Supplemental Material

Functional Validation of Virtual Screening for Novel Agents with General Anesthetic Action at Ligand-Gated Ion Channels

Stephanie A. Heusser, Rebecca J. Howard, Cecilia M. Borghese, Madeline A. Cullins, Torben Broemstrup, Ui S. Lee, Erik Lindahl, Jens Carlsson, R. Adron Harris

Molecular Pharmacology

Supplemental Table 1. Complete list of predicted ligands from the docking screen. The docking rank is the position of the compound in the list of 153,000 screen molecules that was sorted based on their predicted binding energies.

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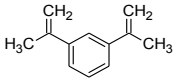
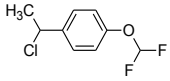
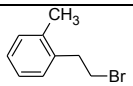
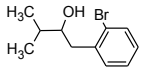
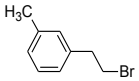
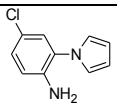
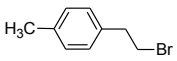
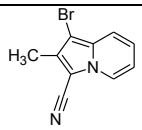
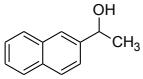
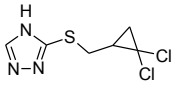
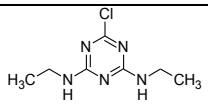
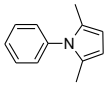
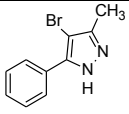
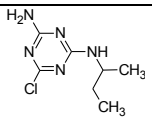
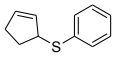
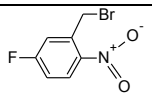
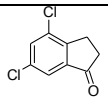
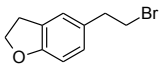
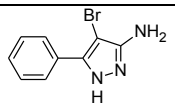
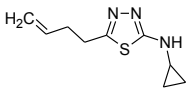
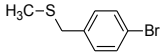
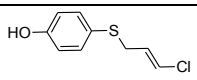
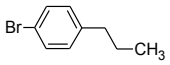
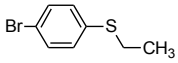
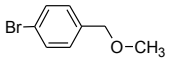
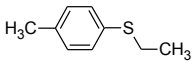
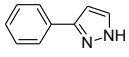
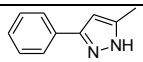
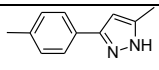
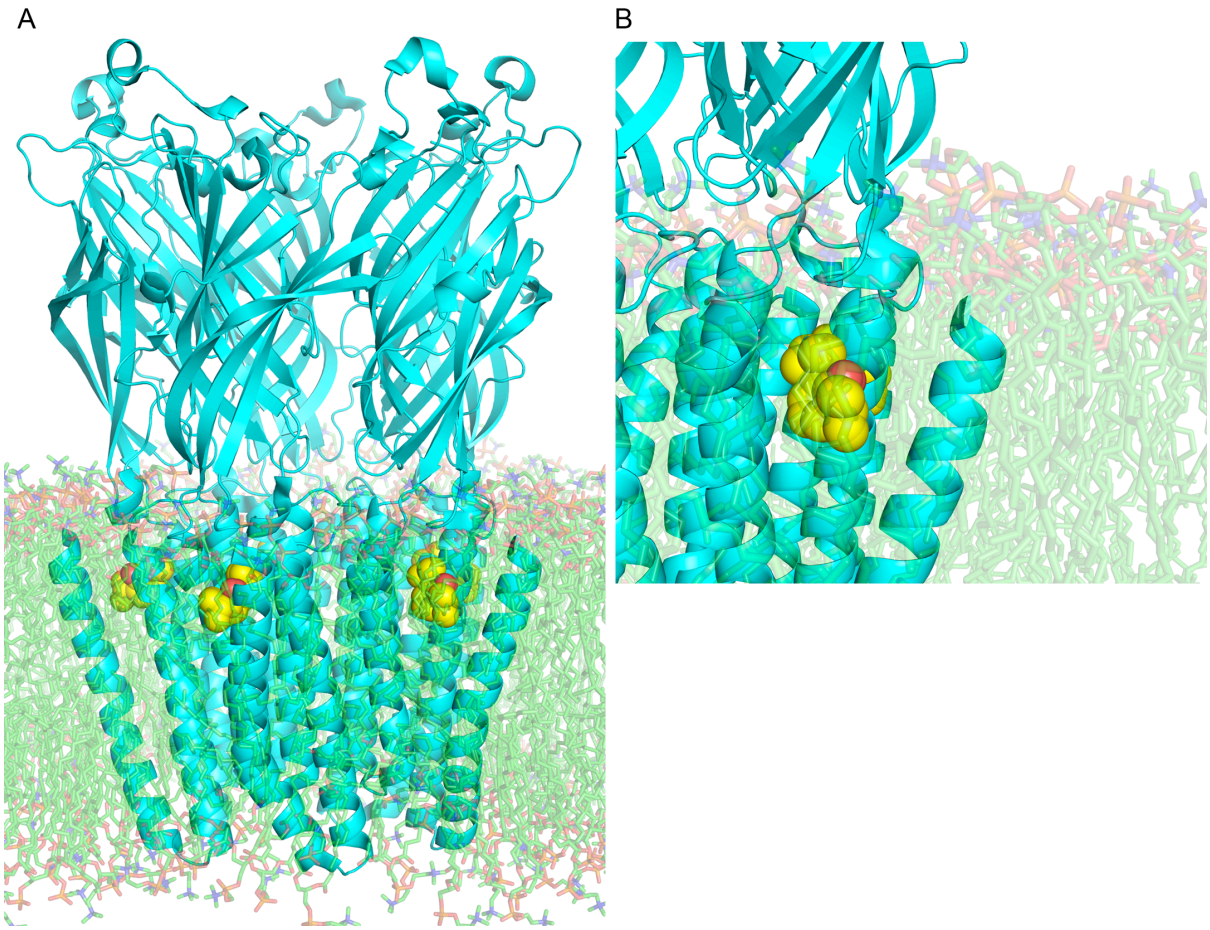
1		156	**12**		419
2		698	**13**		18
3		351	**14**		235
4		350	**15**		67
5		465	**16**		335
6		27	**17**		111
7		9	**18**		166
8		208	**19**		336
9		179	**20**		280

10		68	**21**		497
11		313	**22**		399

Supplemental Table 2. Analogs of hit compounds from the docking screen.

	Structure	Analog to compound
23		**11**
24		**11**
25		**11**
26		**4**
27		**7**
28		**7**
29		**7**

Supplemental Figure 1. Crystal structure of the GLIC-propofol complex in MD equilibrated DOPC membrane. Water molecules and ions have been removed. Propofol is shown as spheres (yellow), the membrane is shown as transparent sticks (green), and GLIC is shown as cartoon (cyan). (A) Side view (B) Propofol binding site. This figure was generated with PyMOL (version 1.4.1).



Supplemental Figure 2. Effect of compounds identified on the virtual screen on propofol modulation of GABA responses. Compounds (50 μM) were co-applied with propofol (2 μM) and EC_{10} GABA on α1β2γ2 $GABA_A$ receptors expressed in oocytes. The compound alone (50 μM) was pre-applied for 1 min, immediately followed by co-application of the compound with 2 μM propofol for 1 min, and then co-application of the compound, propofol and EC_{10} GABA for 30s. As with other protocols, EC_{10} GABA was applied for 30s before and after each co-application. The potentiation obtained when each compound was co-applied with propofol was then calculated as the percentage of the potentiation by propofol alone (assigned a 100% value) obtained in that same oocyte. *p< 0.05 versus potentiation induced by propofol alone (100%), one-sample t-test versus a hypothetical value of 100, n= 4-5.