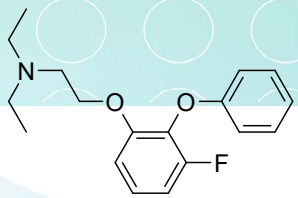
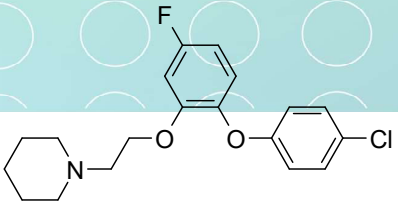
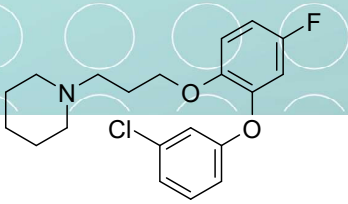
SL-05. Ion Channel Modulators. $Na_v1.8$

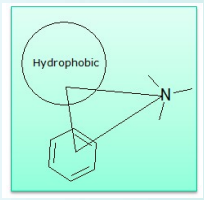
The blockage of voltage-gated sodium channels may effectively control such pathological conditions as chronic pain, epilepsy, and different arrhythmias. Those located in nervous system tetrodotoxin-resistant $Na_v1.8$ and tetrodotoxin-sensitive $Na_v1.7$ are known to be critical for the sensation of pain and have a relatively small number of side effects [1]

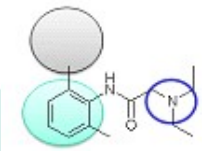
The analysis of several well-known ion-channel blockers revealed common pharmacophoric features: two hydrophobic regions and a basic nitrogen (i.e. lidocaine and amitriptyline). To exploit this pharmacophore model, a library of structurally novel biaryl ethers was created and tested *in vitro* in the human $Na_v1.8/\beta3$ sodium channel cell line. Some compounds demonstrated activity at $Na_v1.8$ channel comparable with the activity of amitriptyline – a nonspecific modulator of Na and K ion channels.



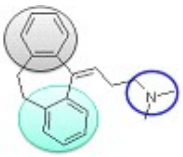








Lidocaine



Amitriptyline

Signature Library 05

Formats	Supplementary Information
80 compounds per plate	$Na_v1.8$ Inhibition% TP1/TP2 @1 µM
0.1 mg; 1 mg; 2 mg dry film/powder	Solubility data in PBS
0.1 µmol; 1 µmol DMSO solutions	SL#5_ICh_04-16.sdf

References:

1. *ChemMedChem* Special Issue: Ion Channel Drug Discovery Volume 7, Issue 10, pages 1712–1740 doi: 10.1002/cmdc.201200298.

Contact us:

USA:	+1 336 721 1617	mparisi@asinex.com
Japan:	+81-80-3401-9097	sota@asinex.com
Europe/Global:		lsadovenko@asinex.com