

**Table S13.** The Nature of the interactions of CO1/1P8D complex

Hydrophobic Interactions										
Index	Residue	AA	Distance		Ligand Atom		Protein Atom			
1	243A	PHE	3.23		4123		196			
2	243A	PHE	3.79		4125		197			
3	271A	PHE	3.62		4134		388			
4	272A	THR	3.93		4144		401			
5	274A	LEU	3.84		4126		415			
6	312A	MET	3.83		4130		708			
7	315A	GLU	3.38		4149		732			
8	329A	PHE	3.73		4147		853			
9	329A	PHE	3.41		4132		857			
10	329A	PHE	3.71		4126		854			
11	340A	PHE	3.91		4132		954			
12	442A	LEU	3.19		4145		1784			
13	457A	TRP	3.99		4144		1913			
Hydrogen Bonds										
Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle		Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	239A	ASN	2.75	3.29	116.15				4121 [O3]	159 [O2]
Water Bridges										
Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor?	Donor Atom	Acceptor Atom	Water Atom
1	319A	ARG	3.07	4.03	100.13	106.50		770 [Ng+]	4121 [O3]	4223

**Table S14.** The nature of the interactions of 7PP/3NMQ complex

Hydrophobic Interactions										
Index	Residue	AA	Distance		Ligand Atom		Protein Atom			
1	107A	LEU	3.99		1738		767			
2	107A	LEU	3.83		1732		766			
3	138A	PHE	3.45		1728		986			
4	138A	PHE	3.84		1733		987			
5	162A	TRP	3.82		1733		1187			
Hydrogen Bonds										
Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle		Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	184A	THR	2.93	3.70	136.96				1341 [O3]	1718 [N2]
Water Bridges										
Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor?	Donor Atom	Acceptor Atom	Water Atom
1	51A	ASN	2.97	3.05	158.33	79.50		338 [Nam]	1721 [Npl]	1812
2	52A	ALA	3.06	3.80	101.91	96.10		339 [Nam]	1720 [Npl]	1745
3	93A	ASP	3.49	3.88	100.45	73.51		660 [Nam]	1720 [Npl]	1758
4	93A	ASP	2.70	4.03	124.43	109.72		1720 [Npl]	666 [O3]	1746
5	93A	ASP	2.78	3.49	108.10	114.11		1720 [Npl]	667 [O2]	1758
6	97A	GLY	2.93	3.16	158.71	99.27		1744 [O3]	690 [O2]	1840
7	184A	THR	3.01	4.03	124.43	99.75		1720 [Npl]	1341 [O3]	1746
π-Stacking										
Index	Residue	AA	Distance		Angle		Offset	Stacking Type	Ligand Atoms	
1	138A	PHE	3.57		3.15		1.11	P	1726, 1727, 1729, 1732, 1734, 1735	
Halogen Bonds										
Index	Residue	AA	Distance		Donor Angle		Acceptor Angle	Donor Atom	Acceptor Atom	
1	97A	GLY	3.26		146.64		98.37	1716 [Cl]	690 [O2]	
Salt Bridges										
Index	Residue	AA	Distance		Protein positive?		Ligand Group	Ligand Atoms		
1	93A	ASP	4.43				Guanidine	1718, 1721, 1720		

**Table S15.** The nature of the interactions of IQO/3096 complex

Hydrophobic Interactions										
Index		Residue		AA	Distance	Ligand Atom	Protein Atom			
1		84A		ILE	3.86	3034	668			
2		210A		LEU	3.66	3072	1342			
3		264A		LEU	3.64	3073	1791			
4		268A		LYS	3.81	3063	1823			
5		272A		TYR	3.50	3039	1855			
6		292A		ASP	3.79	3070	2021			
Hydrogen Bonds										
Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom	
1	205A	SER	2.50	2.89	104.35			1295 [O3]	3067 [Nar]	
2	268A	LYS	2.71	3.26	113.86			1826 [N3]	3067 [Nar]	
Water Bridges										
Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor?	Donor Atom	Acceptor Atom	Water Atom
1	54A	ASN	3.68	3.25	103.13	72.57		422 [Nam]	3050 [O2]	3085
$\pi$ -Stacking										
Index	Residue	AA	Distance	Angle	Offset	Stacking Type	Ligand Atoms			
1	80A	TRP	4.06	4.76	1.92	P	3044, 3060, 3061, 3062, 3063, 3064			
2	80A	TRP	3.73	4.71	1.38	P	3044, 3060, 3061, 3062, 3063, 3064			
3	80A	TRP	3.68	4.42	0.88	P	3043, 3057, 3058, 3059, 3060, 3064			

**Table S16.** The nature of the interactions of 4ACG/6LQ complex

Hydrophobic Interactions										
Index			Residue		AA	Distance	Ligand Atom	Protein Atom		
1			62A		ILE	3.63	5627	208		
2			188A		LEU	3.79	5631	1261		
3			200A		ASP	3.48	5643	1348		
Hydrogen Bonds										
Index	Residue	AA	Distance H-A		Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	133A	ASP	1.87		2.84	165.75			5635 [Npl]	787 [O2]
2	135A	VAL	2.44		3.42	169.68			804 [Nam]	5633 [Nar]
3	141A	ARG	3.65		4.09	109.79			862 [Ng+]	5621 [O2]
Water Bridges										
Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor?	Donor Atom	Acceptor Atom	Water Atom
1	141A	ARG	3.92	3.72	139.59	95.69		863 [Ng+]	5614 [N3]	5759
π-Stacking										
Index	Residue	AA	Distance	Angle	Offset	Stacking Type	Ligand Atoms			
1	67A	PHE	4.88	23.92	1.92	P	5639, 5640, 5641, 5642, 5643, 5644			

**Table S17.** The nature of the interactions of 6FJ/5J20 complex

Hydrophobic Interactions										
Index			Residue		AA	Distance	Ligand Atom		Protein Atom	
1			54A		ASP	3.81	3338		614	
2			103A		LEU	3.67	3342		1383	
Hydrogen Bonds										
Index	Residue	AA	Distance H-A		Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	51A	ASN	2.06		2.90	138.53			581 [Nam]	3336 [O2]
2	58A	LYS	1.94		2.80	140.47			671 [N3+]	3332 [O2]
3	93A	ASP	1.70		2.61	160.72			3329 [O3]	1249 [O3]
4	97A	GLY	3.23		3.82	118.19			1294 [Nam]	3327 [Nar]
5	97A	GLY	2.00		2.79	135.70			3331 [Nar]	1297 [O2]
6	184A	THR	2.77		3.54	134.06			2597 [O3]	3327 [Nar]
Water Bridges										
Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor?	Donor Atom	Acceptor Atom	Water Atom
1	48A	LEU	3.07	2.67	165.34	83.40		3330 [O3]	528 [O2]	3359
2	95A	GLY	2.93	3.88	112.60	79.33		1268 [Nam]	3329 [O3]	3416
$\pi$ -Stacking										
Index	Residue		AA	Distance	Angle	Offset	Stacking Type	Ligand Atoms		
1	138A		PHE	5.18	68.97	1.17	T	3322, 3323, 3340, 3341, 3342		
2	162A		TRP	4.73	82.54	1.28	T	3322, 3323, 3340, 3341, 3342		
3	162A		TRP	4.81	82.59	1.46	T	3322, 3323, 3340, 3341, 3342		
$\pi$ -Cation Interactions										
Index	Residue	AA	Distance	Offset	Protein charged?		Ligand Group	Ligand Atoms		
1	58A	LYS	4.15	1.35			Aromatic	3313, 3319, 3320, 3333, 3334, 3338		