Supplementary Material

Molecular simulations of unexplored Philippine plant constituents on the inhibition of the proinflammatory marker NF-κB p50 subunit

Jasmine U. Ting [1,*], Maria Carmen S. Tan [1], Vincent Antonio S. Ng [1], Stephani Joy Y. Macalino [1], Virgilio C. Linis [2] and Glenn G. Oyong [3,*]

[1] Department of Chemistry, De La Salle University, 2401 Taft Avenue, Malate, Manila 0922, Philippines; maria.carmen.tan@dlsu.edu.ph (M.C.S.T.); vincent.ng@dlsu.edu.ph (V.A.S.N.); stephani.macalino@dlsu.edu.ph (S.J.Y.M.)

[2] School of Multidisciplinary Studies, De La Salle-College of Saint Benilde, 2544 Taft Avenue, Malate, Manila 0922, Philippines; virgilio.linis@benilde.edu.ph

[3] Department of Physics, De La Salle University, 2401 Taft Avenue, Malate, Manila 0922, Philippines; glenn.oyong@dlsu.edu.ph

* Correspondence: jasmine.u.ting@outlook.com (J.U.T.); glenn.oyong@dlsu.edu.ph (G.G.O.)

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Table S1. List of previously reported new or novel compounds from plants available in the Philippines

Compound	Name	CID	Classification of the Compound	Plant	Family	Part	Ref
1 [a,c]	lβ-acetoxy-4α,9α-dihydroxy-6β-isobutyroxyprostatolide	n/a	Eudesmanolide sesquiterpene	*Wollastonia dentata* (H.Lév. & Vaniot) Orchard (syn. *Eclipta dentata* H.Lév. & Vaniot; *Melanthera prostrata* (Hemsl.) W.L. Wagner & H.Bob.; *Wedelia prostrata* Hemsl.)	Asteraceae	Leaves	[15]
2 [a,c]	lβ-acetoxy-4α,9α-dihydroxy-6β-methacryloxyprostatolide	n/a	Eudesmanolide sesquiterpene	*W. dentata* (H.Lév. & Vaniot) Orchard	Asteraceae	Leaves	[15]
3 [a,c]	lβ,9α-diacetoxy-4α-hydroxy-6β-isobutyroxyprostatolide	n/a	Eudesmanolide sesquiterpene	*W. dentata* (H.Lév. & Vaniot) Orchard	Asteraceae	Leaves	[15]
4 [a,c]	lβ,9α-diacetoxy-4α-hydroxy-6β-methacryloxyprostatolide	n/a	Eudesmanolide sesquiterpene	*W. dentata* (H.Lév. & Vaniot) Orchard	Asteraceae	Leaves	[15]
5 [a,b]	Spicatolide A	**4**4445367	Germacranolides	*Pseudelephantopus spicatus* (Juss. ex Aubl.) Rohr	Asteraceae	Leaves	[16]
6 [a,b]	Spicatolide B	n/a	Germacranolides	*P. spicatus* (Juss. ex Aubl.) Rohr	Asteraceae	Leaves	[16]
7 [c]	Phytyl heptanoate	n/a	Diterpene	*Bidens pilosa* L.	Asteraceae	Leaves	[45]
8 [b]	azadirachtolide	n/a	Tetranortriterpenoids	*Azadirachta indica* A.Juss.	Meliaceae	Leaves	[17]
9 [b]	deoxyazadirachtolide	n/a	Tetranortriterpenoids	*A. indica* A.Juss.	Meliaceae	Leaves	[17]
10 [b]	22β-acetoxylantic acid/ 22β-acetyl lantoic acid	n/a	Triterpene	*Lantana camara* L.	Verbenaceae	Leaves	[44]
11 [a, b]	eudesm-11-en-4α-O-β-D-3-senecioyloxy-6-deoxyglucopyranoside	n/a	Sesquiterpene glycosides	*Pittosporum pentandrum* (Blanco) Merr.	Pittosporaceae	Leaves	[18]
12 [a, b]	eudesm-11-en-4α-O-β-D-3-tigoyloxy-6-deoxy-glucopyranoside	n/a	Sesquiterpene glycosides	*P. pentandrum* (Blanco) Merr.	Pittosporaceae	Leaves	[18]
13 [a, b]	α-pinene-7β-O-β-D-2,6-diacetylglucopyranoside	n/a	Acetylated pinene glucosides	*Erigeron sumatrensis* Retz. (syn. *Erigeron bonariensis* L.)	Asteraceae	Leaves	[19]
14 [a, b]	α-pinene-7β-O-β-D-2-acetylglucopyranoside	n/a	Acetylated pinene glucosides	*E. sumatrensis* Retz.	Asteraceae	Leaves	[19]
15 [c]	(3R,3aR,5aS,5bR,8S,9S,11aR)-8-(hydroxymethyl)-3-isopropyl-3a,5a,5b,8,11a-pentamethyl-1H,2H,3H,4H,5H,6H,7H,7aH,9H,10H,11H,11bH,12H,13H-cyclopenta[a]chrysen-9-ol	n/a	Triterpene	*Ficus pumila* L.	Moraceae	Leaves	[20]

16 [a, c]	(2aβ,3α,5aβ,6β,7α,8aα)-6-[2-(3-furanyl)ethyl]-2a,3,4,5,5a,6,7,8,8a,8b-decahydro-2a,3-dihydroxy-6,7,8b-trimethyl-2H-naphtho[1-8-bc]furan-2-one	n/a	Diterpene	*Tinospora crispa* (L.) Hook. f. & Thomson (syn. *Tinospora rumphii* Boerl.)	Menispremac-eae	Leaves	[21]
17 [a, c]	Methyl(1α,4αa,5α,6β,8aα)-5-[2-(3-furan-3-ene-2-one)ethyl]-1,2,3,4,4a,5,6,7,8,8a-decahydro-1,2-dihydroxy-1-napthalenecarboxylate	n/a	Diterpene	*T. crispa (*L.) Hook. f. & Thomson	Menispremac-eae	Leaves	[21]
18 [c]	2-[(4bR,6S)-6-(acetyloxy)-1,3,4,9-tetrahydroxy-4b,8,8-trimethyl-10-oxo-6,7-dihydro-5H-phenanthren-2-yl]-3-hydroxypropyl acetate	n/a	Diterpene	*Coleus scutellarioides* (L.) Benth. (syn. *Plectranthus scutellarioides* (L.) R.Br.	Lamiaceae	Leaves	[22]
19 [c]	(4S,6R,6aS,9R,10S)-6,10-bis(acetyloxy)-3-(ethoxymethyl)-6a,9-dihydroxy-6,9-dimethyl-2-oxo-4H,5H,7H,8H,10H-naphtho[4a,4-b]furan-4-yl acetate	n/a	Sesquitepene lactone	*Pseudelephantopus spicatus* (Juss. ex Aubl.) Rohr	Asteraceae	Leaves	[23]
20 [c]	(4S,5R)-4-[(1E,3S)-3,4-dihydroxybut-1-en-1-yl]-4-hydroxy-3,3,5-trimethylcyclohexan-1-one	n/a	Ionone	*Alternanthera sessilis* (L.) DC.	Amaranthaceae	Leaves	[24]
21 [a, c]	(4S,5R)-4-[(1E,3R)-3,4-dihydroxybut-1-en-1-yl]-4-hydroxy-3,3,5-trimethylcyclohexan-1-one	n/a	Ionone	*A. sessilis* (L.) DC.	Amaranthaceae	Leaves	[24]
22 [c]	Isovoucapenol A	n/a	Cassane-type furanoditerpenoids	*Caesalpinia pulcherrima* (L.) Sw.	Fabaceae	Leaves	[25]
23 [c]	Isovoucapenol B	n/a	Cassane-type furanoditerpenoids	*C. pulcherrima* (L.) Sw.	Fabaceae	Leaves	[25]
24 [c]	Isovoucapenol C	n/a	Cassane-type furanoditerpenoids	*C. pulcherrima* (L.) Sw.	Fabaceae	Leaves	[25]
25 [c]	Isovoucapenol D	n/a	Cassane-type furanoditerpenoids	*C. pulcherrima* (L.) Sw.	Fabaceae	Leaves	[25]
26 [c]	Isovoucapenol E	n/a	Cassane-type furanoditerpenoids	*C. pulcherrima* (L.) Sw.	Fabaceae	Leaves	[26]
27 [c]	16-hydroxycycloartenol-palmittic acid ester	n/a	Cycloartenol esters	*Ixora coccinea* L.	Rubiaceae	Flowers	[27]
28 [c]	16-hydroxycycloartenol-myristic acid ester	n/a	Cycloartenol esters	*I. coccinea* L.	Rubiaceae	Flowers	[27]
29 [c]	31-norlargerenol acetate	n/a	Triterpenoid	*Lagerstroemia speciosa (*L.) Pers	Lythraceae	Leaves	[28]
30 [a, c]	Lappaceolide A	*11622716*	Monoterpene lactones	*Nephelium lappaceum* L.	Sapindaceae	Seeds	[29]
31 [a, c]	Lappaceolide B	*11572139*	Monoterpene lactones	*N. lappaceum* L.	Sapindaceae	Seeds	[29]

32 [a, c]	(1S,4S,7S,11S)-4-hydroxy-7-methyl-2,10-dioxatricyclo[5.3.1.0^{4},^{11}]undec-5-en-9-one	n/a	Iridiod	*Gardenia jasminoides* J. Ellis	Rubiaceae	Flowers	[30]
33 [a, c]	(4S,4aR,7aR)-7-(hydroxymethyl)-1-oxo-3H,4H,4aH,5H,7aH-cyclopenta[c]pyran-4-yl acetate	n/a	Iridiod	*G. jasminoides* J. Ellis	Rubiaceae	Flowers	[30]
34 [a, c]	(4R,4aR,7aR)-7-(hydroxymethyl)-1-oxo-3H,4H,4aH,5H,7aH-cyclopenta[c]pyran-4-yl acetate	n/a	Iridiod	*G. jasminoides* J. Ellis	Rubiaceae	Flowers	[30]
35 [a, c]	(5R)-5-(4-{(1S,5R)-1-hydroxy-4-oxo-5-[(3E)-2-oxopent-3-en-1-yl-]cyclopent-2-en-1-yl}butyl)dihydrofuran-2(3H)-one	n/a	Chromomoric acid	*Tectona philippinensis* Benth & Hook.f.	Lamiaceae	Leaves	[31]
36 [a, c]	(5R)-5-(4-{(1S,5E)-5-{[(2S,3S)-3-ethyloxiran-2-yl]methylidene}-1-hydroxy-4-oxocyclopent-2-en-1-yl]butyl}dihydrofuran-2(3H)-one	n/a	Chromomoric acid	*T. philippinesis* Benth & Hook.f.	Lamiaceae	Leaves	[31]
37 [a, c]	(5R)-5-(4-{(1S,5R)-1-hydroxy-5-[(2R,3E)-2-hydroxypent-3-en-1-yl]-4-oxocyclopent-2-en-1-yl}butyl)dihydrofuran-2(3H)-one	n/a	Chromomoric acid	*T. philippinesis* Benth & Hook.f.	Lamiaceae	Leaves	[31]
38 [a, c]	(5R)-5-(4-{ (1S,5R)-1-hydroxy-5-[(2S,3E)-2-hydroxypent-3-en-1-yl]-4-oxocyclopent-2-en-1-yl}butyl)dihydrofuran-2(3H)-one	n/a	Chromomoric acid	*T. philippinesis* Benth & Hook.f.	Lamiaceae	Leaves	[31]
39 [a, c]	11,12,12a-nonahydrocyclopentacycloundecene	n/a	Sesquiterpene	*Artemisia indica* Willd.	Asteraceae	Leaves	[32]
40 [a, c]	(1S,5R,6R)-3-(hydroxymethyl)-6-isopropyl-5-{[(2Z)-2-methylbut-2-enoyl]oxy}-2-oxocyclohex-3-en-1-yl (2R,3R)-2,3-dimethyloxirane-2-carboxylate	n/a	Carvotanacetone	*Sphaeranthus africanus* L.	Asteraceae	Leaves	[33]
41 [a, c]	(1S,5R,6R)-3-(hydroxymethyl)-6-isopropyl-5-{[(2Z)-2-methylbut-2-enoyl]oxy}-2-oxocyclohex-3-en-1-yl (2Z)-2-methylbut-2-enoate	n/a	Carvotanacetone	*S. africanus* L.	Asteraceae	Leaves	[33]
42 [a, c]	(1R,5S,6R)-5-{[(2R)-2-hydroxy-2-methylbutanoyl]oxy}-3-(hydroxymethyl)-6-isopropyl-4-oxocyclohex-2-en-1-yl (2Z)-2-methylbut-2-enoate	n/a	Carvotanacetone	*S. africanus* L.	Asteraceae	Leaves	[33]
43 [a, c]	(1R,5S,6R)-5-{[(2S)-2-hydroxy-2-methylbutanoyl]oxy}-3-(hydroxymethyl)-6-isopropyl-4-oxocyclohex-2-en-1-yl (2Z)-2-methylbut-2-enoate	n/a	Carvotanacetone	*S. africanus* L.	Asteraceae	Leaves	[33]
44 [c]	germanicol caffeoyl ester	53248580	Triterpene	*Barringtonia asiatica* (L.) Kurz	Lecythiadaceae	Leaves	[34]
45 [a, c]	Camelliagenone	53248544	Triterpene	*B. asiatica* (L.) Kurz	Lecythiadaceae	Leaves	[34]
46 [c]	Retusenol	n/a	Triterpene	*Atalantia retusa* Merr.	Rutaceae	Leaves	[35]
47 [c]	(3α,11β)-11-hydroxyolean-12-en-3-yl palmitate	n/a	Triterpene	*B. asiatica* (L.) Kurz	Lecythiadaceae	Bark	[36]
48 [a, c]	(1R)-8-isopropyl-4-methoxy-1-methyltricyclo[6.2.2.0^{2},^{7}]dodeca-4,9-diene-3,6-dione	n/a	Sesquiterpene	*Cinnamomum cebuense* Kosterm	Lauraceae	Bark	[37]

49 [a, c]	3-[(5Z)-5-methylhept-5-en-2-yl]-6-methylidenecyclohex-1-ene	n/a	Monoterpene	*C. cebuense* Kosterm	Lauraceae	Leaves	[37]
50 [c]	Dysoxylumglabretol A	n/a	Glabretal-type triterpenoids	*Didymocheton mollissimus* (Spreng.) Mabb. (syn. *Dysoxylum mollissimum* (Spreng.) Blume ex G.Don)	Meliaceae	Leaves	[38]
51 [c]	Dysoxylumglabretol B	n/a	Glabretal-type triterpenoids	*D. mollissimus* (Spreng.) Mabb.	Meliaceae	Leaves	[38]
52 [c]	Asperol A	n/a	Triterpene	*Canarium asperum* Benth. in Hook.f.	Burseraceae	Resins of the bark	[39]
53 [c]	Asperol B	n/a	Triterpene	*C. asperum* Benth. in Hook.f.	Burseraceae	Resins of the bark	[39]
54 [a, c]	Oppositifolone	n/a	Triterpene	*Glinus oppositifolius* (L.) A.DC.	Molluginaceae	Leaves	[40]
55 [a, c]	2α,18-dihydroxy-isopimara-7,15-diene	n/a	Diterpene	*Cycas sancti-lasallei* Agoo & Madulid	Cycadaceae	Leaflet	[41]
56 [a, c]	Wadeiol	n/a	Isoflavonoid phtoalexin	*Cycas wadei* Merr.	Cycadaceae	Roots	[42]
57 [c]	Selin-4(5)-en-1β,11-diol	n/a	Sesquitepene alcohol	*C. wadei* Merr.	Cycadeceae	Roots	[42]
58 [a, c]	Grandiflorolide	n/a	Sesquitepene lactone	*Chrysanthemum* x *morifolium* (Ramat.) Hemsl. (*syn. Dendranthema* x *grandiflorum* (Ramat.) Kitam)	Asteraceae	Flower	[43]

[a] Compounds that passed the drug-likeness screening (Lipinski's Rule of Five); [b] classified as novel compounds; [c] classified as new compounds

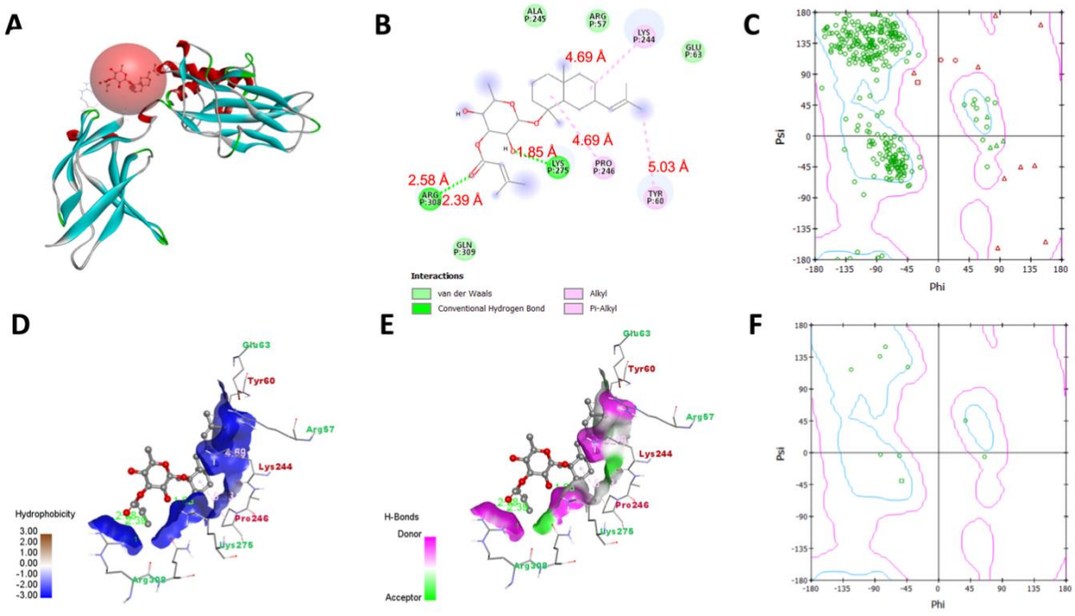


Figure S1. Binding interaction of p50 and Compound **11** (A)Ligand binding sphere and p50 protein, (B) Two-dimensional display of the interaction, (C) Ramachandran plot of p50, (D) Hydrophobic property of binding pocket, (E) H-bond property of binding pocket, (F) Ramachandran plot of ligand-interaction amino acid residues

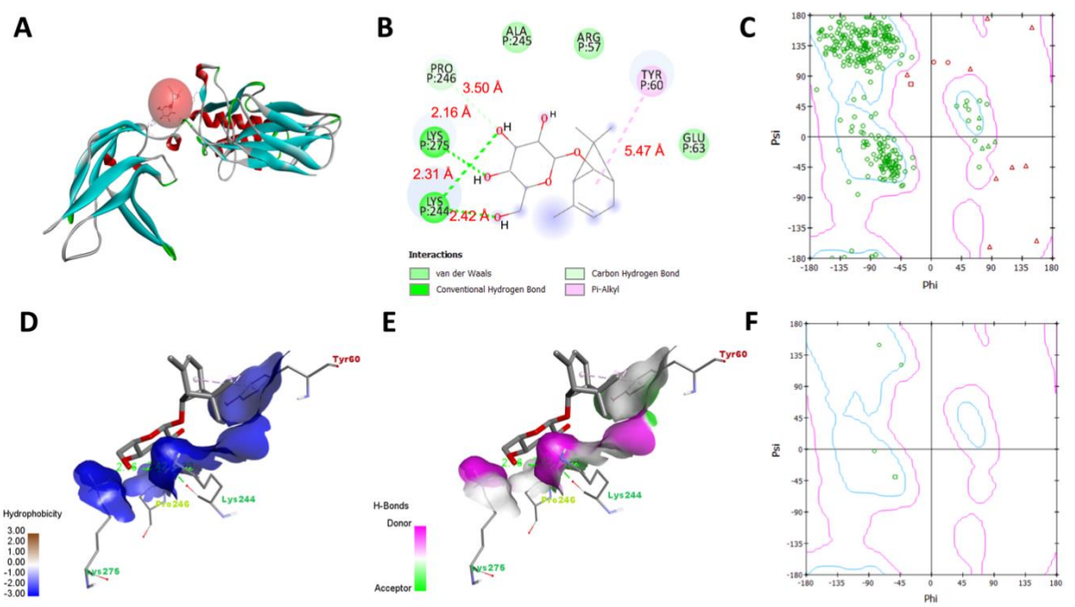


Figure S2. Binding interaction of p50 and Compound **14** (A) Ligand binding sphere and p50 protein, (B) Two-dimensional display of the interaction, (C) Ramachandran plot of p50, (D) Hydrophobic property of binding pocket, (E) H-bond property of binding pocket, (F) Ramachandran plot of ligand-interaction amino acid residues

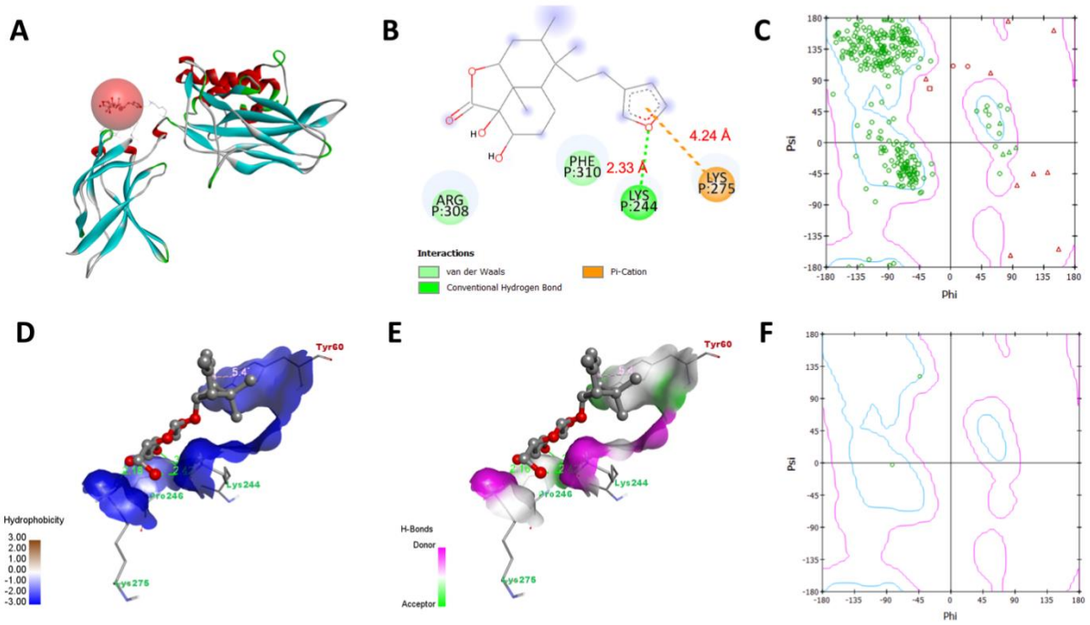


Figure S3. Binding interaction of p50 and Compound **16** (A)Ligand binding sphere and p50 protein, (B) Two-dimensional display of the interaction, (C) Ramachandran plot of p50, (D) Hydrophobic property of binding pocket, (E) H-bond property of binding pocket, (F) Ramachandran plot of ligand-interaction amino acid residues

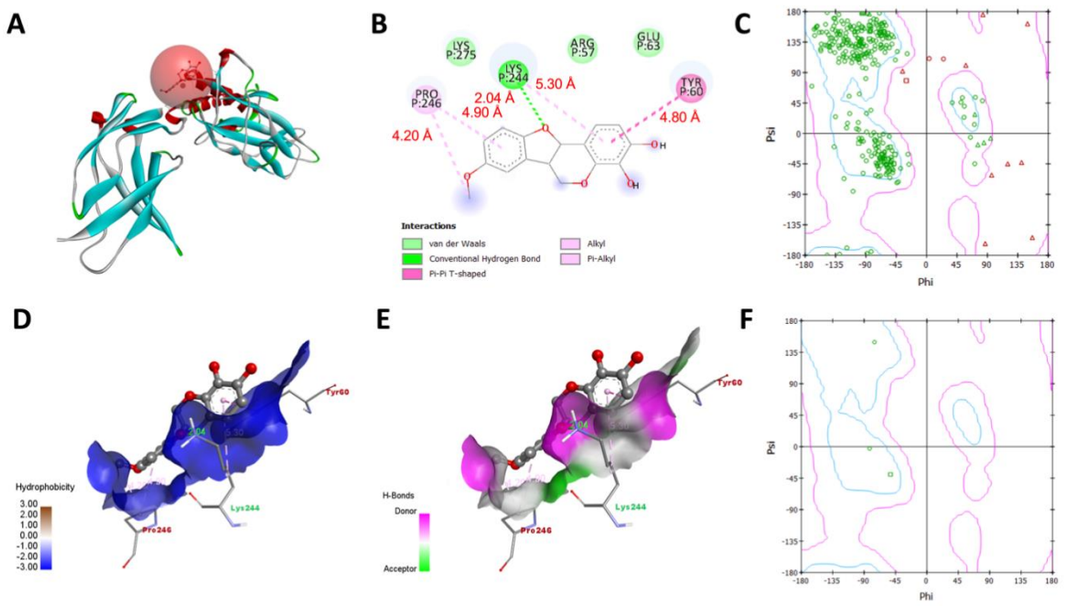


Figure S4. Binding interaction of p50 and Compound **56** (A)Ligand binding sphere and p50 protein, (B) Two-dimensional display of the interaction, (C) Ramachandran plot of p50, (D) Hydrophobic property of binding pocket, (E) H-bond property of binding pocket, (F) Ramachandran plot of ligand-interaction amino acid residues

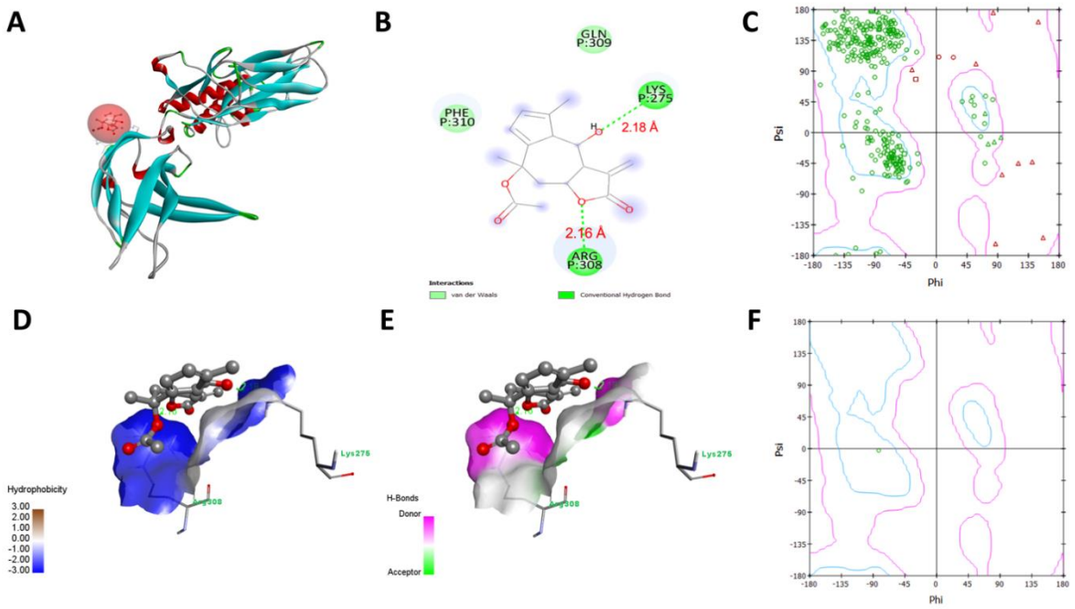


Figure S5. Binding interaction of p50 and Compound **58** (A)Ligand binding sphere and p50 protein, (B) Two-dimensional display of the interaction, (C) Ramachandran plot of p50, (D) Hydrophobic property of binding pocket, (E) H-bond property of binding pocket, (F) Ramachandran plot of ligand-interaction amino acid residues

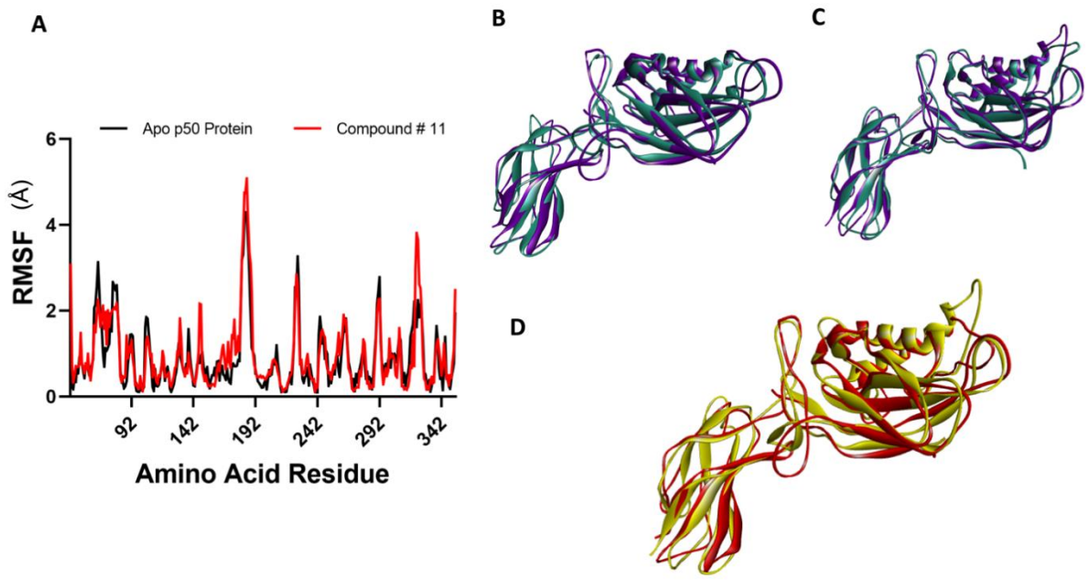


Figure S6. Molecular simulation of of p50 – Compound **11** complex: (A) RMSF values of amino acid residues of Apoprotein vs. protein-ligand **(**Compound **11)** complex and control. Three-dimensional models of (B) Changes in Apoprotein in 0ns *(Teal)* and 10ns *(Violet)*, (C) Changes in Protein-ligand **(**Compound **11)** complex in 0ns *(Teal)* and 10ns *(Violet)*, and (D) overlap model of Apo-protein *(Red)* vs protein-ligand *(Yellow)* complex (at 10ns)

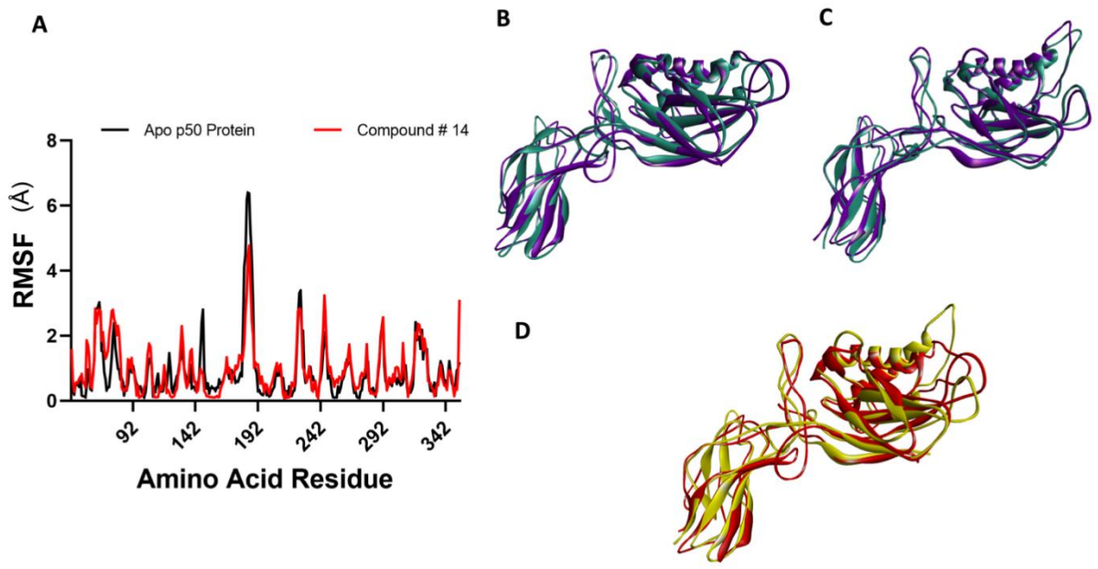


Figure S7. Molecular simulation of of p50 – Compound **14** complex: (A) RMSF values of amino acid residues of Apoprotein vs. protein-ligand **(**Compound **14)** complex and control. Three-dimensional models of (B) Changes in Apoprotein in 0ns *(Teal)* and 10ns *(Violet)*, (C) Changes in Protein-ligand **(**Compound **14)** complex in 0ns *(Teal)* and 10ns *(Violet)*, and (D) overlap model of Apoprotein *(Red)* vs protein-ligand *(Yellow)* complex (at 10ns)

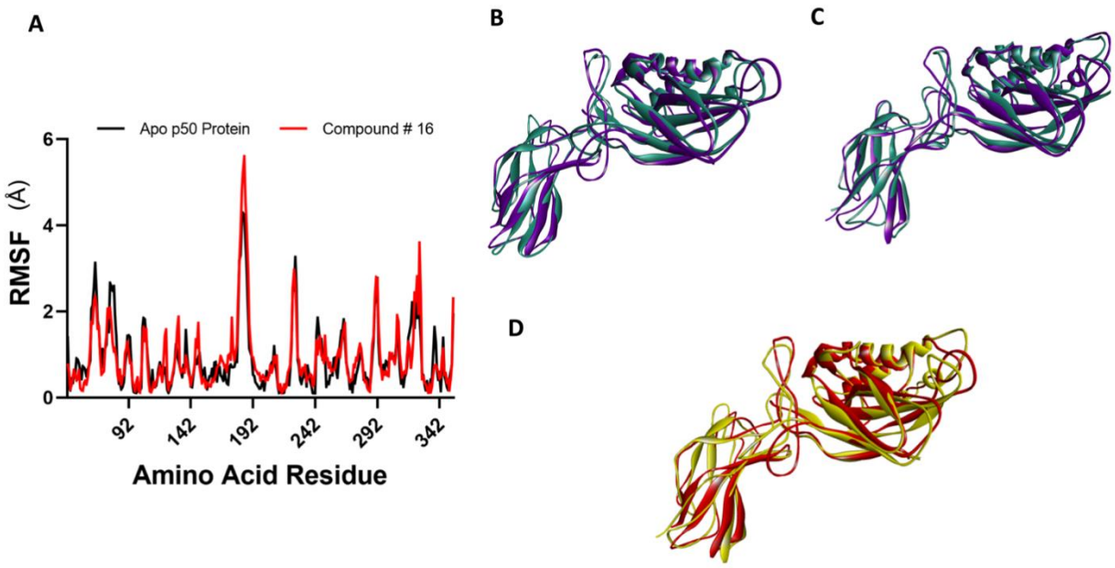


Figure S8. Molecular simulation of of p50 – Compound **16** complex: (A) RMSF values of amino acid residues of Apoprotein vs. protein-ligand **(**Compound **16)** complex and control. Three-dimensional models of (B) Changes in Apoprotein in 0ns *(Teal)* and 10ns *(Violet)*, (C) Changes in Protein-ligand **(**Compound **16)** complex in 0ns *(Teal)* and 10ns *(Violet)*, and (D) overlap model of Apoprotein *(Red)* vs protein-ligand *(Yellow)* complex (at 10ns)

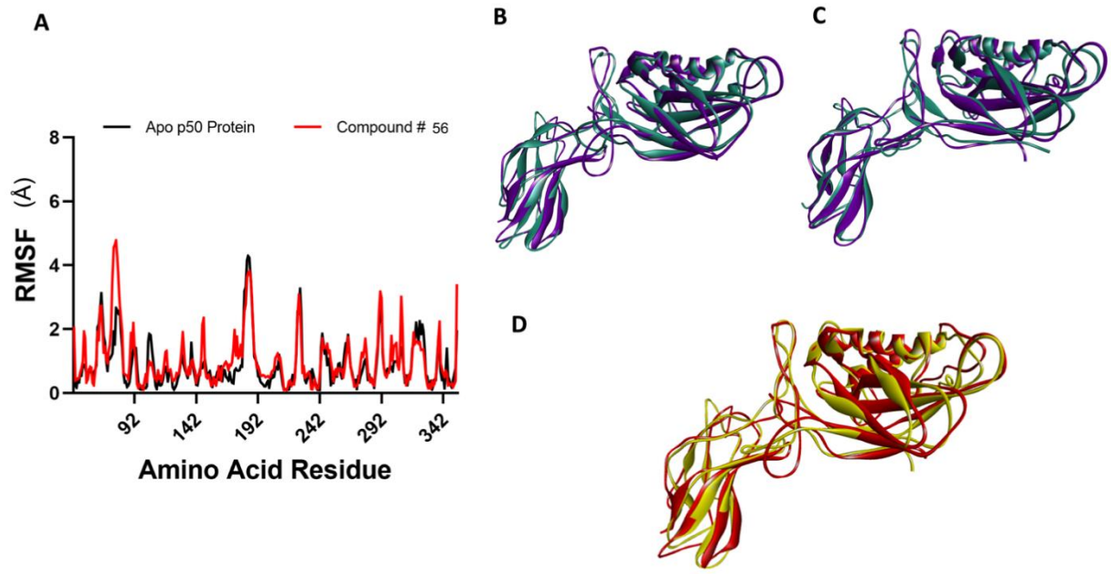


Figure S9. Molecular simulation of of p50 – Compound **56** complex: (A) RMSF values of Apoprotein vs. protein-ligand **(**Compound **56)** complex and control amino acid residues. Three-dimensional models of (B) Changes in Apoprotein in 0ns *(Teal)* and 10ns *(Violet)*, (C) Changes in Protein-ligand **(**Compound **56)** complex in 0ns *(Teal)* and 10ns *(Violet)*, and (D) overlap model of Apoprotein *(Red)* vs protein-ligand *(Yellow)* complex (at 10ns)

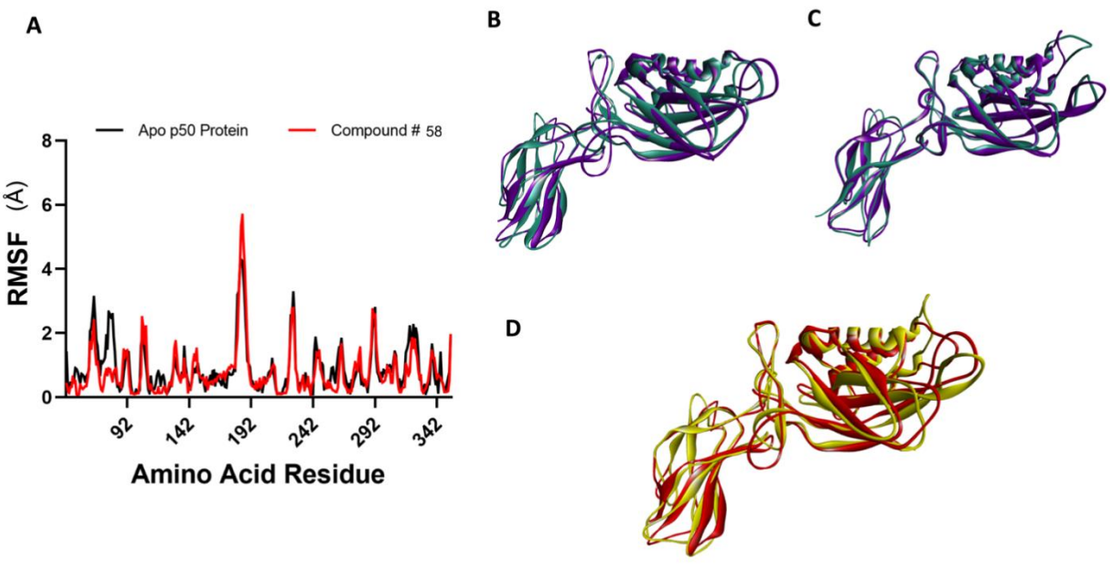
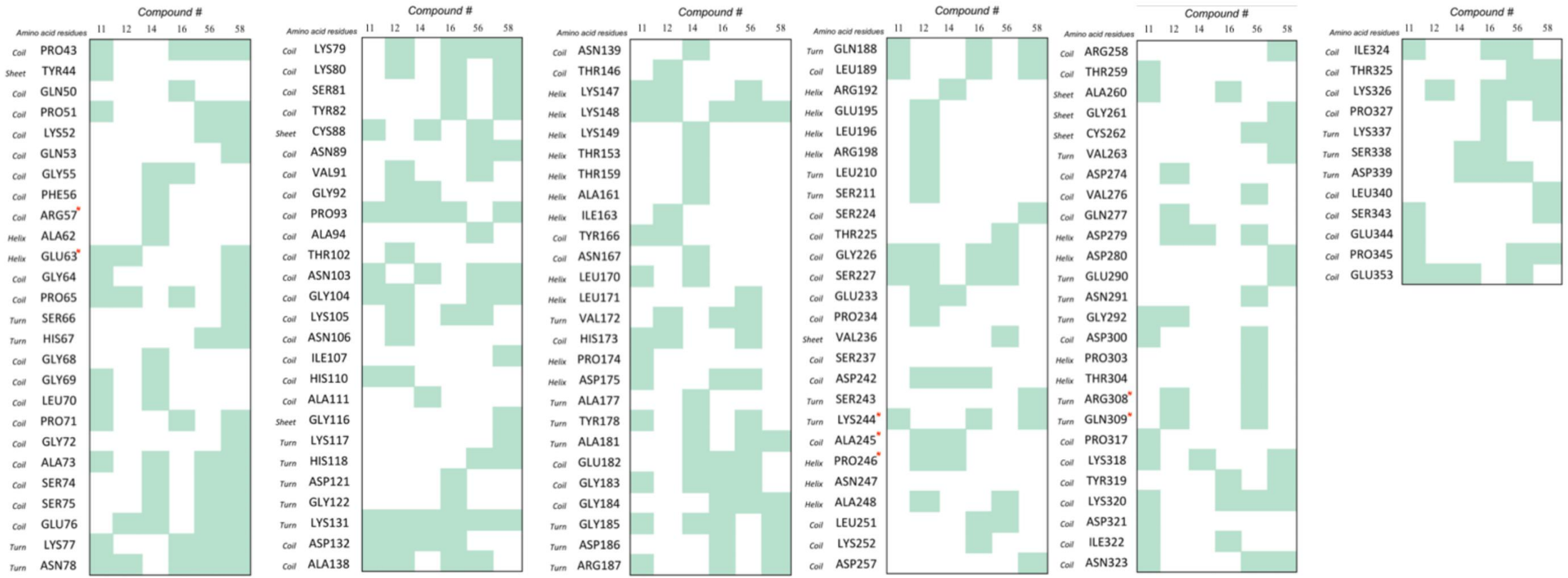


Figure S10. Molecular simulation of of p50 – Compound **58** complex: (A) RMSF values of amino acid residues of Apoprotein vs. protein-ligand **(**Compound **58)** complex and control. Three-dimensional models of (B) Changes in Apoprotein in 0ns *(Teal)* and 10ns *(Violet)*, (C) Changes in Protein-ligand **(**Compound **58)** complex in 0ns *(Teal)* and 10ns *(Violet)*, and (D) overlap model of Apoprotein *(Red)* vs protein-ligand *(Yellow)* complex (at 10ns)



* *Amino acid residues interacting with the ligand during binding*

Figure S11. Amino acid residues with significant vibration motion during the simulation

Table S2. Evolution of non-covalent bonding interaction between the protein and ligand in 10 ns.

Cmp	0 ns		2 ns		4 ns		6 ns		8 ns		10 ns	
	Amino acids	Type	Amino acids	Type	Amino acids	Type	Amino acids	Type	Amino acids	Type	Amino acids	Type
11	LYS275	Conventional Hydrogen Bond	ARG308	Conventional Hydrogen Bond	LYS244	Alkyl	PHE58	Pi-Alkyl	LYS244	Alkyl	LYS244	Alkyl
	ARG308	Conventional Hydrogen Bond	LYS244	Alkyl	ALA245	Alkyl	ARG59	Van der Waals	HIS307	Van der Waals	TYR60	Pi-Alkyl
	LYS244	Alkyl	ALA248	Alkyl	ALA248	Alkyl	TYR60	Van der Waals	GLN277	Van der Waals	ALA62	Van der Waals
	PRO246	Alkyl	TYR60	Pi-Alkyl	TYR60	Van der Waals	ALA62	Van der Waals	LYS275	Van der Waals	GLU63	Van der Waals
	TYR60	Pi-Alkyl	GLN277	Van der Waals	GLU63	Van der Waals	PRO65	Van der Waals	ALA248	Van der Waals	ALA245	Van der Waals
	ARG57	Van der Waals	PRO246	Van der Waals	SER243	Van der Waals	LYS244	Van der Waals	ASN247	Van der Waals	PRO246	Van der Waals
	GLU63	Van der Waals	ALA245	Van der Waals	PRO246	Van der Waals	ALA245	Van der Waals	LYS244	Van der Waals	ALA248	Van der Waals
	ALA245	Van der Waals	PHE58	Van der Waals	VAL276	Van der Waals	LYS275	Van der Waals	ALA245	Van der Waals	LYS275	Van der Waals
	GLN309	Van der Waals	ARG59	Van der Waals			LYS278	Van der Waals	TYR60	Van der Waals	LYS278	Van der Waals
			ALA62	Van der Waals							ARG308	Van der Waals
			GLU63	Van der Waals							*GLN309*	Van der Waals
			GLY64	Van der Waals								
12	LYS275	Conventional Hydrogen Bond	ARG308	Alkyl	LYS244	Alkyl	ARG308	Alkyl	ARG308	Conventional Hydrogen Bond and Alkyl	ARG308	Conventional Hydrogen Bond
	LYS244	Alkyl	TYR60 -	Pi-Alkyl	ALA245	Alkyl	LYS244	Alkyl	ALA245	Alkyl	ALA245	Alkyl
	ARG308	Alkyl	LYS244	Van der Waals	GLN309	Van der Waals	ARG59	Van der Waals	GLN309	Van der Waals	TYR60	Van der Waals
	TYR60	Pi-Alkyl	ALA245	Van der Waals	GLN277	Van der Waals	PHE58	Van der Waals	ASN247	Van der Waals	GLU63	Van der Waals
	PHE310	Pi-Alkyl	ASN247	Van der Waals	LYS275	Van der Waals	TYR60	Van der Waals	PRO246	Van der Waals	LYS244	Van der Waals
	GLN309	Van der Waals	GLN309	Van der Waals	ASN247	Van der Waals	ALA245	Van der Waals	LYS244	Van der Waals	PRO246	Van der Waals
	PRO246	Van der Waals			PRO246	Van der Waals	PRO246	Van der Waals	GLU63	Van der Waals	ASN247	Van der Waals
	ALA245	Van der Waals			SER243	Van der Waals	ASN247	Van der Waals	TYR60	Van der Waals	ALA248	Van der Waals
	ARG57	Van der Waals					LYS275	Van der Waals			LYS278	Van der Waals
	TYR60	Van der Waals					GLN277	Van der Waals			GLN309	Van der Waals
	GLU63	Van der Waals					GLN309	Van der Waals				

(Continue Table S2…)

14	LYS244	Conventional Hydrogen Bond	ALA62	Alkyl	ARG57	Van der Waals	TYR60	Conventional Hydrogen Bond and Pi-Alkyl	TYR60	Van der Waals	TYR60	Pi-Alkyl
	LYS275	Conventional Hydrogen Bond	TYR60	Pi-Alkyl	TYR60	Van der Waals	LYS275	Van der Waals	ASP242	Van der Waals	LYS275	Van der Waals
	PRO246	Carbon Hydrogen Bond	PHE58	Van der Waals	GLU63		GLU63				HIS144	Van der Waals
	TYR60	Pi-Alkyl	ARG59	Van der Waals	LYS244		ARG59				GLU63	Van der Waals
	GLN309	Van der Waals	VAL61	Van der Waals	ASN247						ARG59	Van der Waals
	ALA245	Van der Waals	ALA62	Van der Waals	LYS275						VAL61	Van der Waals
	GLU63	Van der Waals	GLU63	Van der Waals								
	ARG59	Van der Waals	GLY64	Van der Waals								
	PHE58	Van der Waals	ASP242	Van der Waals								
			LYS275	Van der Waals								
16	LYS244	Conventional Hydrogen Bond	ALA245	Pi-Alkyl	ARG308	Conventional Hydrogen Bond	LYS275	Pi-Cation	ARG308	Conventional Hydrogen Bond	ARG308	Van der Waals
	LYS275	Pi-Cation	PRO246	Pi-Alkyl	ALA245	Pi-Alkyl	ALA245	Pi-Alkyl	ALA245	Pi-Alkyl	GLN309	Van der Waals
	ARG308	Van der Waals	PHE310	Van der Waals	PRO246	Van der Waals	GLN309	Van der Waals	PRO246	Van der Waals	PHE310	Van der Waals
	GLN309	Van der Waals	GLN309	Van der Waals	HIS307	Van der Waals	PHE310	Van der Waals	LYS275	Van der Waals	LYS275	Van der Waals
	PHE310	Van der Waals	ARG308	Van der Waals	GLN309	Van der Waals	PRO246	Van der Waals	GLN309	Van der Waals	LYS244	Van der Waals
			HIS307	Van der Waals	PHE310	Van der Waals			PHE310	Van der Waals	ALA245	Van der Waals
											PRO246	Van der Waals
56	LYS244	Pi-Alkyl, Conventional Hydrogen Bond, and Alkyl	GLN277	Van der Waals	ALA62	Pi-Alkyl	ALA62	Pi-Alkyl and Conventional Hydrogen Bond	ALA245	Pi-Alkyl and Alkyl	LYS244	Pi-Alkyl and Pi-Lone Pair
	PRO246	Pi-Alkyl and Alkyl	LYS275	Van der Waals	TYR60	Pi-Alkyl	ALA245	Pi-Alkyl and Alkyl	PRO246	Pi-Alkyl	LYS275	Van der Waals
	TYR60	Pi-Pi T-shaped	LYS244	Van der Waals	VAL61	Van der Waals	LYS275	Van der Waals	TYR60	Pi-Alkyl	GLN277	Van der Waals
	GLU63	Van der Waals	ALA245	Van der Waals	GLU63	Van der Waals	PRO246	Van der Waals	PHE58	Van der Waals	ASN247	Van der Waals
	ALA245	Van der Waals	SER243	Van der Waals	GLY64	Van der Waals	LYS244	Van der Waals	ARG59	Van der Waals	PRO246	Van der Waals
	LYS275	Van der Waals	ASN247	Van der Waals	SER66	Van der Waals	SER243	Van der Waals	GLU63	Van der Waals	ALA245	Van der Waals
	GLN309	Van der Waals	ALA62	Van der Waals	SER243	Van der Waals	LEU210	Van der Waals	ASN247	Van der Waals	SER243	Van der Waals
	ARG57	Van der Waals	GLU63	Van der Waals	LYS244	Van der Waals	TYR60	Van der Waals	LYS275	Van der Waals	GLU63	Van der Waals
	ARG59	Van der Waals	TYR60	Van der Waals	ALA245	Van der Waals	VAL61	Van der Waals			ALA62	Van der Waals
			PHE58	Van der Waals	LYS275	Van der Waals	GLU63	Van der Waals			TYR60	Van der Waals
							GLY64	Van der Waals			PHE58	Van der Waals
							PRO65	Van der Waals			ARG57	Van der Waals

(Continue Table S2…)

58	LYS275	Conventional Hydrogen Bond	ARG308 -	Alkyl, Conventional Hydrogen Bond, and Carbon Hydrogen Bond	LYS275	Alkyl	HIS307	Van der Waals	ASN247	Van der Waals	HIS307	Van der Waals
	ARG308	Conventional Hydrogen Bond	PHE310	Van der Waals	ARG308	Van der Waals	ARG308	Van der Waals	LYS275	Van der Waals	ARG308	Van der Waals
	PHE310 -	Pi-Alkyl	GLN309	Van der Waals	GLN309	Van der Waals	GLN309	Van der Waals	ARG308	Van der Waals	GLN309	Van der Waals
	HIS307	Van der Waals	LYS275	Van der Waals	PHE310	Van der Waals	PHE310	Van der Waals	GLN309	Van der Waals	PHE310	Van der Waals
	GLN309	Van der Waals					LYS275	Van der Waals	PHE310	Van der Waals	LYS275	Van der Waals