Curation and Analysis of Multi-targeting Agents for Polypharmacological Modeling

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(Supporting Information)

(16 Pages)

Table S1. Minimum and maximum cutoff values of the parameters used to screen and obtain the drug-like ligands using the filter module of Openeye software program.

S. No	Property	Lower Limit	Higher limit
1	Molecular weight	130	781
2	Heavy atom count	9	55
3	Number of ring systems	0	5
4	Ring size	0	20
5	Carbon count	3	41
6	Hetero count	1	14
7	Hetero atom to carbon ratio	0.04	4.0
8	Number of rotatable bonds	0	16
9	Number of rigid bonds	4	55
10	Hydrogen-bond acceptors	0	13
11	Hydrogen-bond donors	0	9
12	Lipinski acceptors	1	14
13	Lipinski donors	0	6
14	Chiral count	0	21
15	LogP	-3.0	6.85
16	Total formal charge	-2	+2
17	Number of atoms with a formal charge	0	4
18	Halide fraction	0.0	0.66
19	Un-branched chains	1	13
20	Topological polar surface area	0.0	205.0
21	Connected non-ring	0	19
22	Un-branched chains	1	13
23	Total functional group count	0	7
24	Maximum number of Lipinski violations	-	3
26	Allowed elements	H,C,N,O,F,P,S,Cl,Br,I	
27	Eliminate metals	Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Y, Zr, Nb, Mo, Tc, Ru, Rh, Pd, Ag, Cd	
28	Minimum Solubility	insoluble	

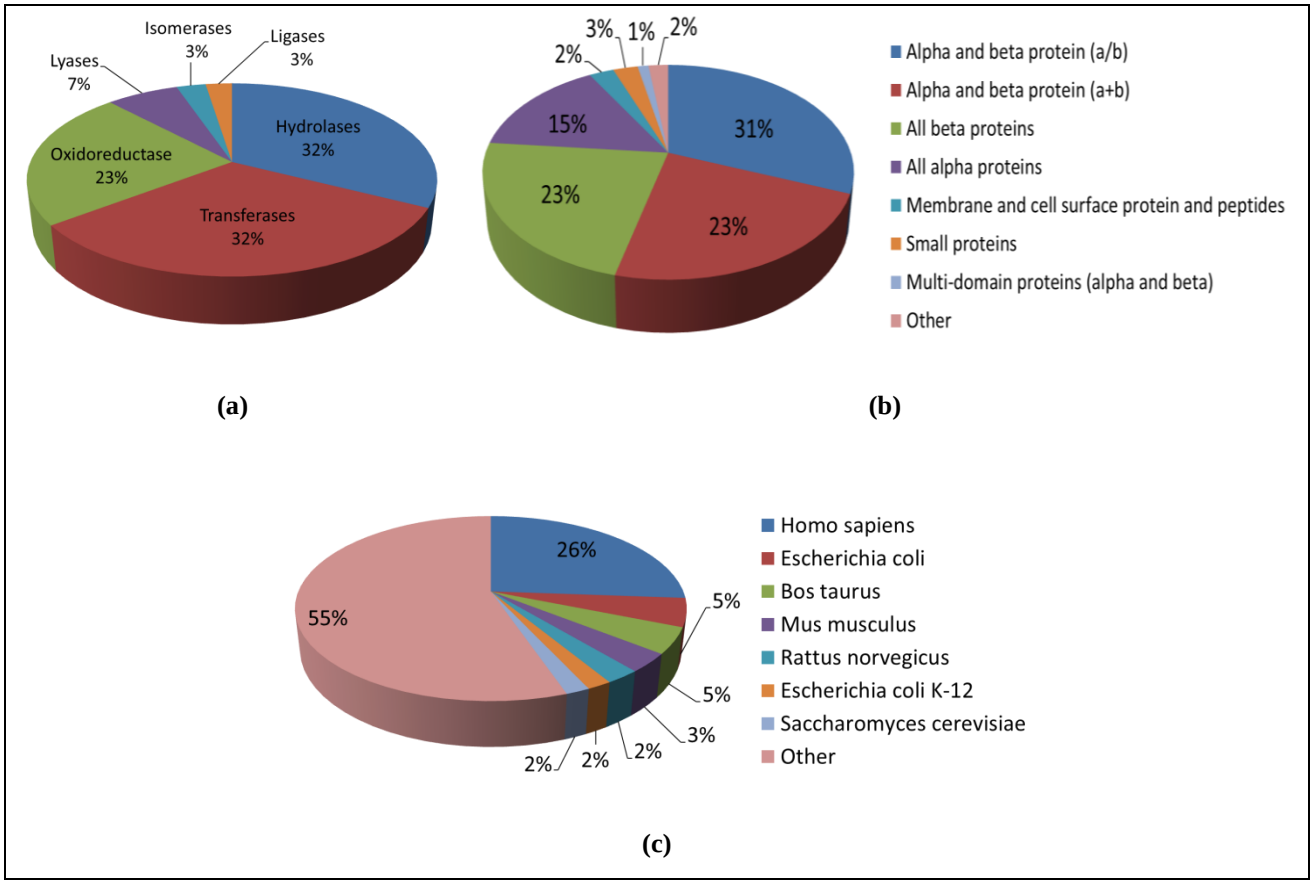

Figure S1. Classification of 4,167 PDB IDs bound with 953 ligands based on (a) EC numbers (b) SCOP IDs (c) Organism species.

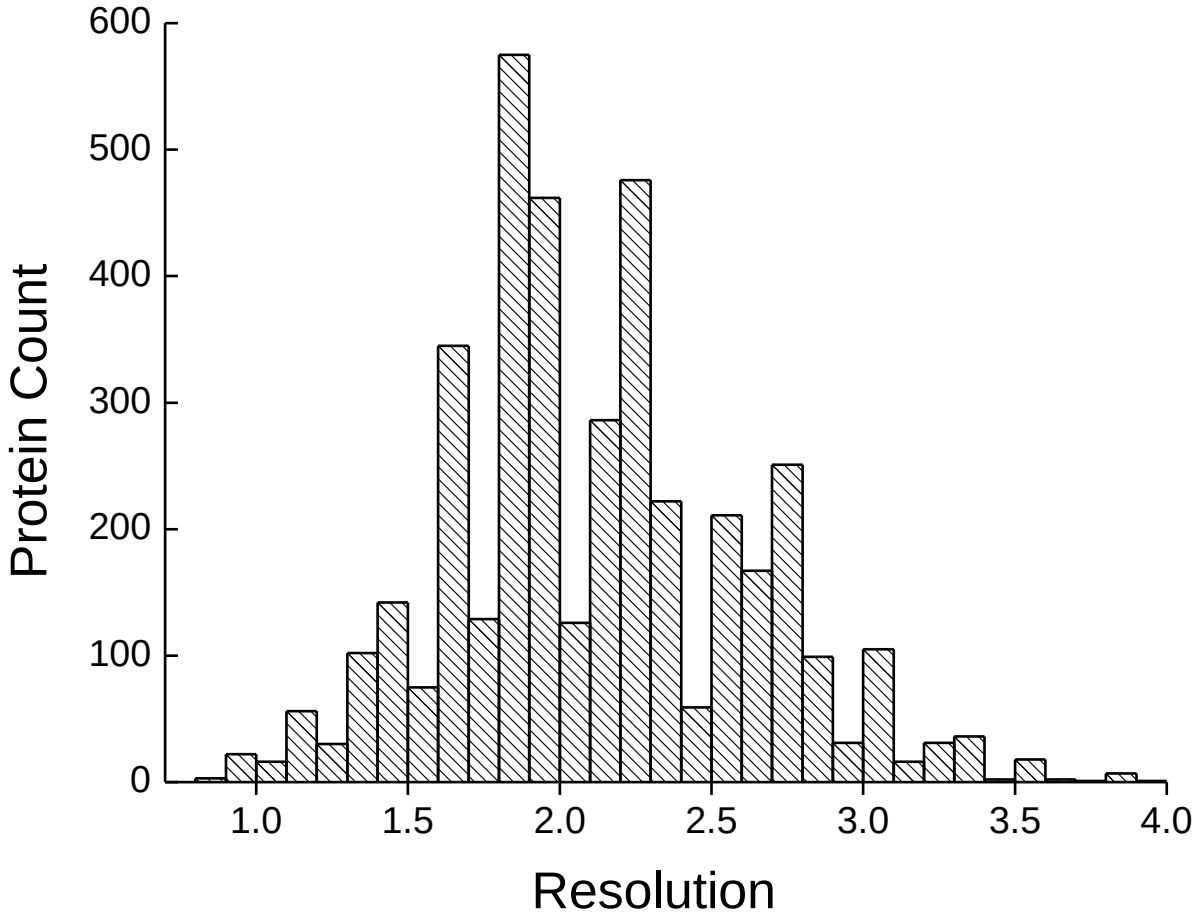

Figure S2. Distribution of resolution of the target structures present in the *Polypharma* database.

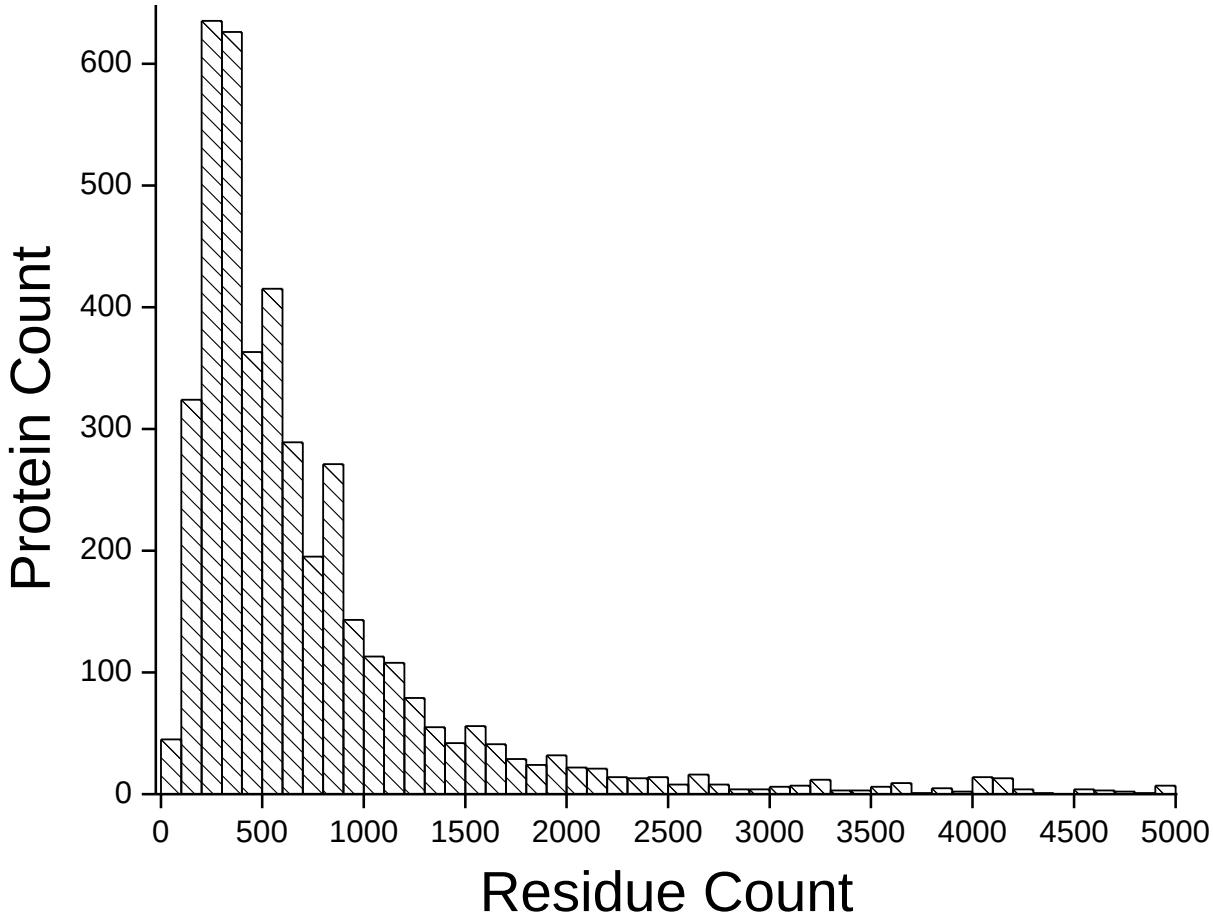

Figure S3. Distribution of number of residues of the target structures present in the *Polypharma* database.

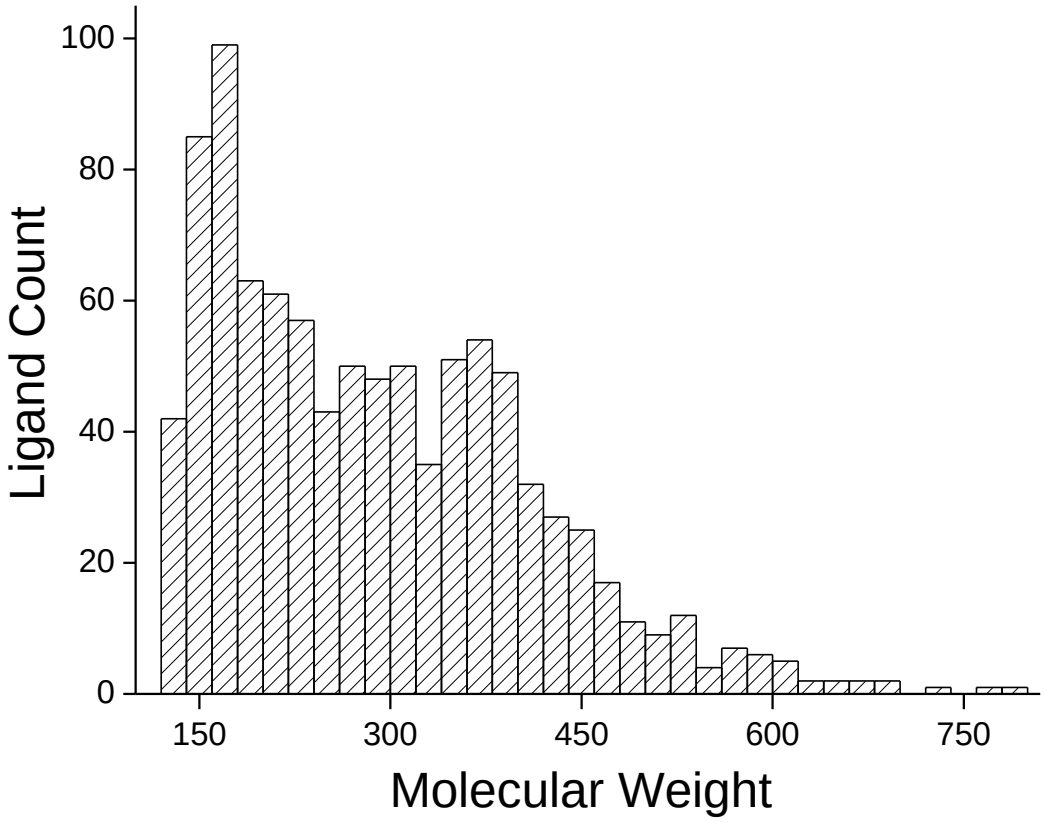

Figure S4. Distribution of the molecular weights of the ligands present in the *Polypharma* database.

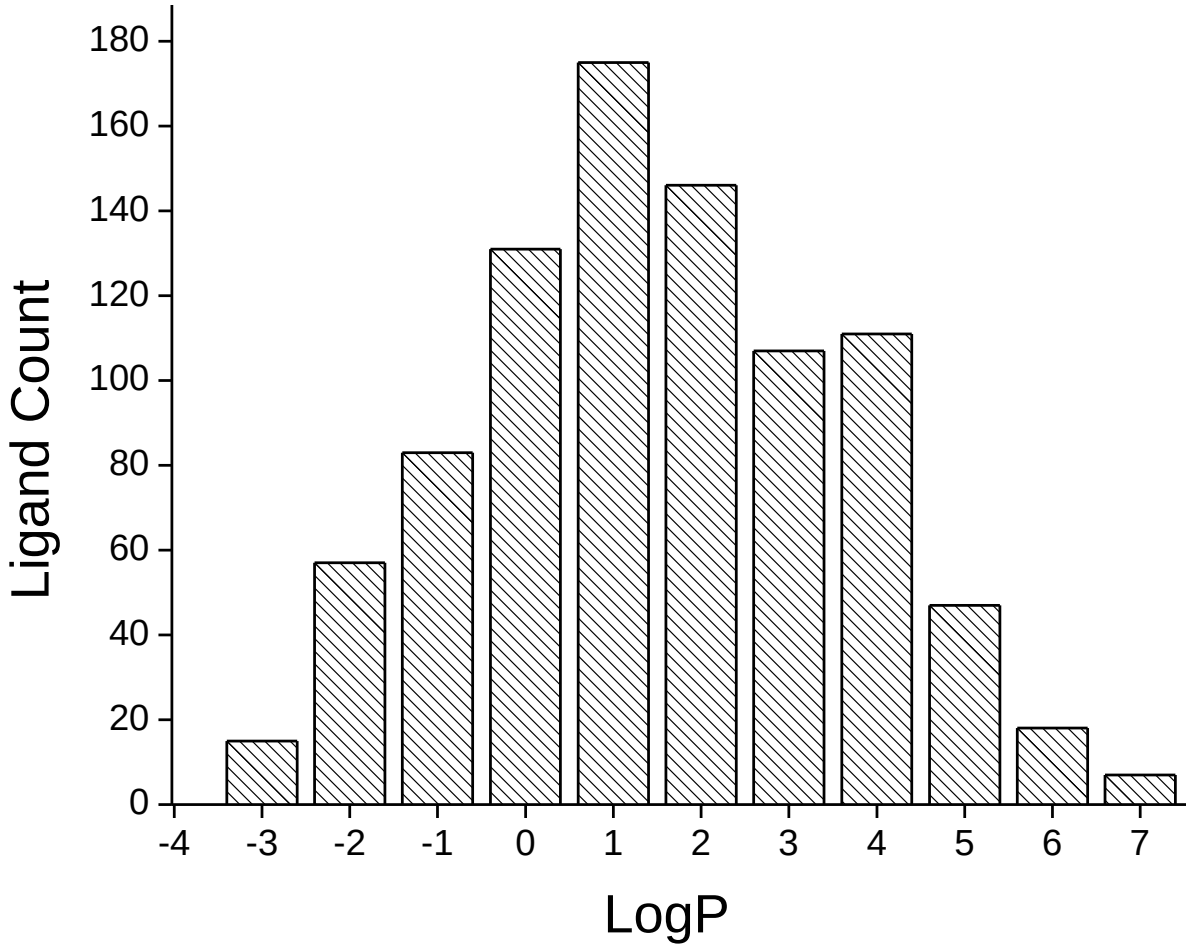

Figure S5. Distribution of the LogP of the ligands present in the *Polypharma* database.

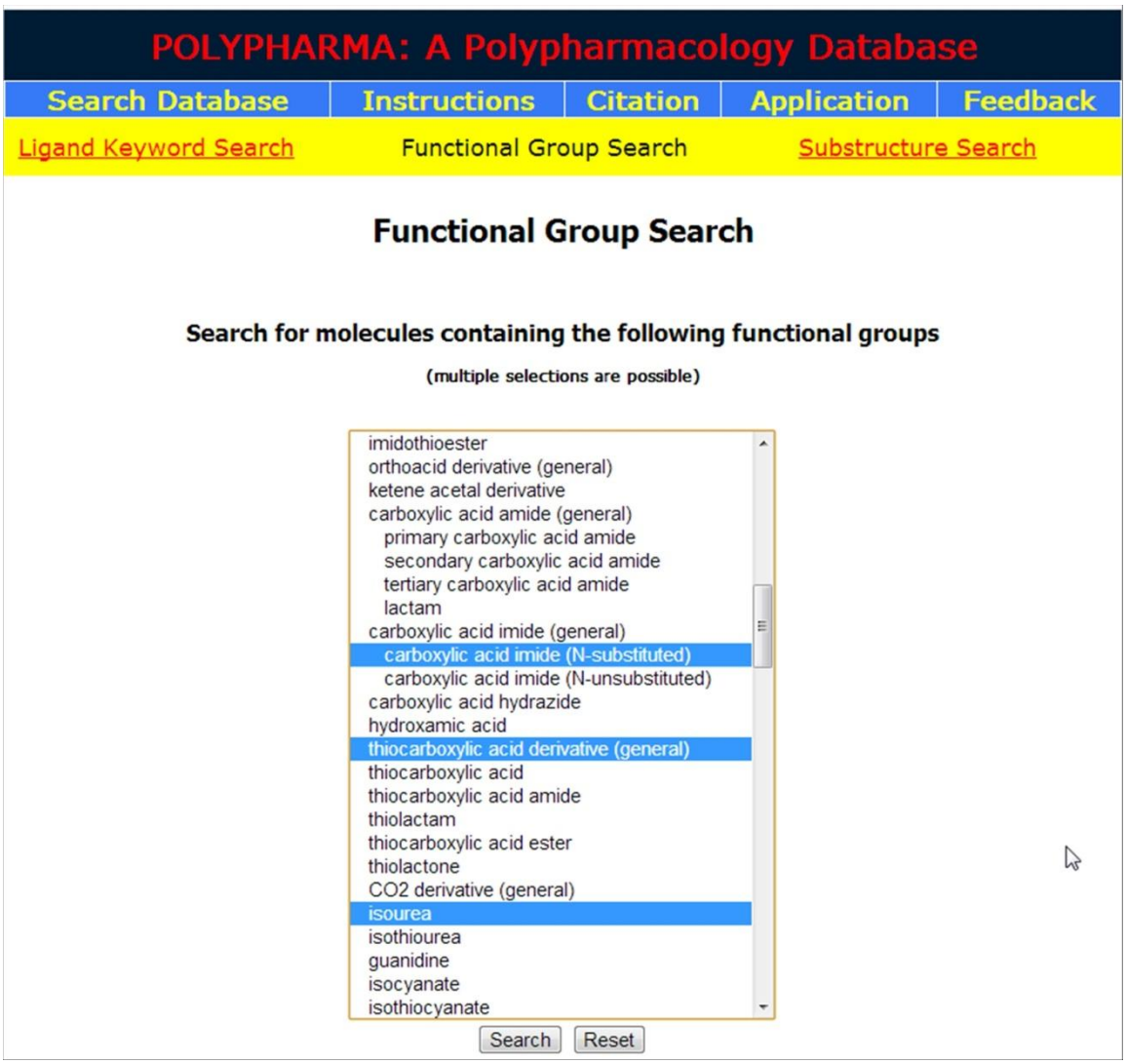

Figure S6. Screenshot of *functional group based search* page of the *Polypharma* database.

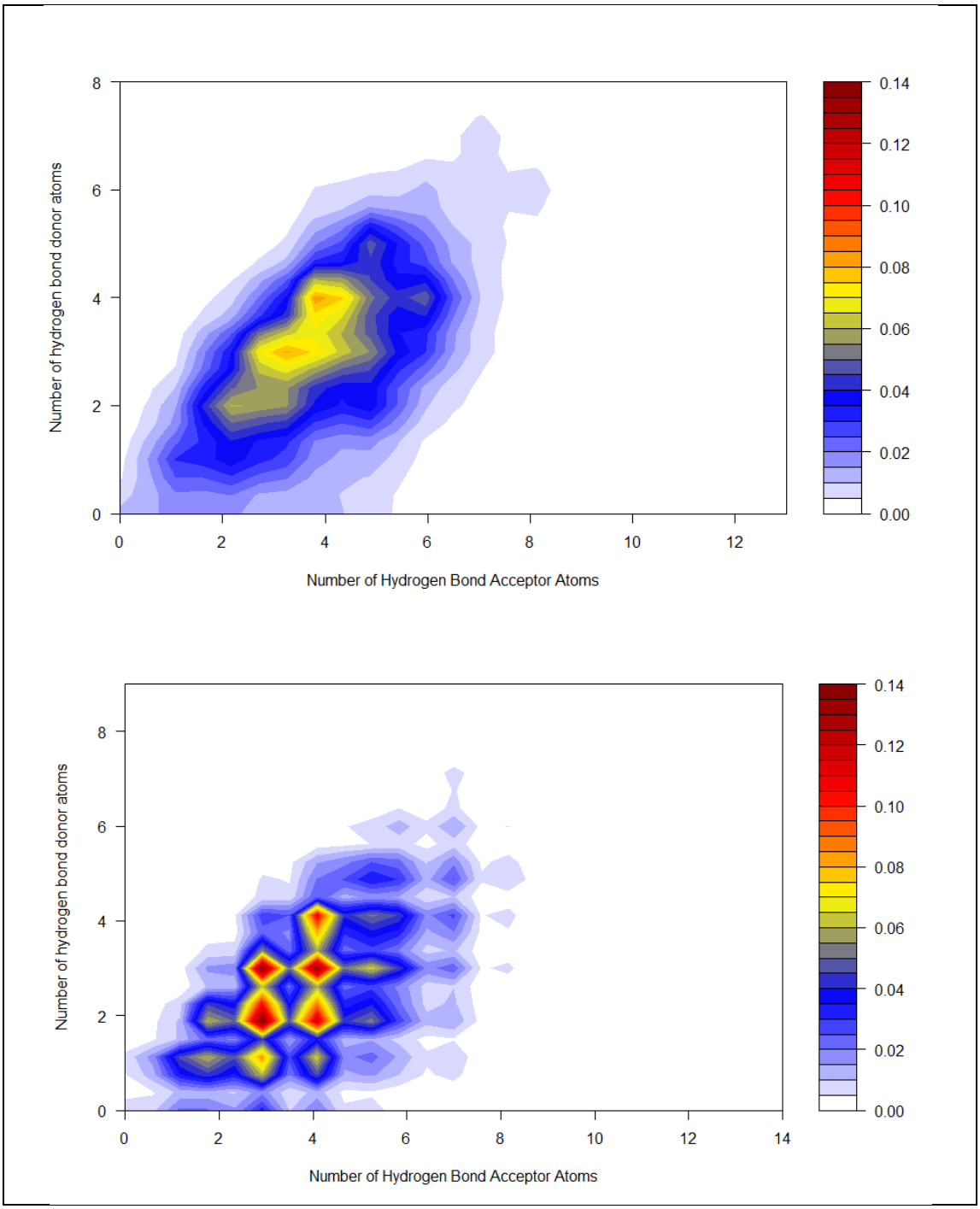

Figure S7A. Comparison of multi-targeted ligands vs. single-targeted ligands. The plots represent the distribution density of the ligands in the 2D space in terms of Number of Hydrogen Bond Acceptors vs. Number of Hydrogen Bond Donors. The color represents the density as demonstrated by the bar. The color code and scale is the same for multi-targeting and single-targeting ligands.

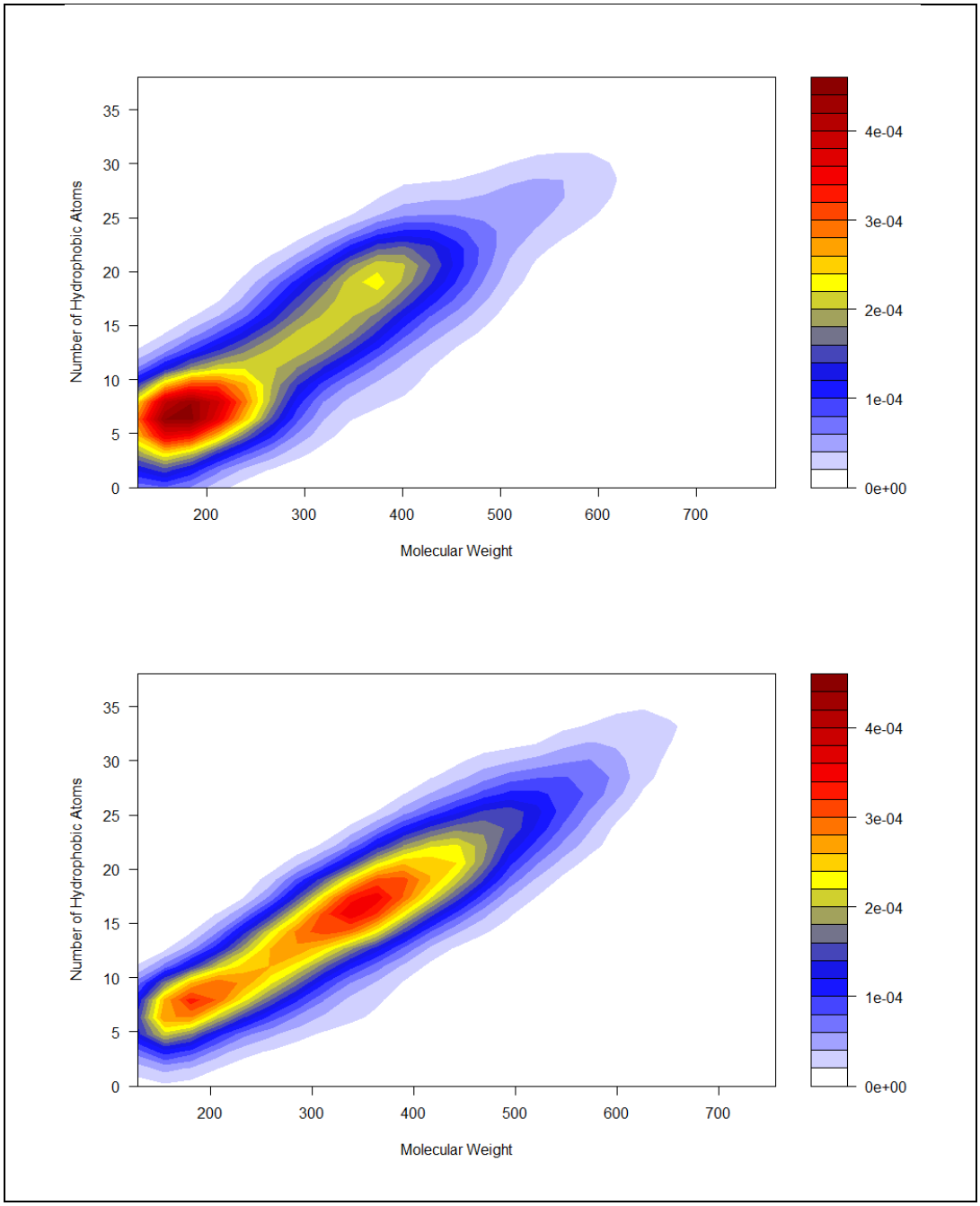

Figure S7B. Comparison of multi-targeted ligands vs. single-targeted ligands. The plots represent the distribution density of the ligands in the 2D space in terms of Molecular Weight vs. Number of Hydrophobic Atoms. The color represents the density as demonstrated by the bar. The color code and scale is the same for multi-targeting and single-targeting ligands.

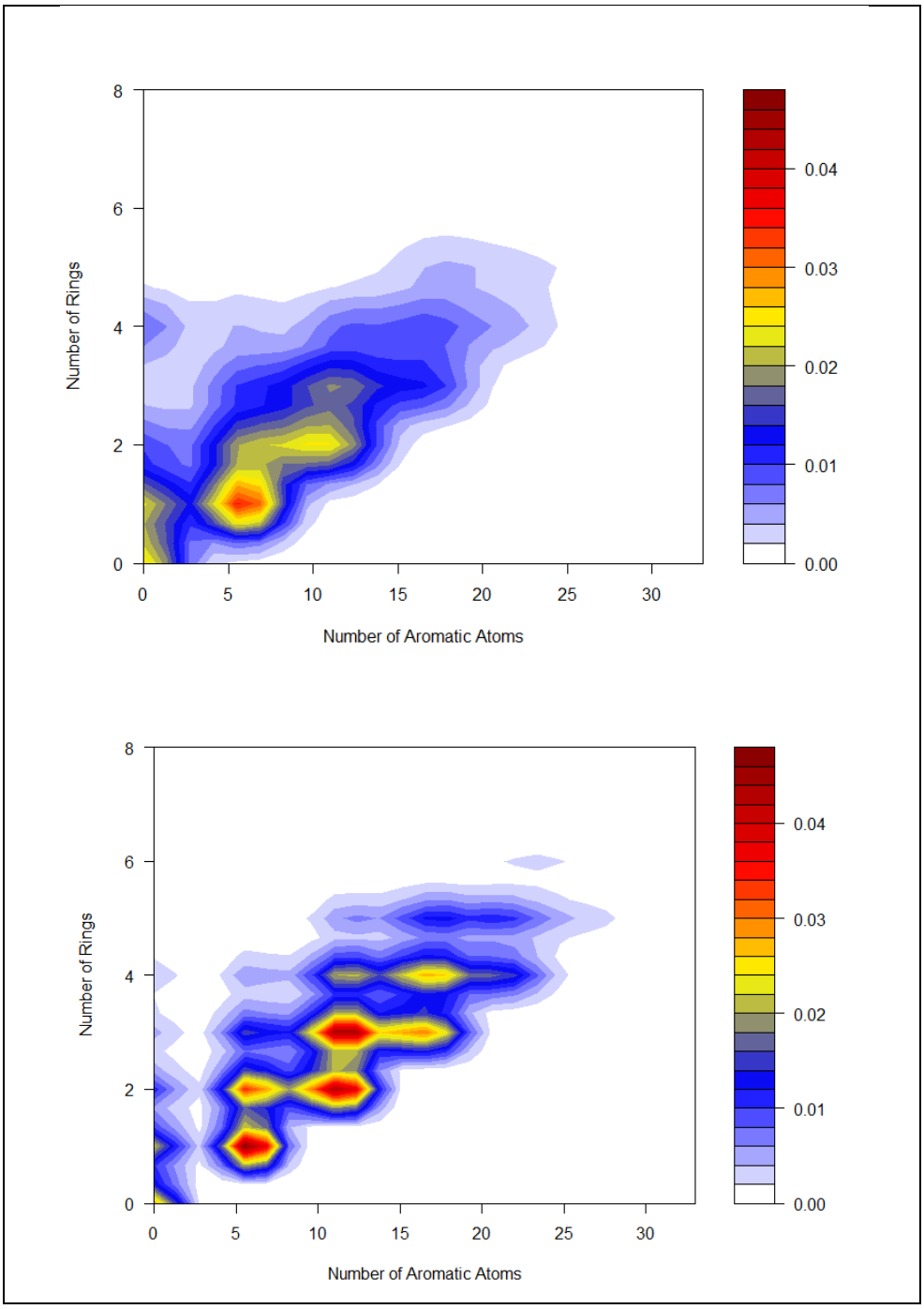

Figure S7C. Comparison of multi-targeted ligands vs. single-targeted ligands. The plots represent the distribution density of the ligands in the 2D space in terms of Number of Aromatic Atoms vs. Number of Rings. The color represents the density as demonstrated by the bar. The color code and scale is the same for multi-targeting and single-targeting ligands.

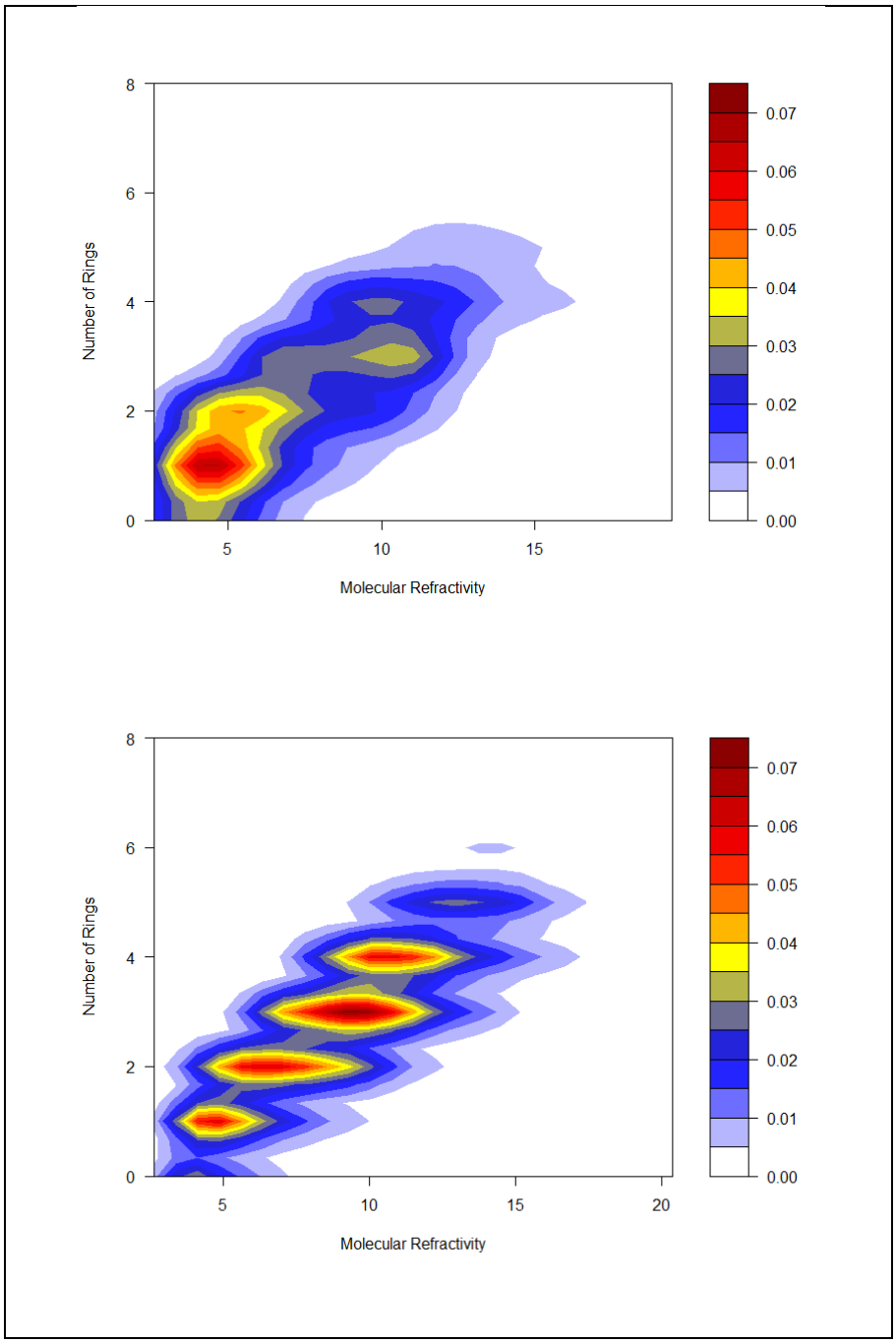

Figure S7D. Comparison of multi-targeted ligands versus single-targeted ligands. The plots represent the distribution density of the ligands in the 2D space in terms of Molecular Refractivity vs. Number of Rings. The color represents the density as demonstrated by the bar. The color code and scale is the same for multi-targeting and single-targeting ligands.

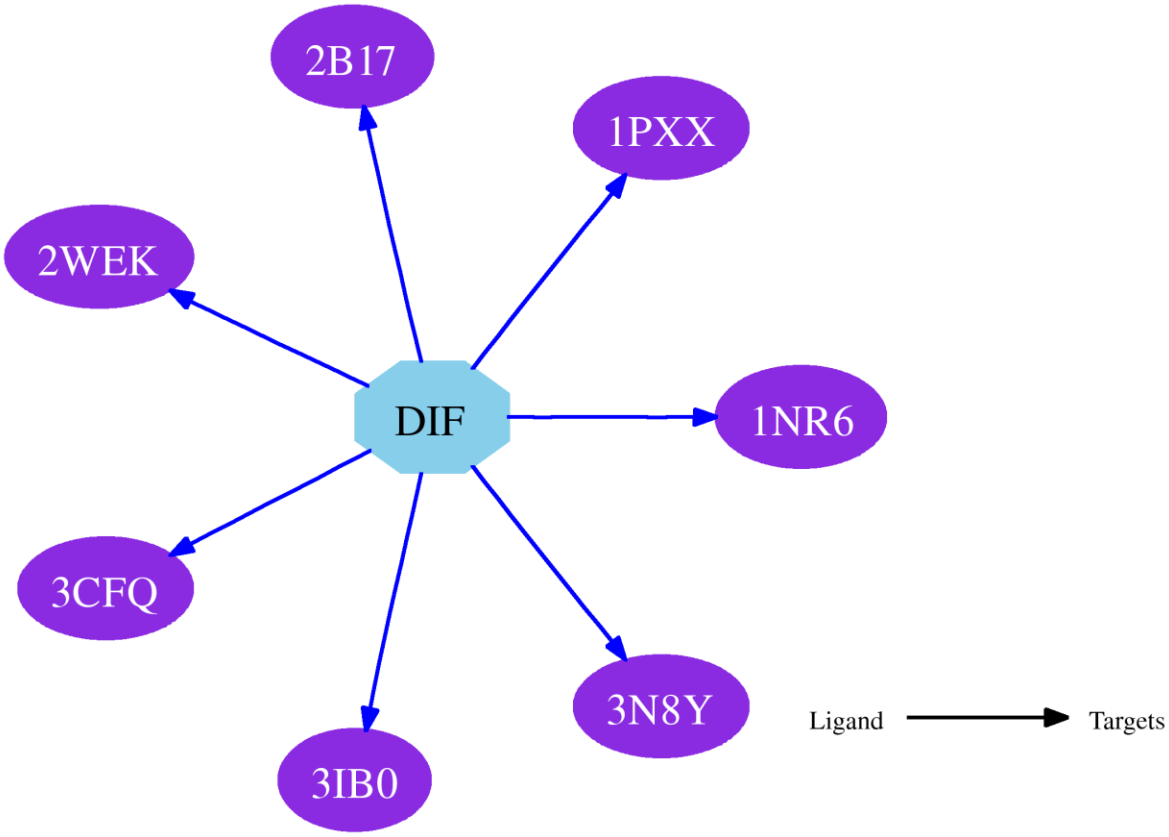

Figure S8. Depiction of ligand-protein network of diclofenac.

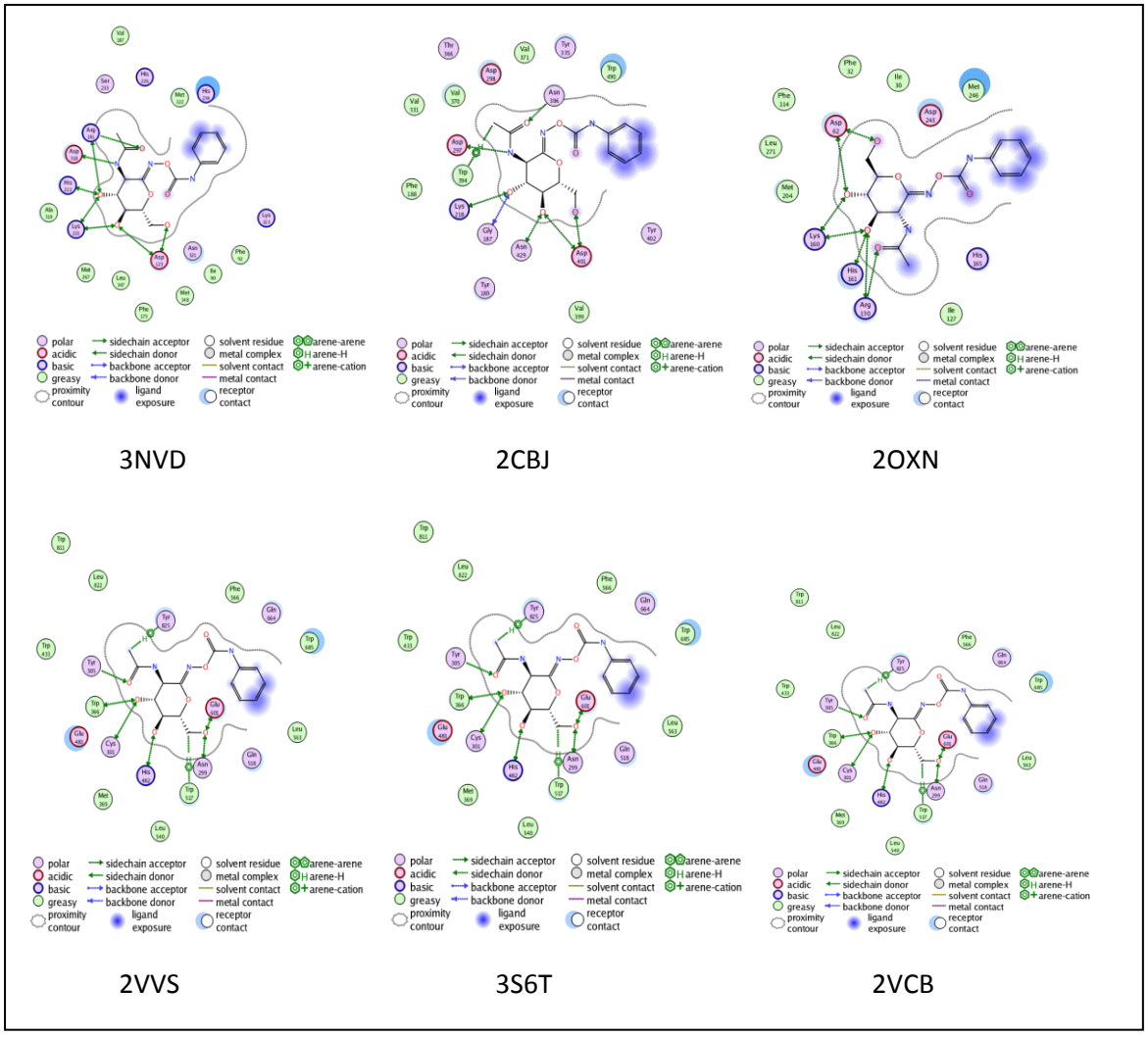

Figure S9A. Analysis of active sites and target-ligand interactions for OAN (PUGNAc) binding proteins.

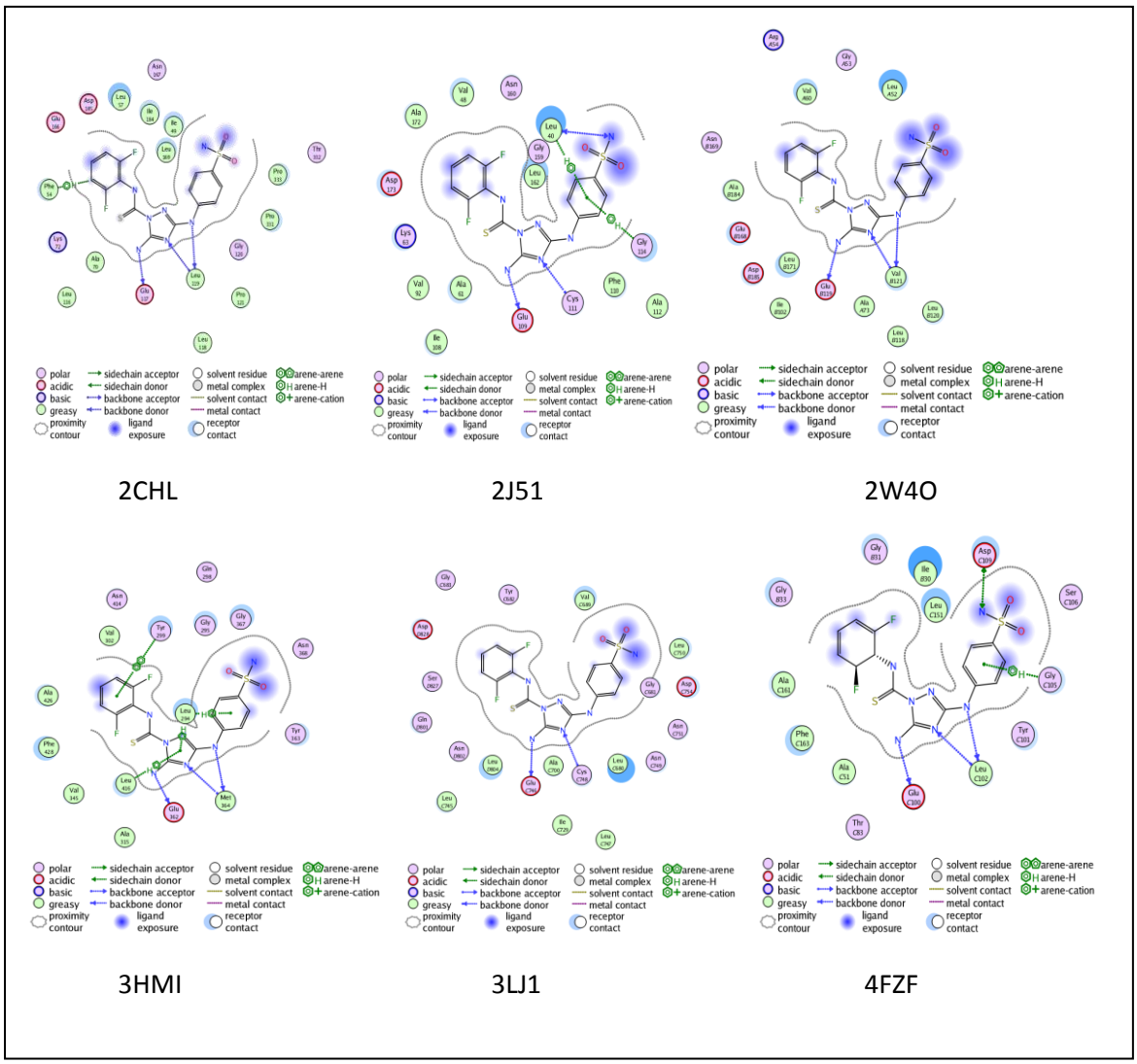

Figure S9B. Analysis of active sites and target-ligand interactions for DKI (5-amino-N-(2,6-difluorophenyl)-3-[(4-sulfamoylphenyl)amino]-1,2,4-triazole-1-carbothioamide) binding proteins.

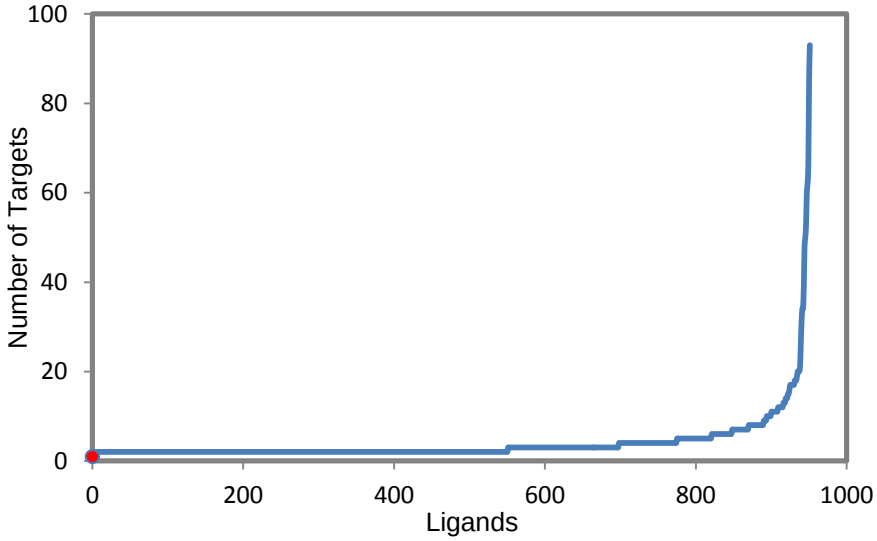

Figure S10. **Number of ligand-target complex structures for each ligand**. The red dot represents all of those single-targeting ligands (only a single crystal structure available for them).