS 83/H-donor/3.14/-2.0 GLU 81/H-donor/3.49/-0.4 GLU 81/H-donor/3.49/-0.4 VAL 18/H-acceptor/4.32/-0.2 VAL 18/H-acceptor/4.36/-0.2 CYS 83/H-acceptor/3.86/-0.3 CYS 83/H-acceptor/3.86/-0.3 LEU 133/H-acceptor/3.58/-0.2 LEU 133/H-acceptor/3.51/-0.2 ILE 10/pi-H/4.46/-0.4 VAL 18/pi-H/4.25/-0.7 GLN 85/pi-H/3.81/-1.0 ASN 144/pi-H/3.99/-0.2 ILE 10/pi-H/4.56/-0.5 VAL 18/pi-H/4.22/-0.7 GLN 85/pi-H/3.81/-1.0 ASN 144/pi-H/3.95/-0.3

Table. S3. Receptor interaction of compounds 1-3 and the ligand 66F into the 66F binding site in the BACE 1, PDB: 7D2V.

Compound	S dG Kcal/mole	E_conf Kcal/mole	rmsd_refine	Receptor Amino acid/Type of bonding/Distance (Å) / Binding Energy (Kcal/mole)
1	-5.6644	-74.9125	1.3282	GLY 11/H-donor/3.13/-0.1 GLY 11/H-donor/3.13/-0.1 SER 229/H-donor/3.51/-0.4 SER 229/H-donor/3.51/-0.4 SER 229/H-donor/3.32/-0.4 SER 229/H-donor/3.32/-0.4 ARG 307/Ionic/3.80/-1.0 ARG 307/Ionic/3.80/-1.0 SER 10/pi-H/4.62/-0.3 ARG 307/pi-cation/3.21/-2.1 SER 10 /pi-H/4.62/-0.3 ARG 307/pi-cation/3.21/-2.1
2	-5.39809465	1.68075621	-15.7678709	THR 232/H-donor/3.62/-0.1 THR 232/H-donor/3.62/-0.1 SER 10/pi-H/4.09/-0.1 ARG 307/ pi-H/ 4.97/-0.1 SER 10/pi-H/4.09/-0.1 ARG 307/pi-H/ 4.97/-0.1
3	-5.0369	3.0587	1.6280	SER 10/H-donor/3.37/-0.1 SER 10/H-donor/3.37/-0.1 GLU 339/H-donor/4.03/-0.1 GLU 339/H-donor/4.03/-0.1 VAL 170/H-acceptor/3.54/-0.1 VAL 170/H-acceptor/3.63/-0.1

				VAL 170/H-acceptor/3.54/-0.1 VAL 170/H-acceptor/3.63/-0.1 ARG 307/H-acceptor/3.44/-0.2 ARG 307/H-acceptor/3.22/ -0.2 ARG 307/H-acceptor/3.44/-0.2 ARG 307/H-acceptor/3.22/-0.2 SER 10/pi-H/3.99/-0.9 GLY 11/pi-H/3.44/-0.2 SER 10/pi-H/3.99/ -0.9 GLY 11/ pi-H/3.44/-0.2
Ligand 66F	-8.0110	-345.3253	1.57711	ASP 228/H-donor/3.47/-0.2 ASP 228/H-donor/3.47/ -0.2 ASP 32/H-donor/2.92/-7.5 ASP 228/H-donor/2.94/-9.1 ASP 32/H-donor/2.92/-7.5 ASP 228/H-donor/2.94/ -9.1 ASP 32/H-donor/2.93/-2.9 ASP 32/H-donor/2.93/-2.9 GLY 230/H-donor/3.39/-0.2 GLY 230/H-donor/3.39/-0.2 GLY 230/H-donor/3.07/-3.0 GLY 230/H-donor/3.07/-3.0 SER 229/H-donor/3.37/-0.3 SER 229/H-donor/3.37/-0.3 GLY 11/H-donor/3.21/-0.1 GLY 11/H-donor/3.21/-0.1

				LEU 30/H-acceptor/3.66/-0.1 TRP 115/H-acceptor/3.59/-0.1 LEU 30/H-acceptor/3.66/-0.1 TRP 115/H-acceptor/3.59/-0.1 PHE 108/H-acceptor/3.32/-0.1 PHE 108/H-acceptor/3.32/-0.1 ASP 228/Ionic/ 4.21/-0.2 ASP 228/Ionic / 4.21/-0.2 ASP 32/Ionic/2.92/-5.0 ASP 32/ Ionic /3.64/-1.4 ASP 228/Ionic/3.04/-4.2 ASP 228/Ionic/2.94/-4.9 ASP 32/Ionic/2.92/-5.0 ASP 32 / Ionic/3.64/-1.4 ASP 228/Ionic/ 3.04/-4.2 ASP 228/Ionic/2.94/-4.9 ASP 32 /Ionic/3.63/-1.4 ASP 32/Ionic/2.93/-4.9 ASP 32 / Ionic/3.63/-1.4 ASP 32/ Ionic/2.93/-4.9 TYR 71/H-pi/3.67/-0.5 TYR 71/H-pi /3.67/ -0.5

Table. S4. Receptor interaction of compounds 1-3 and the ligand 65A into the 65A binding site in the glycogen synthase kinase 3 PDB: 5HLP.

Compound	S	E_conf	rmsd_refine	Receptor
	dG Kcal/mole	Kcal/mole		Amino acid/Type of bonding/Distance (Å) / Binding Energy (Kcal/mole)
1	-5.4860	-78.8546	1.89496088	VAL 135/H-donor/3.31/-0.1 LYS 85/H-acceptor/3.26/-0.1 LYS 85/H-acceptor/2.85/-12.7 VAL 70/H-acceptor/3.55/-0.1 LYS 85/Ionic/2.85/-5.6 TYR 134/H-pi/4.89/-0.2 LYS 85/pi-H/4.88/-0.1 LEU 188/pi-H/3.55/-0.2 CYS 199/pi-H/4.42/-0.1 ASP 200/pi-H/3.57/-0.1
2	-5.1836	-18.9100	1.4032954	GLU 97/H-donor/3.16/-2.2 LYS 85/H-acceptor/3.05/-0.4 LEU 132/pi-H/3.87/-0.1 CYS 199/pi-H/4.31/-0.1 ASP 200/pi-H/3.72/-0.4
3	-5.3032	2.7724	0.8087	GLU 97/H-donor/3.24/-0.1 MET 101/H-donor/3.69/-0.1 CYS 199/H-donor/4.36/-0.1 VAL 110/H-acceptor/3.97/-0.1 LEU 188/H-acceptor/3.97/-0.1 LYS 85/H-acceptor/3.34/-0.1 LYS 85/H-acceptor/3.07/-7.6 ASP 200/H-acceptor/3.46/-0.2 LEU 132/pi-H/3.87/-0.1

				CYS 199/pi-H/4.25/-0.1 ASP 200/pi-H/3.76/-0.2
65A	-6.56960344		1.8019	CYS 199/H-donor/4.32/-0.1 VAL 135/H-donor/3.54/-0.1 PRO 136/H-donor/3.35/-0.1 LEU 188/H-acceptor/3.82/-0.1 TYR 134/H-pi/4.97/-0.3 LEU 132/pi-H/4.21/-0.1 LEU 188/pi-H/4.29/-0.3 LEU 188/pi-H/4.53/-0.1 LEU 188/pi-H/4.06/-0.1 CYS 199/pi-H/3.94/-0.9 ASP 200/pi-H/4.27/-0.3