

## Supplementary Document

**Table S1.** Frequency distribution of ligands by the number of distinct families they bind to.

Number of distinct IUPHAR families	Frequency
1	98750
2	16191
3	11

**Table S2.** List of the 11 ligands that bind to 3 different IUPHAR families.

Ligands InChIKey <sup>a</sup>	Abbreviation	Compound Class
XLWJPQQFJNGUPA-UHFFFAOYSA-N	XLWJ	Synthetic Organic
DTZDSNQYNPNCPK-UHFFFAOYSA-N	DTZD	Synthetic Organic
CLQVVPDAXJGBV-UHFFFAOYSA-N	CLQV	Synthetic Organic
AJLFQFYMLRXVHV-UHFFFAOYSA-N	AJLF	Not known
IKSHHOBCKJKOG-UHFFFAOYSA-N	IKSH	Not known
FQUAFMNPXPXOJE-UHFFFAOYSA-N*	FQUA	Not known
MLQFOEOUNIRULR-UHFFFAOYSA-N*	MLQF	Not known
YKMSTUDOGGAJEH-UHFFFAOYSA-N	YKMS	Not known
USZPQRMQYJIDII-UHFFFAOYSA-N	USZP	Not known
BYBLEWFAAKGYCD-UHFFFAOYSA-N*	BYBL	Not known
NKOPNLUYOHOGFZ-UHFFFAOYSA-N	NKOP	Not known

<sup>a</sup>InChIKey: International Chemical Identifier compact hashed code

\*Were excluded from further analysis

**Table S3.** List of ligands and the proteins they bind to for the control dataset.

Ligands PDB ID	Proteins UniProt ID	Protein PDB ID	GPCR	GPCR Class
0HK	P08173	5DSG	Yes	A
	P11229	5CXV	Yes	A
7LD	P28223	6WGT	Yes	A
	P41595	5TVN	Yes	A
7MA	O43613	6TOD	Yes	A
	O43614	5WQC	Yes	A
8NU	P14416	6CM4	Yes	A
	P28223	6A93	Yes	A
40F	Q14416	4XAQ	Yes	C
	Q14832	4XAR	Yes	C
89F	P28222	5V54	Yes	A
	P28223	6WH4	Yes	A
ADN	P29274	2YDO	Yes	A
	P30542	6D9H	Yes	A
GGL	O00222	6BSZ	Yes	C
	Q14416	5CNI	Yes	C
	Q14832	5CNK	Yes	C
GLU	A0A173M0G2	5X2P	Yes	TR2
	E9P5T5	4IO2	No	-
	P41594	3LMK	Yes	A

	P42264	3S9E	No	-
	Q14416	7MTR	Yes	A
SRO	P08908	7E2Y	Yes	A
	P37231	3ADV	No	-
97V*	P43220	5VEX	Yes	B
	P47871	5XF1	Yes	B
Z99	P41594	7FD9	Yes	C
	Q13255	3KS9	Yes	C
	Q14831	3MQ4	Yes	C
	Q14832	7WI6	Yes	C

\*Predicted pockets did not include the pocket for ligand, as a result was excluded from further analysis.