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ProductInformation

ADRENERGIC LIGAND-SET™

Product Number **L 0383**
Storage Temperature –20 °C

Product Description

The Adrenergic LIGAND-SET™ is a set of 48 small organic ligands to adrenergic 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.

The adrenergic receptors are divided into three types, α_1, α_2 and β, each with several subtypes. Each type has a distinct function and pharmacology.

There are three subtypes of α_1 adrenergic receptors, α_{1A}, α_{1B} and α_{1D}. α_1 Adrenergic receptors are widely distributed in the central and peripheral nervous systems, where their activation generally results in depolarization and increased neuronal firing rate. In the periphery, they are activated by either norepinephrine released from sympathetic nerve terminals or epinephrine released from the adrenal medulla. Activation of these receptors mediates a wide variety of functions, including contraction of smooth muscle, cardiac stimulation, cellular proliferation and activation of hepatic gluconeogenesis and glycogenolysis. Most of the peripheral actions of α_1 adrenergic receptors are mediated through the inositol phosphate second messenger pathway, while there is evidence that α_1 receptors in the CNS activate adenylyl cyclase within the CNS.

There are four subtypes of α_2 adrenergic receptors, α_{2A}, α_{2B}, α_{2C} and α_{2D}. The α_2 adrenergic receptors are also widely distributed and activated by norepinephrine and epinephrine. The most well-characterized action is the inhibition of the release of neurotransmitter from many peripheral and central neurons by prejunctional α_2 receptors. α_2 receptors are also present at postjunctional sites, where they mediate actions such as smooth muscle contraction, platelet aggregation and inhibition of insulin secretion.

There are three subtypes of β adrenergic receptors, β_1, β_2 and β_3. These are also activated by norepinephrine and epinephrine and are widely distributed. Activation of β adrenergic receptors results in stimulation of cardiac rate and force, relaxation of vascular, urogenital and bronchial smooth muscle, stimulation of renin secretion from the juxta-glomerular apparatus, stimulation of insulin and glucagon secretion from the endocrine pancreas, stimulation of glycogenolysis in liver and skeletal muscle, and stimulation of lipolysis in adipocytes. Prejunctional β adrenergic receptors are present on some central and peripheral nerve terminals, where their activation results in facilitation of stimulation-evoked neurotransmitter release. However, in contrast to the prejunctional α_2 receptors, activation of prejunctional β receptors do not appear to have major physiologic significance.

Components/Reagents

The Adrenergic 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 an ISIS/Base Structure Data (SD) file and a Microsoft Excel file containing structural information as well as the catalog number, name, rack position and pharmacological characteristics of each ligand. The following is a listing of all the ligands included:

A0779	p-Aminoclonidine hydrochloride
A7655	(±)-Atenolol
A-131	Alprenolol hydrochloride
A9512	L(-)-Arterenol (Norepinephrine) bitartrate
B-012	6-Fluoronorepinephrine hydrochloride
B-016	Benoxathian hydrochloride
B-019	Phenoxybenzamine hydrochloride
B-154	BU224 hydrochloride
B-161	B-HT 933 dihydrochloride
B-162	B-HT 920 dihydrochloride
B-169	BRL 37344 sodium
B2656	Benextramine tetrahydrochloride
B8406	Bretylium tosylate
C-125	(±)-CGP-12177A hydrochloride
C-223	Cirazoline hydrochloride
C-231	CGP 20712A methanesulfonate
C-247	Cyclazosin hydrochloride
C7897	Clonidine hydrochloride
D0411	WB-4101 hydrochloride
D0676	Dobutamine hydrochloride
D5290	(-)-alpha-Methylnorepinephrine
E4375	(-)-Epinephrine bitartrate
G-110	Guanabenz acetate
I-114	p-Iodoclonidine hydrochloride
I-127	ICI 118,551 hydrochloride
I2760	R(-)-Isoproterenol (+)-bitartrate
I5627	(±)-Isoproterenol hydrochloride
I8005	S(+)-Isoproterenol (+)-bitartrate
M3656	Mephentermine hemisulfate
M6524	Methoxamine hydrochloride
N-153	Nylidrin hydrochloride
N-158	Naftopidil dihydrochloride
O2378	Oxymetazoline hydrochloride
P0778	Pindolol
P0884	(±)-Propranolol hydrochloride
P-119	(±)-Pindobind
P6126	Phenylephrine hydrochloride
P7561	Phentolamine mesylate
P7791	Prazosin hydrochloride
R-104	Rauwolscine hydrochloride
R-134	Rilmenidine hemifumarate
S5013	Salbutamol hemisulfate
T6394	S(-)-Timolol maleate
U-100	Urapidil hydrochloride
U-101	Urapidil, 5-Methyl-
U-104	UK 14,304
X1251	Xylazine hydrochloride
Y3125	Yohimbine hydrochloride

Preparation Instructions

To create a new database in ISIS™/BASE :

- Open ISIS™/BASE.
- Choose **File>New database**.
- Enter **Adrenergic** 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 Adrenergic 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 Adrenergic.sdf will not be visible in the import window.*
- Enter **Adrenergic.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. Leonardi, A., et al. "α_1-adrenoceptor subtype and organ-selectivity of different agents." in *Perspectives in Receptor Research*, **Vol. 24**, Eds. D. Giardina, A. Piergentili and M. Pigini, pp. 135-152 Elsevier, Amsterdam (1996).
2. Macdonald, E., et al., "Gene targeting-homing in on alpha 2-adrenoceptor subtype function." *Trends Pharmacol. Sci.*, **18**, 211-219 (1997).
3. Ruffolo, R.R., et al., "Alpha- and beta-adrenoceptors: From the gene to the clinic. Part 2." *J. Med. Chem.*, **38**, 3681-3716 (1995).

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