3050 Spruce Street
Saint Louis, Missouri 63103 USA
Telephone (800) 325-5832 (314) 771-5765
Fax (314) 286-7828
email: techserv@sial.com
sigma-aldrich.com

ProductInformation

ION CHANNEL MODULATOR LIGAND-SET™

Product Number **L 6912**
Storage Temperature –20 °C

Product Description

The Ion Channel Modulator LIGAND-SET™ is a set of 80 small organic ligands which modulate the activity of monovalent and calcium ion channels. These ligands are arrayed in a standard 96-well plate format; each well has a capacity of 1 ml.

This set can be used for screening new drug targets, for guiding secondary screens of larger, more diverse libraries and for standardizing and validating new screening assays.

Ion channels are gated pores within the cell membrane that regulate the passage of ions into and out of the cell. The ions of primary importance for signal transduction are Ca^{2+}, K^{+}, Cl^{-} and Na^{+}. The entry of these ions triggers certain events within the cell and allows for the transduction of electricochemical signals between the cells.

Structurally, ion channels are composed of several protein subunits that form the channel. These subunits often have modulatory sites or receptors that can be targeted by certain ligands. Antibodies have also helped to elucidate the nature of these channels and their functions. By developing antibodies to the subunits, their activity can be monitored to determine their function within the channel architecture and to elucidate the function of the channel in the cell. More recently, small organic ligands with specificity for one or two subunits have been developed which have been used to further to characterize the structure and function of the ion channel.

Dysfunctions of ion channels have been implicated in numerous pathologies, from heart disease to epilepsy to hair loss. Ligands active at certain ion channel receptors have found use as anesthetics, typically in topical applications. The most potent blockers of ion channels are toxins isolated from various species of spiders, scorpions, snails and snakes.

Components/Reagents

The Ion Channel Modulator LIGAND-SET™ contains 2 mg of each ligand per well. Stock solutions can be readily prepared by adding 1 ml of DMSO to each well. The set also comes with a diskette containing a structure database, or SD file, and a Microsoft Excel file containing the catalog number, name, rack position and pharmacological characteristics of each ion channel modulator. The following is a listing of all the modulators included:

A1052	4-Aminopyridine
A2129	GABA
A-251	A-85380 dihydrochloride
A-263	ATPA
A5909	N-Acetylprocainamide hydrochloride
A7410	Amiloride hydrochloride
A8423	Amiodarone hydrochloride
B0753	2,3-Butanedione monoxime
A9959	S-MAP4
B-171	1-BCP
B2296	(+/-)-Bay K 8644
B5016	Bepridil hydrochloride
C-105	CGS 19755
C-128	Clofilium tosylate
C-144	1-m(Chlorophenyl)-biguanide
C-191	Capsazepine
C-195	L-CCG-IV
C-271	CX546
C4024	Carbamazepine
C6019	Clotrimazole
C7522	Calcimycin
D1260	Decamethonium dibromide

D-129	R(+)-Butylindazone
D-149	Dihydro-beta-erythroidine hydrobromide
D-221	L-cis-Diltiazem hydrochloride
D2521	D-cis-Diltiazem hydrochloride
D4505	Phenytoin sodium
D5891	1,1-Dimethyl-4-phenyl-piperazinium iodide
D6035	Disopyramide phosphate
D9035	Diazoxide
D9175	Dantrolene sodium
F-131	FPL 64176
F4381	Furosemide
F8257	Flunarizine dihydrochloride
G-017	AMPA hydrobromide
G0639	Glibenclamide
G-117	Glipizide
G-154	Gabapentin
H-133	5-HTQ iodide
H2138	Hexamethonium dichloride
I-117	R(+)-IAA-94
O-104	Omeprazole
L5783	Lidocaine N-ethyl bromide quaternarysalt
L-110	LY-278,584 maleate
L5647	Lidocaine hydrochloride
M-107	MK-801 hydrogen maleate
M-109	2-Methylserotonin maleate
M-116	Metolazone
M-140	Methylcarbamylcholine chloride
M2028	Capsaicin
M4145	Minoxidil

M5644	(±)-Methoxyverapamil hydrochloride
M9020	Mecamylamine hydrochloride
N-134	(±)-Niguldipine hydrochloride
N-144	Nitrendipine
N-149	Nimodipine
N-170	NS-1619
N4779	5-Nitro-2-(3-phenylpropylamino)benzoic acid
N7510	Nicardipine hydrochloride
N7634	Nifedipine
P-154	Pinacidil
P-160	N-Phenylanthranilic acid
P-203	Phenamil methanesulfonate
P4543	Valproic acid sodium
P9391	Procainamide hydrochloride
Q0875	Quinidine sulfate
Q1250	Quinine sulfate
R-130	RJR-2403 hemigalacatarate
R-131	RJR-2429 dihydrochloride
S8251	Succinylcholine chloride
T0517	TMB-8 hydrochloride
T2265	Tetraethylammonium chloride
T4143	Triamterene
T5515	Thio-NADP sodium
T7508	Tetracaine hydrochloride
T8160	MDL-72222
V4629	(±)-Verapamil hydrochloride
W-105	S(-)-Willardiine
Y-101	YS-035 hydrochloride
Z4900	Zopiclone

Preparation Instructions

To create a new database in ISIS™/BASE :

- Open ISIS™/BASE.
- Choose **File>New database**.
- Enter **Ion Channel** or a preferred name in the File name field.
- Click **Save**.

The "Create Database" window will now be open.

- Enter **Catnum** for the Field name.
- Choose **Variable text** from the drop down window of the Type field.
- Click Add.
- Repeat the above steps for the following:

Field name	Type
Name	**Variable text**
Position	**Variable text**
Action	**Variable text**
Class	**Variable text**
Selectivity	**Variable text**
SecName	**Variable text**
Description	**Variable text**

- Enter **Structure** for the Field name.
- Choose **Structure** from the drop down window of the Type field.
- Enter ***Structure** for the External name.
- Click **Add**.
- Click **Save**.

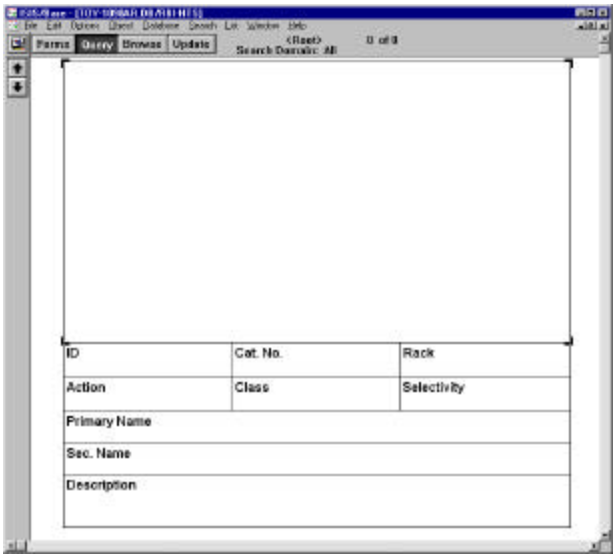
The main ISIS™/BASE window will now be open.

To create the Form:

- Click on the "Draw a box" button (second button down on the left of the screen).
- Move the mouse to the bottom left hand corner and draw a box, ½ inch high, the length of the screen by clicking on the left mouse button and dragging the mouse across the screen. (see figure below)
- Above this box, draw another ½ inch high box the length of the screen. (see figure below)
- Above this box, draw a third ½ inch high box the length of the screen. (see figure below)
- Above these long boxes draw 3 ½ inch high x 3 inch wide boxes. (see figure below)
- Above these 3 boxes, draw another three the same size. (see figure below)
- Draw a final box to fit the remaining space of the screen above these boxes. (see figure below)

Double click on the top box. This will open the Box properties window.

- Click on **Structure**.
- Click **OK**.



- Repeat the same steps, clicking on the appropriate field name for the appropriate box:

Box	Field name
First small box	**ID**
Second small box	**Catnum**
Third small box	**Position**
Fourth small box	**Action**
Fifth small box	**Class**
Sixth small box	**Selectivity**
First long box	**Name**
Second long box	**SecName**
Bottom long box	**Description**

- Choose **File>Save form**.
- Enter Ion Channel or preferred name.
- Click **OK**.

Importing an SD file:

- Click **Update**.
- Choose **File>Import>SD File**. ***NOTE:*** *For MAC users, you must hold down the* ***option key*** *while choosing* **File>Import>SD File**. *If you do not, the Ion Channel.sdf will not be visible in the import window.*
- Enter **Ion Channel.sdf** (Located on the floppy diskette provided with the plate).
- Click **Open**.

  The Import SD File window will now be open.
- Click on **Add a new record including structure**, on both sides of the table.
- Click **OK**.

The database is now ready to use.

Storage/Stability
Store plate -20°C with cap strips firmly in place. Plate cover should only be removed when plate is in use to prevent loss of caps strips.

References

1. De Waard, M., et al., "Structural and functional diversity of voltage-activated calcium channels." In *Ion Channels*, Volume 4 (T. Narahashi, Ed.), pp. 41, 87, Plenum Press, NY (1996).
2. Jentsch, T.J. and Gunther, W., "Chloride channels: An emerging molecular picture." *Bioessays* **19**, 117-126 (1997).
3. Chandy, K.G. and Gutman, G.A. "Voltage-gated potassium channel genes." In *Handbook of Receptors and Channels: Ligand and Voltage-Gated Ion Channels* R.A. North (Ed.) **1**, pp 1-71, CRC, Boca Raton, FL (1995).
4. Macdonald, R.L. and Kelly, K.M. "Mechanisms of action of currently prescribed and newly developed antiepileptic drugs." *Epilepsia* **35**, 541-550 (1994).

SMS 8/00