

# NEUROSCIENCE



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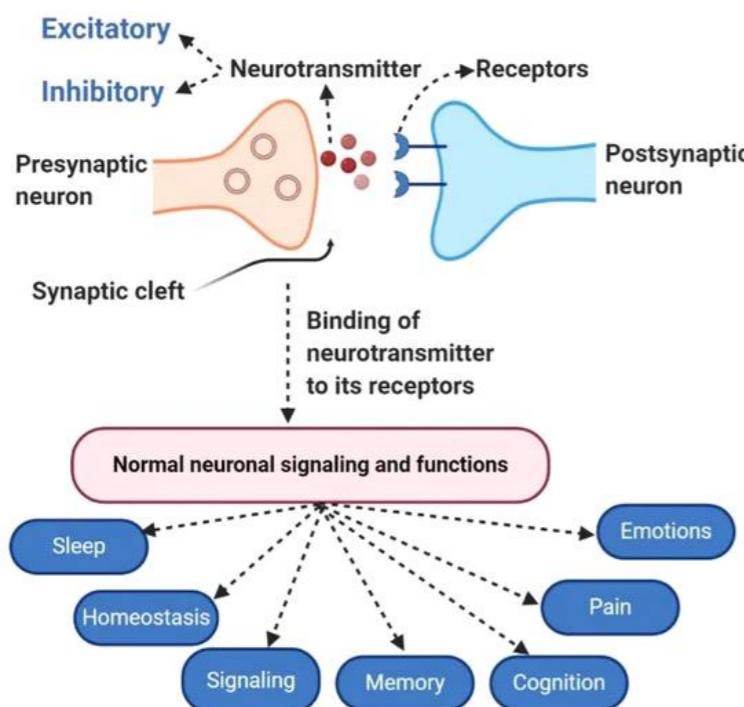
# Neuroscience

Neuroscience is the scientific study of the nervous system, including the brain, spinal cord, and peripheral nervous system, along with their functions and diseases. The core of neuroscience is to understand how the brain and nervous system work and how they influence behavior, cognition, and perception. Neuroscience encompasses multiple levels, from the molecular and cellular levels to systems and behavioral levels, and involves fields such as neuroanatomy, neurophysiology, neurodevelopment, and neuropathology. Neuroscientists conduct research across these areas to uncover the complex mechanisms of the nervous system and apply this knowledge to treat neurological disorders.

## Neurotransmitters and Neurotransmitter Receptors

Neurotransmitters and neurotransmitter receptors are two crucial components of the nervous system, working together to transmit and regulate nerve signals. Neurotransmitters are chemical substances released by neurons to transmit nerve signals. Common neurotransmitters include acetylcholine, dopamine, serotonin, norepinephrine, GABA, and glutamate. Neurotransmitter receptors are protein structures located on the neuronal cell membrane, capable of specifically binding to corresponding neurotransmitters. These receptors can be categorized into ionotropic receptors and metabotropic receptors.

Both types of neurotransmitters (inhibitory and excitatory) are released from synaptic vesicles into the synaptic cleft. In the synaptic cleft, neurotransmitters are received by receptors on the target cells, triggering a series of intracellular biochemical reactions. These reactions regulate neuronal excitability and provide signals for various functions, including sleep, homeostasis, pain, mood, and cognition.



The basic mechanism of neurotransmission<sup>[1]</sup>

### Inhibitors & Agonists

Catalog No.	Product Name	Description
T7044	Norepinephrine	Norepinephrine (Levophed) is an alkaloidal natural product, a neurotransmitter, an adrenergic receptor (AR) agonist, with activating activity on $\alpha_1$ , $\alpha_2$ , and $\beta_1$ ARs.
T1644	Dopamine hydrochloride	Dopamine hydrochloride (ASL279) is a naturally occurring catecholamine and a precursor of norepinephrine and epinephrine. Dopamine hydrochloride binds to $\alpha_1$ and $\beta_1$ adrenergic receptors.
TN2437	Serotonin	Serotonin (5-hydroxytryptamine) is a monoamine neurotransmitter and endogenous 5-HT receptor agonist in the CNS. Serotonin is also an inhibitor of catechol O-methyltransferase (COMT).
T0508	$\gamma$ -Aminobutyric acid	$\gamma$ -Aminobutyric acid (4-Aminobutyric acid) is the major inhibitory neurotransmitter in the adult mammalian brain, and is able to act by binding to ionotropic GABA <sub>A</sub> and GABA <sub>B</sub> receptors.
T1221	Acetylcholine chloride	Acetylcholine chloride (Pilofrin) is a neurotransmitter and cholinergic agonist that modulates dopaminergic neuronal activity through stimulation of nicotinic acetylcholine receptors.
T0326L	L-Glutamine	L-Glutamine (L-Glutamic acid 5-amide), a non-essential amino acid, is synthesized from glutamic acid and ammonia.
T7173	[Leu5]-Enkephalin	[Leu5]-Enkephalin (Leu-enkephalin) is an endogenous neuropeptide involved in nociception and an agonist of $\delta$ -opioid and $\mu$ -opioid receptors.
T0450	Fluoxetine	Fluoxetine (LY-110140) is a highly specific serotonin uptake inhibitor and selective 5-hydroxytryptamine (5-HT) reuptake inhibitor. Fluoxetine has antidepressant activity.
T1566	Aripiprazole	Aripiprazole (OPC-14597) is a partial agonist at serotonin receptor 5-HT <sub>1A</sub> and dopamine D <sub>2</sub> receptors, and is also used as a postsynaptic antagonist and an antagonist at serotonin receptor 5-HT <sub>2A</sub> .
T22240	Amitriptyline	Amitriptyline (MK-230) is a tricyclic antidepressant (TCA) with analgesic properties. Amitriptyline is widely used to treat depression and neuropathic pain.
T1247	Clonidine hydrochloride	Clonidine hydrochloride (Catapres) is a centrally active $\alpha$ -adrenergic agonist used predominantly as an antihypertensive agent.
T0102	Naloxone hydrochloride	Naloxone hydrochloride (Naloxone HCl) is a specific opiate antagonist that has no agonist activity. It is a competitive antagonist at mu, delta, and kappa opioid receptors.
T0351	Risperidone	Risperidone (R 64 766) is a selective blocker of dopamine D <sub>2</sub> receptors and serotonin 5-HT <sub>2</sub> receptors that act as an atypical antipsychotic agent.
T8708	Paroxetine	Paroxetine is a inhibitor of serotonin uptake that is effective in the treatment of depression. Paroxetine has weaker inhibitory function on adrenaline uptake, but is more effective than other SSRIs at this site.
T1083	Theophylline	Theophylline (1,3-Dimethylxanthine) is a methyl xanthine derivative from tea with diuretic, smooth muscle relaxant, bronchial dilation, cardiac and central nervous system stimulant activities.

Compound Libraries

Catalog No.	Product Name	Quantity	Description
L2610	Neurotransmitter Receptor Compound Library	1,500+	A unique collection of neurotransmitter receptor compounds, can be used for HTS and HCS screening. Targets include 5-HT receptor, AChR, GABA receptor, dopamine receptor, Opioid receptor, Ionotropic Glutamatergic receptor, Metabotropic Glutamatergic receptor, Purinergic receptor, etc.
L2700	Adrenergic Receptor-Targeted Compound Library	200+	A unique collection of bioactive compounds includes blockers, agonists, endogenous neuron transmitters, and approved drugs, and is an effective tool for screening or identifying recombinant orphan G-protein coupled receptors, new target identification, second screening, and other pharmacological applications.
L2800	Serotonin Receptor-Targeted Compound Library	200+	A unique collection of compounds targeting serotonin receptors for high throughput screening and high content screening. Targets include serotonin receptors: 5-HT1, 5-HT2, 5-HT3, 5-HT4, 5-HT6, 5-HT7, etc.
L1500	GPCR Compound Library	2,200+	A unique collection of GPCR-active agents for high throughput screening and high content screening for GPCR drug discovery, and new GPCR target identification and research. Potential to find new GPCR drug candidates by screening against orphan GPCRs.
-	Neurotransmitter Transporter Inhibitors library	12,000+	A collection of compounds related to neurotransmitter transporters. Neurotransmitter transporters are a class of membrane transport proteins that span the neuronal cell membrane. Their primary function is to transport neurotransmitters across the cell membrane and further relocate them to specific intracellular locations.
-	GABA Targeted Library	7,200+	A collection of compounds targeting GABA. In the central nervous system, GABA is the primary inhibitory neurotransmitter. GABA receptor antagonists are drugs that inhibit the effects of GABA. Generally, these drugs produce excitatory and convulsive effects and are mainly used to counteract the overdose of sedatives.

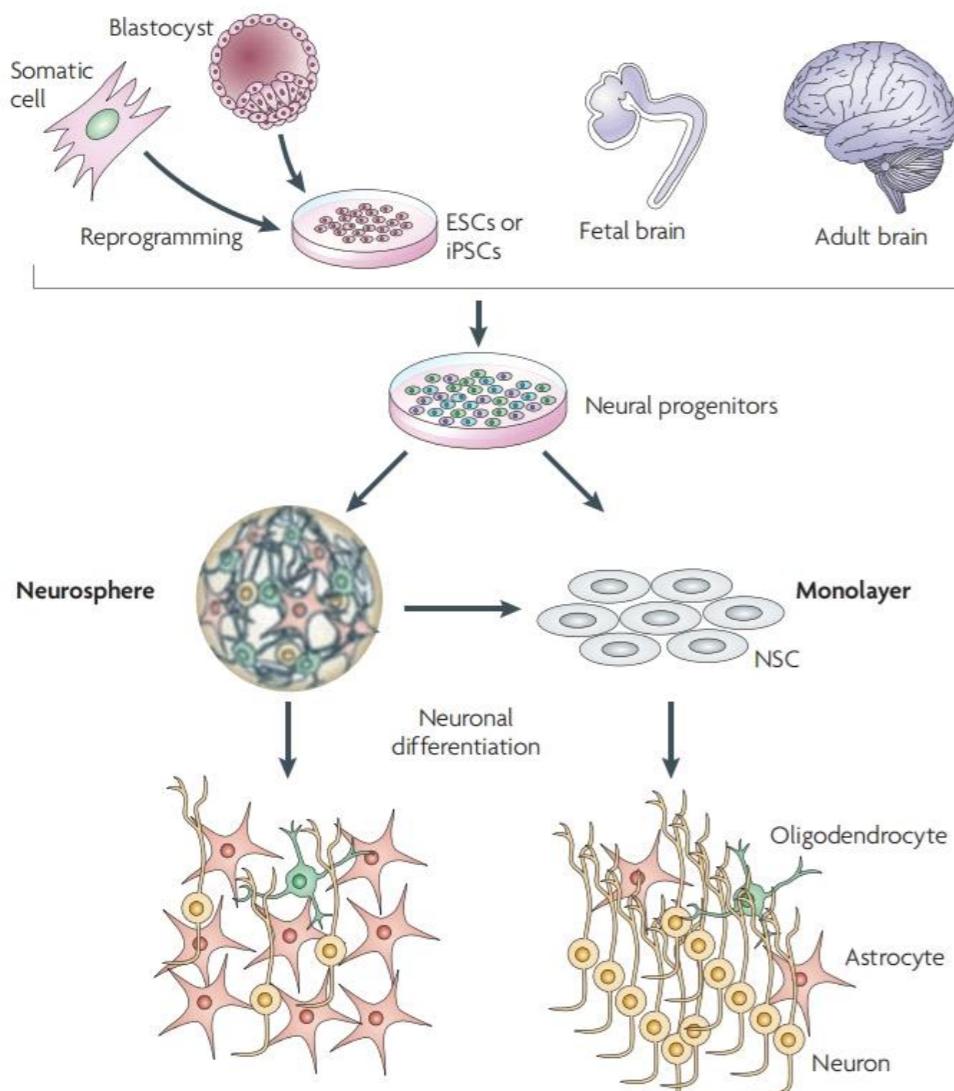
Recombinant Proteins

Catalog No.	Product Name	Description
TMPY-02245	SNAP-25 Protein, Human, Recombinant (His)	Synaptosomal-associated protein 25 (SNAP25) is a cytoplasm and cell membrane protein that belongs to the SNAP-25 family. SNAP25 / SUP is involved in the molecular regulation of neurotransmitter release.
TMPJ-00016	GABARAP Protein, Human, Recombinant (GST)	Gamma-Aminobutyric Acid Receptor-Associated Protein (GABARAP) is a ligand-gated chloride channel protein that mediates inhibitory neurotransmission and belongs to the MAP1 LC3 family.
TMPJ-01379	TAC3 Protein, Human, Recombinant (His)	Tachykinin 3 (TAC3) is a secreted protein that belongs to the Tachykinin family. TAC3 is primarily expressed in the central and peripheral nervous systems and functions as a neurotransmitter.
TMPY-01959	Tryptophan Hydroxylase 1/TPH-1 Protein, Human, Recombinant (His)	Tryptophan hydroxylase catalyzes the biopterin-dependent monooxygenation of tryptophan to 5-hydroxytryptophan (5HT), which is subsequently decarboxylated to form the neurotransmitter serotonin.
TMPY-02025	CPLX2 Protein, Human, Recombinant (His)	Complexin-2 (CPLX2), a member of the complexin/synaphin family, is a soluble pre-synaptic protein believed to regulate neurotransmitter release from pre-synaptic terminals.
TMPY-04422	Casein Kinase 1 gamma 2 Protein, Human, Recombinant (His)	Casein kinase I gamma 2 isoform (CSNK1G2) is a member of the large casein kinase I (CKI) subfamily. CSNK1G2 may affect the development of brain, and associate with vesicular trafficking and neurotransmitter releasing from small synaptic vesicles.
TMPY-02340	HNMT Protein, Human, Recombinant (GST)	Histamine N-methyltransferase (HNMT) catalyzes the N tau-methylation of histamine and structurally related compounds. HNMT is believed to be the sole pathway for termination of the neurotransmitter action of histamine in the mammalian brain.
TMPY-01742	Acetylcholinesterase Protein, Mouse, Recombinant (His)	Acetylcholinesterase (ACHE) is an enzyme that degrades the neurotransmitter acetylcholine. Acetylcholinesterase plays a crucial role in nerve impulse transmission at cholinergic synapses by rapid hydrolysis of the neurotransmitter ACh.
TMPY-00186	GHRH Protein, Human, Recombinant (hFc)	Growth hormone releasing hormone (GHRH) has recently been shown to increase the level of gamma-aminobutyric acid (GABA) and activate GABA receptors (GABARs) in the cerebral cortex.
TMPY-03445	Aspartate Aminotransferase Protein, Human, Recombinant (His)	Aspartate aminotransferase is an enzyme that in humans is encoded by the GOT1 gene. GOT1 is an important regulator of levels of glutamate, the major excitatory neurotransmitter of the vertebrate central nervous system.

# Neural Stem Cells

Neural Stem Cells (NSCs) are self-renewing and multipotent cell populations found in the central nervous system (CNS) of developing and adult mammals. NSCs differentiate into the primary cell types of the nervous system, including neurons (which transmit neural signals), astrocytes (which support and protect neurons), and oligodendrocytes (which form myelin sheaths to accelerate neural signal transmission).

NSCs are crucial during embryonic development for the formation of the brain and spinal cord, responsible for constructing the structures of the CNS. They also persist in specific regions of the adult brain, contributing to tissue repair and regeneration. Due to their regenerative capabilities, NSCs hold significant research value and clinical potential for treating neurodegenerative diseases, stroke, spinal cord injuries, and other neurological disorders.



Sources of neurospheres and monolayer NSCs and results of differentiation <sup>[2]</sup>

## Inhibitors & Agonists

Catalog No.	Product Name	Description
T3031	A 83-01	A 83-01 is an ALK4/5/7 inhibitor that can promote the reprogramming of mouse fibroblasts into iPSCs and is used for organoid culture.
T1870	Y-27632	Y-27632 is an orally potent, ATP-competitive inhibitor of ROCK-I and ROCK-II. Y-27632 also inhibits isolation-induced apoptosis in mouse prostate stem or progenitor cells.
T6202	DAPT	DAPT is a $\gamma$ -secretase inhibitor and Notch inhibitor that can induce cell differentiation and is used for organoid differentiation culture.
T2310	CHIR-99021	CHIR-99021 is an activator of the Wnt/ $\beta$ -catenin signaling pathway and a GSK-3 $\alpha$ / $\beta$ inhibitor with selective and oral activity. It induces cellular autophagy, which enhances self-renewal in human embryonic stem cells.
T1726	SB-431542	SB-431542 is an inhibitor of ALK5/TGF- $\beta$ type I Receptor (IC <sub>50</sub> =94 nM) and is selective. SB 431542 also has inhibitory activity against ALK4 and ALK7 but not other proteins. SB 431542 can be used for induced differentiation of stem cells.
T2301	SB 202190	SB 202190 is a p38 MAPK inhibitor that can induce the differentiation of human embryonic stem cells into cardiomyocytes and promote the self-renewal of neural stem cells.
T1051	Retinoic acid	Retinoic acid is a natural agonist of the retinoic acid receptor (RAR) and plays an important role in cell growth, differentiation, and organogenesis.
T1935	LDN193189	LDN193189 (DM-3189) is a selective inhibitor of the BMP type I receptor that inhibits ALK2 and ALK3. LDN193189 can be used in studies of progressive ossifying fibrous dysplasia.
T7064	Valproic Acid	Valproic Acid (2-Propylpentanoic Acid) is an HDAC inhibitor that inhibits HDAC1 activity, induces HDAC2 degradation, and is orally active. Valproic Acid can be used in epilepsy and bipolar disorder research.
T6337	RepSox	RepSox (ALK5 Inhibitor II) is a TGF $\beta$ R-1/ALK5 inhibitor that selectively inhibits the binding of ATP to ALK5 and the autophosphorylation of ALK5. RepSox induces adipogenesis in MEFs cells.
T2003	ISX-9	ISX-9 (Isoxazole 9) is a potent inducer of neural stem cell differentiation and induces myocardial differentiation of Notch-activated epicardium-derived cells (NEC).
T0196	Diclofenac	Diclofenac (CGP-45840B) is a non-steroidal anti-inflammatory agent. Diclofenac Potassium induces apoptosis of neural stem cells through activation of caspase cascades.
T4674	SB297006	SB297006 is a CCR3 antagonist with an IC <sub>50</sub> of 39 nM. SB297006 significantly inhibits the proliferation and neurosphere formation of CCL11-treated neural stem cells.
T64353	4-tert-Octylphenol	4-tert-Octylphenol, an endocrine-disrupting chemical with estrogenic properties, notably induces apoptosis in offspring mouse brain neuronal progenitor cells.
TN1674	Garcinone D	Garcinone D, a xanthone from mangosteen, promotes the proliferation of C17.2 neural stem cells. Garcinone D shows significant cytotoxicity against the CEM-SS cell line.

Compound Libraries

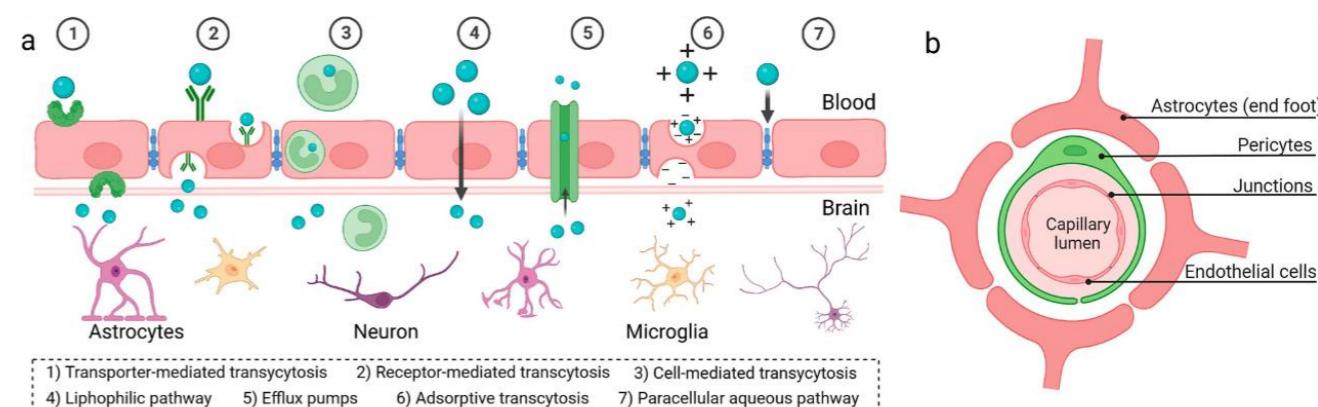
Catalog No.	Product Name	Quantity	Description
L8000	Stem Cell Differentiation Compound Library	1,200+	A unique collection of bioactive small molecule compounds related to stem cell differentiation signaling pathways. Suitable for 1. high-throughput and high-content screening; studying stem cell regeneration mechanisms, regenerative therapies; an effective tool for studying stem cell differentiation signaling pathways and screening new drugs based on stem cells.
L8110	Reprogramming Compound Library	1,800+	A unique collection of bioactive small molecule compounds related to reprogramming signaling pathways. Small molecule-induced pluripotent stem cells have great potential in drug discovery, cell therapy, and disease modeling, opening new avenues for treating major diseases.
-	PI3K-Targeted Library	19,000+	A collection of drug-like compounds targeting PI3K, showing similar binding patterns to reported PI3K inhibitors. The PI3K/Akt signaling pathway is closely related to the self-renewal and multi-lineage differentiation potential of embryonic stem cells.

Recombinant Proteins

Catalog No.	Product Name	Description
TMPY-00749	FGF-2 Protein, Human, Recombinant	Basic fibroblast growth factor (bFGF), also known as FGF2, is a member of the fibroblast growth factor (FGF) family. bFGF is a critical component of human embryonic stem cell culture medium.
TMPY-00005	FGF-2 Protein, Human, Recombinant	Fgf8 encodes a key signaling factor, and its precise regulation is essential for embryo patterning. Recombinant FGFs are widely used in 3D organoid cultures.
TMPY-02638	TGF beta 1 Protein, Human/Rhesus/Cynomolgus /Canine, Recombinant	TGF beta 1 regulates cell processes, including division, differentiation, movement, adhesion, and death, and can be used for brain organoid culture.
TMPY-00395	Insulin Protein, Human, Recombinant	Insulin is a peptide hormone essential for regulating carbohydrate and lipid metabolism and can be used for brain and liver organoid culture.
TMPJ-00135	BDNF Protein, Human/Murine/Rat, Recombinant	BDNF is a member of the neurotrophin family. BDNF promotes the survival, growth, and differentiation of neurons and can be used for brain organoid culture.
TMPY-02792	GDNF Protein, Human, Recombinant (HEK293)	GDNF is a neurotrophic factor involved in cell survival, outgrowth, differentiation, and migration and can be used for brain organoid culture.
TMPY-05202	Noggin/NOG Protein, Human, Recombinant	Noggin binds to BMP proteins to coordinate Wnt signaling to activate stem cells and promote their proliferation, widely used for long-term culture of various organoids.
TMPY-00680	BMP-2 Protein, Human, Mouse, Rat, Rhesus, Canine, Recombinant (hFc)	BMP-2 regulates the development of bones and cartilage and has been shown to effectively induce osteoblast differentiation in various cell types, significant for bone formation and repair.
TMPJ-01127	SHH Protein, Human, Recombinant	Sonic Hedgehog Homolog (SHH) belongs to a three-protein family called hedgehog. SHH is expressed in various embryonic tissues and plays critical roles in regulating the patterning of many systems, such as limbs and brain.
TMPY-06987	Wnt Surrogate/Wnt3a Protein, Recombinant	Wnt3a plays a crucial role in regulating cell renewal, proliferation, differentiation, and movement. Wnt3a is one of the most commonly used culture factors for constructing organoids and is used for the culture of various organoids.

## Blood-Brain Barrier

The blood-brain barrier (BBB) is a semi-permeable membrane that includes the microvasculature of the central nervous system (CNS) and serves to protect the CNS from toxins and pathogens in the blood. From a physiological perspective, the BBB is primarily composed of endothelial cells, astroglia, pericytes, and junctional complexes, including tight junctions and adherens junctions, which control the entry and exit of molecules between the vascular compartment and the brain. The intact BBB effectively prevents most blood-borne substances from entering the brain. However, it is noteworthy that while the BBB protects the brain, it also excludes over 98% of small-molecule drugs and all large-molecule therapeutic agents from entering the brain. Therefore, there is an urgent need to address the challenge of brain-targeted therapy by developing effective and safe delivery strategies.



Strategies and materials for BBB regulation and brain-targeted drug delivery.<sup>[3]</sup>  
a Schematic diagram of different mechanisms for BBB crossing.  
b Schematic diagram of BBB structure.

## Inhibitors & Agonists

Catalog No.	Product Name	Description
T1178	Temozolomide	Temozolomide (TMZ) is a DNA alkylating agent with blood-brain barrier permeability and oral activity. Temozolomide has antitumor activity and antiangiogenic activity, and also induces apoptosis and autophagy.
T8526	Metformin	Metformin (1,1-Dimethylbiguanide) is an AMPK activator with blood-brain barrier permeability. Metformin improves glycemic control, and is commonly used in type 2 diabetes research.
T4081	MPTP hydrochloride	MPTP hydrochloride is a precursor of MPP+, a dopamine neurotoxin with blood-brain barrier permeability. MPTP hydrochloride is toxic to dopaminergic neurons, which can lead to Parkinson's disease.
TP1095	Elamipretide	Elamipretide (MTP-131) is a mitochondria-targeted antioxidant tetrapeptide that reduces toxic ROS production and stabilizes cardiolipin, with blood-brain-barrier permeability.

Inhibitors & Agonists

Catalog No.	Product Name	Description
T4494	CLOZAPINE N-OXIDE	Clozapine N-oxide is the major metabolite of Clozapine and is blood-brain barrier permeable. Clozapine N-oxide is an agonist of DREADDs and activates the DREADD receptors hM3Dq and hM4Di.
T2274	SC79	SC79 is an AKT agonist with specificity and blood-brain barrier permeability. SC79 specifically binds to the PH domain of AKT, activates cytoplasmic AKT, and inhibits AKT membrane translocation.
T6961	PX-478	PX-478 is a HIF-1 $\alpha$ inhibitor with selectivity, oral activity, and blood-brain barrier permeability. PX-478 has antitumor activity and is used in type 2 diabetes mellitus research.
T0795	Rutin	Rutin (Quercetin 3-O-rutinoside) is a natural flavonoid with blood-brain barrier permeability. Rutin has a wide range of biological activities including antioxidant, anti-inflammatory and anti-tumor.
T1079	Metronidazole	Metronidazole (Metronidazol) is a synthetic nitroimidazole derivative, an antibiotic and antiprotozoal agent with oral activity and blood-brain barrier penetration.
T6S0444	Salvianolic acid A	Salvianolic acid A (Dan Phenolic Acid A) is a natural product and an inhibitor of MMP-9. Salvianolic acid A has antioxidant and anti-inflammatory activity and protects the blood-brain barrier.
T3678	Entrectinib	Entrectinib (RXDX-101) is a Trk, ROS1, and ALK inhibitor that inhibits TrkA, TrkB, TrkC, ROS1, and ALK with oral activity and blood-brain-barrier penetration. Entrectinib exhibits both antitumor and CNS activity.
T0458	Indomethacin	Indomethacin (Indomethacin) is a COX1 and COX2 inhibitor with blood-brain barrier permeability and non-selectivity. Indomethacin is a non-steroidal anti-inflammatory agent.
T0492	Dimethyl fumarate	Dimethyl fumarate (DMF) is an Nrf2 activator with oral activity and blood-brain barrier permeability. Dimethyl fumarate has antimicrobial, anti-inflammatory, and immunomodulatory activities.
T7100	PLX5622	PLX5622 is a CSF1R inhibitor with selectivity, oral activity, and blood-brain barrier permeability. PLX5622 induces sustained and specific elimination of microglia.
T18988	FITC-Dextran (MW 10000)	FITC-Dextran (MW 10000) is capable of determining the solute, ion and protein permeability of the blood-brain barrier according to the size of the dextran used.

Compound Libraries

Catalog No.	Product Name	Quantity	Description
L5900	CNS-Penetrant Compound Library	500+	A unique collection of 509 CNS-Penetrant compounds for high throughput screening (HTS) and high content screening (HCS). Targets include Kinases, GPCR, and ion channels, etc.
-	CNS BBB Library	23,000+	An exclusive collection of carefully selected small molecules for the treatment of central nervous system disorders. The latest computational models were used to predict physicochemical properties, and cutting-edge machine learning and artificial intelligence algorithms were employed to predict blood-brain barrier permeability.

Application Case

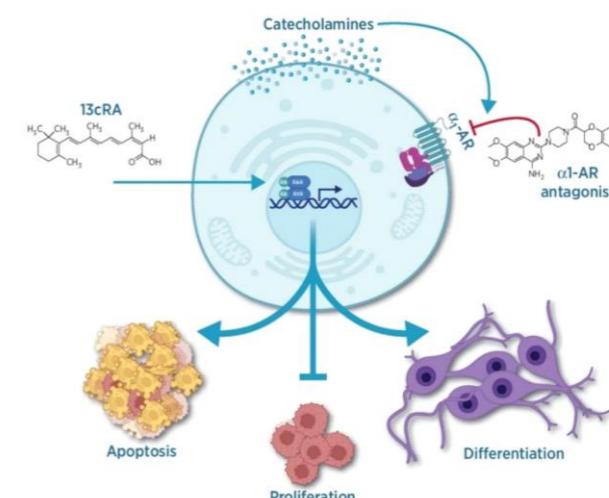
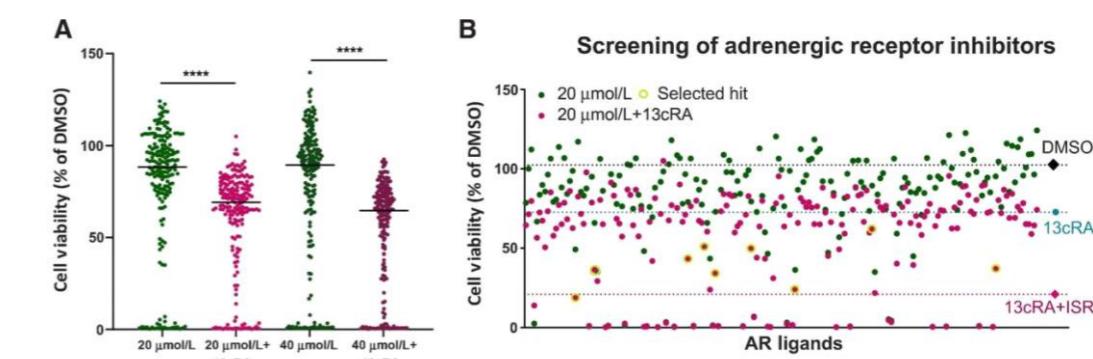
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**Screening with a focused library of adrenergic receptor binding molecules**

NB cells were seeded in white TC 384-well plates with a final volume of 60  $\mu$ L. After 24 hours, cells were treated with molecules of the adrenergic receptor ligands **Adrenergic Receptor Compound Library (L2700T, TargetMol)** and SCREEN-WELL adrenergic ligand library

Neuroblastoma (NB) is an aggressive pediatric tumor, and isotretinoin (13cRA) is one of the common therapeutic drugs. Previous studies have shown that inhibiting ADRA1B can enhance the effect of 13cRA. To explore the possibility of modulating adrenergic receptors (AR) to improve the therapeutic potential of 13cRA, researchers screened a focused library of 201 AR ligands, including **TargetMol's Adrenergic Receptor Compound Library** and other libraries. Hit screening revealed that when co-administered with 13cRA, the hits AH11110A ( $\alpha$ 1B-AR antagonist), doxepin, phenoxybenzamine, and maprotiline (all  $\alpha$ 1-AR antagonists) induced a shift in IC50 towards lower values, indicating reduced cell viability compared to monotherapy. The results suggest that antagonism, rather than agonism, especially the antagonism of  $\alpha$ 1B-AR, enhances the antiproliferative effect of 13cRA, thereby improving its therapeutic efficacy. This study identifies the  $\alpha$ 1B adrenergic receptor as a pharmacological target for NB.



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