PURINES/PYRIMIDINES LIGAND-SET™

ProductInformation

Product Number **L2538**
Storage Temperature -20°C

Product Description

The Purines/Pyrimidines LIGAND-SET™ is a set of 64 small organic ligands to the Adenosine and Purinergic 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.

Adenosine receptors are known to consist of four subtypes, A_1, A_{2A}, A_{2B} and A_3. The majority of the known agonists are derivatives of adenosine. They are of interest as potential anti-arrhythmic, cerebro-protective and cardioprotective agents via the A_1 receptor and as hypotensive and antipsychotic agents via the A_{2A} receptor. The A_3 receptor is the most recently discovered subtype and has a unique pharmacological profile, tissue distribution and effector coupling. The first selective A_3 agonists and antagonists have only recently been identified. A_3 specific antagonists have potential in treating inflammatory disorders.

Surface receptors for extracellular nucleotides were originally called the P2 purinoceptors. They are now collectively known as the P2 receptors since it was found that some are activated by pyrimidine nucleotides as well as by purine nucleotides. Based on both the signal transduction mechanisms and on the molecular structure of the receptors, there are two families of P2 receptors: the P2X receptors are ligand-gated ion channels, and the P2Y receptors are G protein-coupled receptors.

The P2X family is made up of 7 subtypes, $P2X_{1-7}$. The receptors show 30-50% homology at the amino acid level. Recombinant $P2X_{1-7}$ receptors have been shown to form homomultimeric assemblies, but endogenous P2X receptors in tissues may also exist as heteromultimeric assemblies (e.g., $P2X_2$ and $P2X_3$ at the P2X receptor in the nodose ganglion). The P2X receptor family members show pharmacological and operational differences; agonist potency variations between subtypes; and considerable variation in the kinetics of inactivation and deactivation.

The P2Y family is made up of 11 subtypes, $P2Y_{1-11}$. Each receptor binds to a single heterotrimeric G protein, although the $P2Y_{11}$ can couple to both $G_{q/11}$ and G_s. P2Y receptors do not form heteromultimeric assemblies with other P2Y subtypes, but many tissues show coexpression of subtypes (e.g., $P2Y_1$ and $P2Y_2$ subpopulations in endothelial cells). The P2Y receptors show 25-55% homology at the amino acid level.

Components/Reagents

The Purines/Pyrimidines 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 structural 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:

A-001	7-(β-Chloroethyl)theophylline
A-003	1,3-Diethyl-8-phenylxanthine
A-013	8-(p-Sulfophenyl)theophylline
A-022	1,3-Dipropyl-8-p-sulfophenylxanthine
A-023	2-Methylthioadenosine triphosphate tetrasodium
A-024	5'-N-Methyl carboxamidoadenosine
A-025	1-Methylisoguanosine
A-111	Adenosine amine congener
A-144	1-Allyl-3,7-dimethyl-8-phenylxanthine
A-145	1-Allyl-3,7-dimethyl-8-p-sulfophenylxanthine
A1755	Aminophylline
A-202	N6-2-(4-Aminophenyl)ethyladenosine
A-236	N6-(4-Aminobenzyl)-N-methylcarboxamidoadenosine
A-242	Alloxazine
A2754	Adenosine 5'-diphosphate sodium salt

A7699	Adenosine 5'-triphosphate disodium salt
A9251	Adenosine
B-152	N6-Benzyl-5'-N-ethylcarboxamidoadenosine
B6894	N6-Benzyladenosine
C0750	Caffeine
C-101	8-Cyclopentyl-1,3-dipropylxanthine
C-102	8-Cyclopentyl-1,3-dimethylxanthine
C-103	5'-(N-Cyclopropyl)carboxamidoadenosine
C-141	CGS-21680 hydrochloride
C-142	2-Chloro-N6-cyclopentyladenosine
C-145	2-Chloroadenosine triphosphate tetrasodium
C-192	Chlormezanone
C-197	8-(3-Chlorostyryl)caffeine
C-199	CGS-15943
C-277	Chloro-IB-MECA
C5134	2-Chloroadenosine
C8031	N6-Cyclopentyladenosine
D1262	P1,P4-Di(adenosine-5')tetraphosphate triammonium
D-130	DPMA
D5385	1,7-Dimethylxanthine
D6938	Diinosine pentaphosphate
D9766	Dipyridamole
E-114	erythro-9-(2-Hydroxy-3-nonyl)adenine hydrochloride
E2387	5'-N-Ethylcarboxamidoadenosine
I-146	IB-MECA
I5879	3-Isobutyl-1-methylxanthine
M1434	2-Methylthioadenosine monophosphate triethylammonium salt
M-152	2-Methylthioadenosine diphosphate trisodium
M-225	Metrifudil

M-227	MRS-1191
M-228	MRS-1120
M3808	MRS 2179
M5501	N6-Methyladenosine
M6517	α,β-Methylene adenosine 5'-triphosphate dilithium
N-128	S-(4-Nitrobenzyl)-6-thioguanosine
N-154	N6-Cyclopentyl-9-methyladenine
N2255	S-(4-Nitrobenzyl)-6-thioinosine
P-101	2-Phenylaminoadenosine
P-107	N6-2-Phenylethyladenosine
P-108	N6-Phenyladenosine
P-178	PPADS
P4532	R(-)-N6-(2-Phenylisopropyl)adenosine
P5679	3-n-Propylxanthine
S2671	Suramin hexasodium
T1633	Theophylline
T4500	Theobromine
U4125	Uridine 5'-diphosphate sodium salt
U6872	Uridine 5'-triphosphate tris sodium salt
X-103	Xanthine amine congener

Preparation Instructions

To create a new database in ISIS™/BASE :

- Open ISIS™/BASE.
- Choose **File>New database**.
- Enter **Purines-Pyrimidines** 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 Purine-Pyrimidine 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 Purines-Pyrimidines.sdf will not be visible in the import window.*
- Enter **Purines-Pyrimidines.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. Fredholm, B.B., et al., "Nomenclature and classification of purinoceptors." *Pharmacol. Rev.*, **46**, 143-156 (1994).
2. Jacobson, K.A., et al., "Adenosine receptors: Pharmacology, structure-activity relationships and therapeutic potential." *J. Med. Chem.*, **35**, 407-422 (1992).
3. Burnstock, G., "The past, present and future of purine nucleotides as signaling molecules." *Neuropharmacology*, **36** 1127-1139 (1997).

SMS 8/00