

## **Challenges Predicting Ligand-Receptor Interactions of Promiscuous Proteins:**

### **The Nuclear Receptor PXR**

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**Table S6** CoMFA outlier analysis (Bold = outliers).

		Exp. Activity	Pred. Activity	Residual
PR1	Pregnanediol	5.29	5.67	0.378
PR2	Pregnanedione	5.59	5.36	-0.225
PR4	Cortexolone	4.64	5.09	0.452
PR5	Aldosterone	4.26	4.74	0.480
PR7	Progesterone	4.83	5.08	0.247
PR8	17-Hydroxyprogesterone	4.75	4.91	0.158
PR9	Cortexone	5.61	4.64	-0.973
PR10	Cortisol	4.32	4.49	0.168
PR11	<i>17-Hydroxypregnenolone</i>	<b>4.47</b>	<b>2.47</b>	<b>-2.005</b>
PR13	Pregnenolone carbonitrile (PCN)	<b>2.00</b>	<b>3.47</b>	<b>1.470</b>
PR14	Allopregnanolone	5.38	4.52	-0.856
PR15	Allopregnanediol	4.28	5.01	0.730
PR17	Cortol	4.33	4.71	0.384
PR18	Cortolone	4.35	4.18	-0.170
PR19	Tetrahydrocortisone	4.28	4.26	-0.018
PR20	THDOC	4.90	4.78	-0.123
PR22	17 $\alpha$ ,20 $\beta$ -Dihydroxyprogesterone sodium sulfate	5.73	5.07	-0.656
PR23	5 $\beta$ -Pregnan-3 $\alpha$ ,20 $\beta$ ,diol	5.42	5.48	0.061
PR24	Tetrahydrocortisol	4.33	4.10	-0.233
PR25	Pregnanolone	4.98	5.04	0.057
PR26	Pregnenolone sulfate	2.00	2.79	0.790
PR27	Levonorgestrol	5.37	6.11	0.743
PR28	Norethindrone	4.59	4.14	-0.452