

## GLUTAMATERGIC LIGAND-SET™

Product Number **L6537**  
Storage Temperature -20°C

### Product Description

The Glutamatergic LIGAND-SET™ is a set of 80 small organic ligands which modulate Glutamate receptors. 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.

There are two families of glutamate receptors, G protein-coupled receptors (metabotropic) and ion channels (ionotropic). Glutamic acid is the endogenous ligand for both receptor families.

The metabotropic glutamate receptor family consists of 8 subtypes, mGluR<sub>1</sub> – mGluR<sub>8</sub>. These are further divided into three groups. Group I contains mGluR<sub>1</sub> and mGluR<sub>5</sub>, Group II contains mGluR<sub>2</sub> and mGluR<sub>3</sub> and Group III contains mGluR<sub>4,6,7,8</sub>. These groupings are based on amino acid sequence, linkage to second messenger systems, and pharmacological similarities between the members of the groups. Group I receptors signal through phosphoinositol whereas Group II and Group III inhibit adenylyl cyclase. In addition, members of all three groups interact directly with voltage-gated calcium or potassium channels through their G proteins. They are all widely distributed throughout the CNS and evidence exists for postsynaptic, presynaptic and, in some cases, glial localization.

The ionotropic family of glutamate receptors has three major subdivisions based on pharmacology and structural properties. The N-methyl-D-aspartate (NMDA) subtype is hetero-oligomeric consisting of an NR1 subunit combined with one or more NR2 (A-D) subunits. This receptor has two amino acid recognition sites, one for glutamate and one for glycine. Activation of both sites is required for ion channel opening. The channel is permeable to cations, including calcium, and is blocked by magnesium at membrane potentials close to the normal resting potential. NMDA receptors are post-synaptic and play an important role in synapse plasticity in the developing and mature CNS.

The  $\alpha$ -amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) subtype is a hetero-oligomer formed from

## Product Information

combinations of GLUR1-4 subunits. This ion channel is cation-permeable, but calcium permeability is regulated by an RNA editing mechanism in the GLUR2 subunit. AMPA receptors are also post-synaptic and mediate chemical transmission at the majority of fast excitatory synapses in the CNS.

The kainate subtype is a hetero-oligomer which has not been well defined. They are composed of GLUR5-7 and KA1 and KA2 subunits. The specific pharmacology of this receptor is not completely known due to a lack of specific agonists and antagonists for the receptor. The role of kainate receptors is not yet clear, but at least in the hippocampus, there is evidence for a presynaptic location.

### Components/Reagents

The Glutamatergic 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 ligand. The following is a listing of all the ligands included:

A0326	(S)-AMPA zwitterion
A0384	Arcaïne sulfate
A-155	trans-(±)-ACPD
A-172	(±)-1-Aminocyclobutane-cis-1,3-dicarboxylic acid
A1910	(±)-2-Amino-4-phosphonobutyric acid
G3166	GYKI 53655
A-243	cis-Azetidine-2,4-dicarboxylic acid
A-244	trans-Azetidine-2,4-dicarboxylic acid
A-254	AIDA
A-263	ATPA
A-266	(R)-AMPA zwitterion
A4910	(±)-2-Amino-3-phosphonopropionic acid

A5157	(±)-2-Amino-7-phosphonoheptanoic acid
A5282	(±)-2-Amino-5-phosphonopentanoic acid
A5930	N-Acetyl-L-aspartyl-L-glutamic acid
A7250	L-Cysteine, N-Acetyl-
A9256	L-Aspartic acid
A9699	(±)-HA-966
A9950	Aniracetam
A9959	S-MAP4
B-171	1-BCP
C0306	7-Chlorokynurenic acid
C-104	(±)-CPP
C1835	S(+)-4-Carboxyphenylglycine
C-189	D-CPP
C-195	L-CCG-IV
C-237	L-CCG-I
C-239	CNQX disodium
C-271	CX 546
C3909	D-Cycloserine
C7522	Calcimycin
C7880	L-Cysteine hydrochloride
C9847	Cyclothiazide
D0540	DNQX
D-104	4-DAMP methiodide
D-127	Dextrorphan D-tartrate
D-133	6,7-Dichloroquinoxaline-2,3-dione
D-138	5,7-Dichlorokynurenic acid
D2531	Dextromethorphan hydrobromide
D2639	1,10-Diaminodecane
F0778	Felbamate

F-109	5-Fluoroindole-2-carboxylic acid
A7929	L(+)-2-Amino-4-phosphonobutyric acid
G-017	(±)-AMPA hydrobromide
G1001	D-Glutamic acid
G-119	GYKI 52466 hydrochloride
K0250	Kainic acid
G2128	L-Glutamic acid hydrochloride
G2879	Glycine hydrochloride
G3126	L-Glutamine
G3894	D-gamma-Glutamylaminomethanesulfonic acid
H-174	(±)-3-Hydroxy-phenylglycine
I2765	(±)-Ibotenic acid
I2892	Ifenprodil tartrate
K3375	Kynurenic acid
M-107	(+)-MK-801 hydrogen maleate
M-108	(-)-MK-801 hydrogen maleate
M-166	MDL 26,630 trihydrochloride
M1684	(2S,3S,4S)-2-methyl-2-(carboxycyclopropyl)glycine
M-216	MDL 105,519
M3262	N-Methyl-D-aspartic acid
M9292	Memantine hydrochloride
N-179	NS 102
N-183	NBQX disodium
P0547	Pentamidine isethionate
P0878	O-Phospho-L-serine
P1801	L-Glutamic acid, N-phthaloyl-
P-209	Phthalamoyl-L-glutamic acid trisodium
P-234	PMPA tetrasodium
P7575	L-trans-Pyrrolidine-2,4-dicarboxylic acid

P8782	(±)-cis-Piperidine-2,3-dicarboxylic acid
P6320 4	Quinolinic acid
Q2128	(+)-Quisqualic acid
R-116	Riluzole
S2501	Spermidine trihydrochloride
S2876	Spermine tetrahydrochloride
S4250	D-Serine
W-105	S(-)-Willardiine
W-110	S(-)-5-Iodo-willardiine

### Preparation Instructions

To create a new database in ISIS™/BASE :

- Open ISIS™/BASE.
- Choose **File>New database**.
- Enter **Glutamatergic** 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:

<u>Field name</u>	<u>Type</u>
<b>Name</b>	<b>Variable text</b>
<b>Position</b>	<b>Variable text</b>
<b>Action</b>	<b>Variable text</b>
<b>Class</b>	<b>Variable text</b>
<b>Selectivity</b>	<b>Variable text</b>
<b>SecName</b>	<b>Variable text</b>
<b>Description</b>	<b>Variable text</b>

- 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:

<u>Box</u>	<u>Field name</u>
First small box	<b>ID</b>
Second small box	<b>Catnum</b>
Third small box	<b>Position</b>
Fourth small box	<b>Action</b>
Fifth small box	<b>Class</b>
Sixth small box	<b>Selectivity</b>
First long box	<b>Name</b>
Second long box	<b>SecName</b>
Bottom long box	<b>Description</b>

- Choose **File>Save form**.
- Enter Glutamatergic 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 *Glutamatergic.sdf* will not be visible in the import window.
- Enter **Glutamatergic.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. Pin, J.-P. and Duvoisin, R., "The metabotropic glutamate receptors: Structure and functions." *Neuropharmacology* **34**, 1-26 (1995).
2. Nicoletti, F., et al., "Metabotropic glutamate receptors: A new target for the therapy of neurodegenerative disorders." *Trends Neurosci.* **19**, 267-271 (1996).
3. Lerma, J., "Kainate reveals its target." *Neuron* **19**, 1155-1158 (1997).
4. Mori, H., and Mishina, M., "Structure and function of the NMDA receptor channel." *Neuropharmacology* **34**, 1219-1237 (1995).

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