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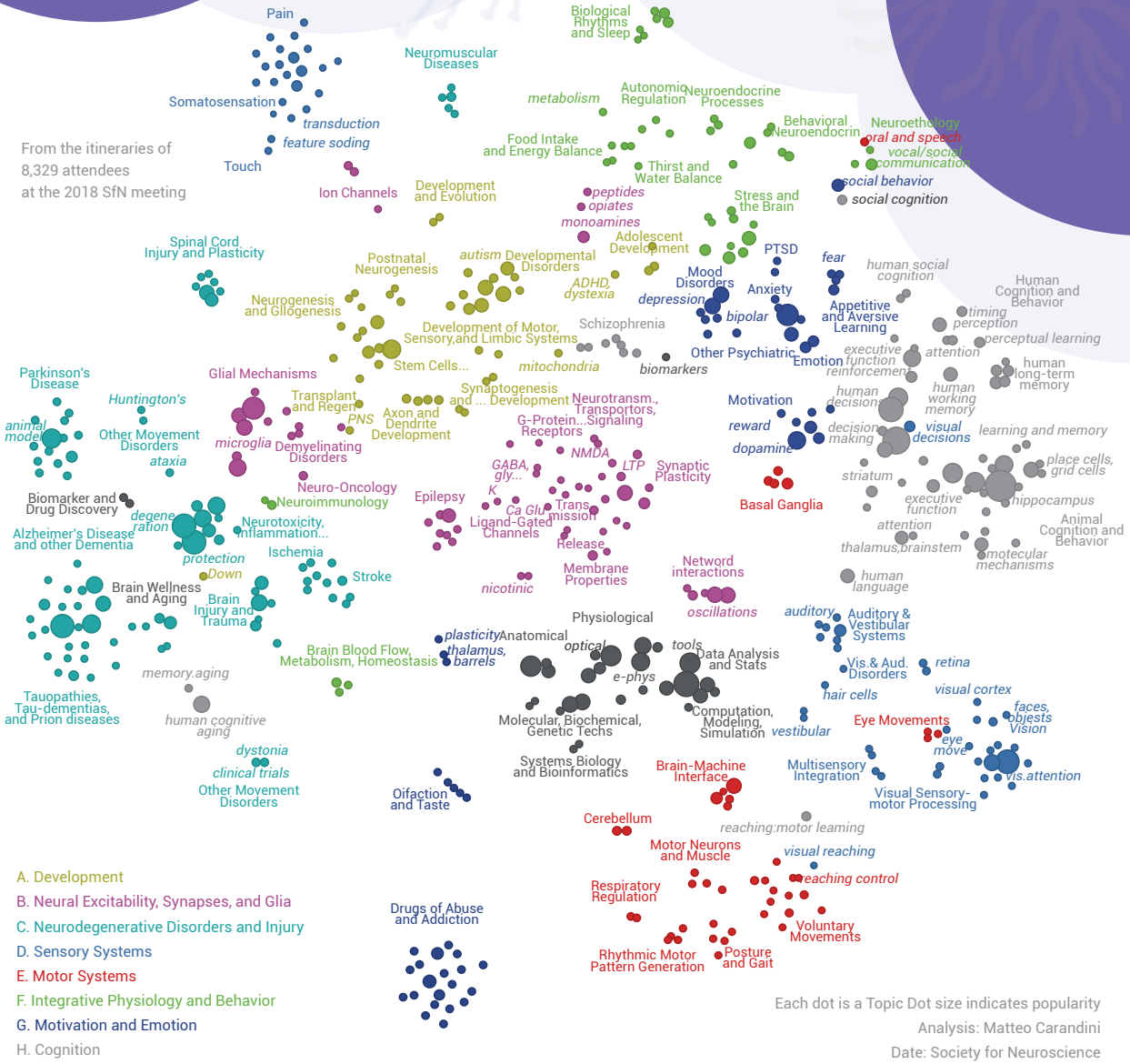
Neuroscience

Product Handbook



A. Development
B. Neural Excitability, Synapses, and Glia
C. Neurodegenerative Disorders and Injury
D. Sensory Systems
E. Motor Systems
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G. Motivation and Emotion
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Each dot is a Topic Dot size indicates popularity
Analysis: Matteo Carandini
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Neuroscience

Introduction

Neuroscience is the most fascinating discipline that attempts to understand the nervous system and to develop potential therapies. There are so many branches of neuroscience, among which development, neural signaling, neurodegenerative disorders, sensory/motor system, integrative neuroscience, motivation and emotion, cognition and techniques are mentioned with high frequencies.

In this handbook, neurotransmitters and their receptors, neuronal stem cells, neurodegenerative diseases, blood-brain barrier will be discussed.

Contents

Neurotransmitters and Neurotransmitter Receptors

Neurotransmitters are the small molecules of chemical substances that carry information between neurons. There are several types of neurotransmitters according to chemical properties, including monoamines and acetylcholine, amino acids, purines, lipids and peptides.

Neurotransmitters induce postsynaptic electrical potentials and biochemical changes through their receptors. The most familiar neurotransmitter receptors are ligand-gated channels and G protein-coupled receptors (GPCRs) (Figure 1). When a ligand (neurotransmitter) binds to the extracellular domain, the ligand-gated channels will open a central pore that permits ions to pass while GPCRs will transmit the signal to activate G proteins and then amplify the signaling cascades through second messengers.

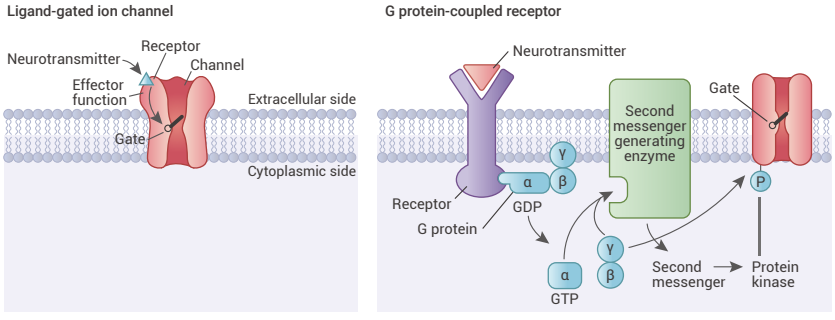

Figure 1. Neurotransmitter receptors [1]

For the central role of neurotransmitters, neurotransmitter receptors are critical targets for the treatment of nervous system related diseases such as psychiatric and neurologic disorders.

		Compounds
Cat. No.	Product Name	Description
HY-B0282	Acetylcholine chloride	A common neurotransmitter found in the central and peripheral nerve system.
HY-106094	CY 208-243	A selective dopamine D1 receptor agonist which exhibits anti-parkinsonian activity.
HY-B1473	Serotonin hydrochloride	A monoamine neurotransmitter in the CNS and an endogenous 5-HT receptor agonist.
HY-B1204	Histamine	An organic nitrogenous compound involved in local immune responses and acts as a neurotransmitter.
HY-N0067	γ-Aminobutyric acid	A major inhibitory neurotransmitter in the adult mammalian brain, binds to GABA receptors.
HY-14608	L-Glutamic acid	Acts as an excitatory transmitter and an agonist at all subtypes of glutamate receptors.
HY-P0288	Leu5-Enkephalin	A pentapeptide with morphine like properties. Acts as an agonist at opioid receptors.
HY-P1866	β-Endorphin, equine	An endogenous opioid peptide that binds to both μ/δ opioid receptors. Analgesic properties.
HY-P0201	Substance P	A neuropeptide, acting as a neurotransmitter and as a neuromodulator in the CNS.
HY-P1480	Neuropeptide Y	A neuropeptide Y receptor agonist.
HY-P1339	Orexin B, human	An endogenous agonist of orexin receptor.
HY-P0049	Argipressin	An endogenous hormone binds to the V1, V2, V3-vascular arginine vasopressin receptor.
HY-17571	Oxytocin	A mammalian neurohypophysial hormone.
HY-P0015	Somatostatin	A tetradecapeptide which can control growth hormone and pituitary hormone secretion in CNS.
HY-P0234	Neurotensin	A gut tridecapeptide that possesses high-affinity neurotensin receptors (NTR).

Cat. No.	Product Name	Description
HY-P0195	Bombesin	A tetradecapeptide that plays an important role in the release of gastrin and the activation of G-protein receptors.
HY-P1765	Galanin (1-19), human	A widely distributed neuropeptide with diverse biological effects.
HY-B0495	Lamotrigine	An anti-convulsant that inhibits voltage-sensitive sodium channels.
HY-P1317A	Nociceptin (1-13), amide	A potent ORL1 receptor (opioid receptor-like 1 receptor, OP4) agonist .
HY-12987	Pimozide	A dopamine receptor antagonist.
HY-15399	Vigabatrin	An inhibitory neurotransmitter GABA vinyl-derivative, is an orally active and irreversible GABA transaminase inhibitor.
HY-12152	PNU-120596	A selective α7 nAChR positive allosteric modulator for psychiatric and neurological disorders research.
HY-14418	VU0361737	A CNS penetrant positive allosteric modulator of metabotropic glutamate receptor 4 (mGluR4 PAM). Neuroprotective effect.
HY-B0527A	Amitriptyline	An inhibitor of serotonin reuptake transporter and noradrenaline reuptake transporter. Antidepressant activity.
HY-15430A	Encenicline	A partial agonist of α7 neuronal nicotinic acetylcholine receptors (nAChRs).
HY-15608	MPTP	A brain penetrant dopamine neurotoxin, inducing Parkinson's Disease.
HY-136390	ML417	A selective and brain penetrant D3 dopamine receptor (D3R) agonist and exhibits neuroprotection.
HY-19918A	Anatabine	A tobacco alkaloid that can cross the blood-brain barrier. A potent α4β2 nAChR agonist for neurodegenerative disorders treatment.

Compound Screening Libraries

Cat. No. : HY-L062

Neurotransmitter Receptor Compound Library

A unique collection of compounds targeting a variety of neurotransmitter receptors.

Cat. No. : HY-L006

GPCR/G Protein Compound Library

A unique collection of compounds targeting GPCRs for various GPCRs-related research and drug development projects.

Neural Stem Cells

Neural stem cells (NSCs) have the ability to self-renew and to differentiate into three neural lineages (i.e. neurons, oligodendrocytes and astrocytes). So, NSCs are promising therapeutics for diseases associated with the nervous system.

Except for direct isolation from primary tissues, NSCs can also be obtained by differentiation from pluripotent stem cells and transdifferentiation from somatic cells. Nowadays, small molecules are reported to gain their roles in transdifferentiating somatic cells into NSCs and some of them are listed as followed.

However, it is also important to maintain the balance between the proliferation and differentiation of NSCs as aberrant NSC proliferation can lead to tumorigenesis.

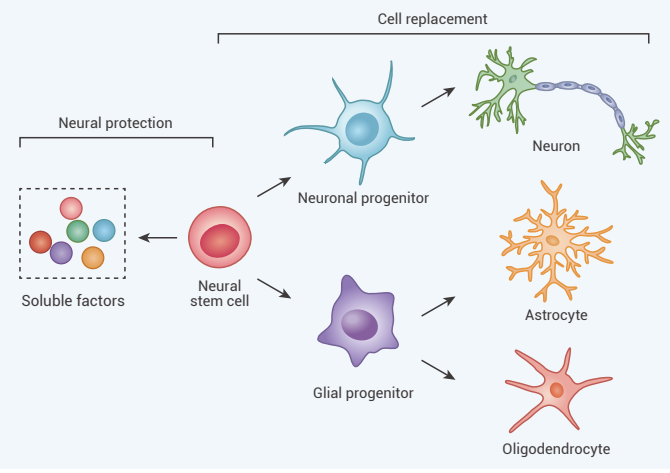

Figure 2. Functions of NSCs [2]

Compounds

Cat. No.	Product Name	Description
HY-15036	Diclofenac	Acts as a COX inhibitor and induces apoptosis of neural stem cells (NSCs).
HY-12323	ISX-9	A potent inducer of adult neural stem cell differentiation.
HY-10585	Valproic acid (VPA)	A potent HDAC inhibitor for the treatment of epilepsy, bipolar disorder and prevention of migraine headaches.
HY-10182	Laduviglusib (CHIR99021)	A potent and selective GSK-3α/β inhibitor, enhances mouse and human embryonic stem cells self-renewal.
HY-13012	Repsox	A potent and selective of the TGFβR-1/ALK5 inhibitor. RepSox can replace Sox2.
HY-10432	A 83-01	A potent inhibitor of TGF-β type I receptor ALK5 kinase, type I nodal receptor ALK4 and type I nodal receptor ALK7.
HY-10587	BIX-01294	An inhibitor of G9a histone methyltransferase.
HY-13642	RG108	A non-nucleoside DNA methyltransferases inhibitor.
HY-B0166	Vitamin C	An electron donor and an endogenous antioxidant agent.
HY-10254	Mirdametinib	An orally active, selective and MEK inhibitor.

Cat. No.	Product Name	Description
HY-14649	Retinoic acid	A natural agonist of RAR nuclear receptors. Plays important roles in cell growth, differentiation, and organogenesis.
HY-12071	LDN193189	A selective BMP type I receptor inhibitor.
HY-124899	Hh-Ag 1.5	A potent Hedgehog agonist that breaks the quiescence of non-injured liver stem cells for rescuing liver failure.
HY-B1496	Tranylcypromine hemisulfate	An irreversible MAO inhibitor for the treatment of depression.
HY-100200	SMER28	A positive regulator of autophagy in an mTOR-independent manner. Prevents the accumulation of Aβ peptide.
HY-13257	Thiazovivin	A ROCK inhibitor that protects human embryonic stem cells. Improves the efficiency of iPSC generation.
HY-15108	Purmorphamine	A smoothened (Smo) receptor agonist that stimulates osteogenic differentiation in murine and human cells.
HY-10591	Neuropathiazol	Induces neuronal differentiation of multipotent hippocampal neural progenitor cells.
HY-103361	SB297006	A CCR3 antagonist that significantly inhibits proliferation and neurosphere formation in CCL11-treated neural progenitor cells.
HY-108439	Neurodazine	A promoter of neurogenesisin pluripotent cells. Promotes neurogenesis by activating Wnt and Shh signaling pathways.
HY-W019870	Glufosinate	A phosphinic acid analogue of glutamic acid, which exerts neurotoxic activity.
HY-N6953	Garcinone D	A natural xanthone that promotes the proliferation of C17.2 neural stem cell.
HY-10046	Plerixafor	A selective CXCR4 antagonist. A hematopoietic stem cell (HSC) mobilizer.
HY-15838	ID-8	A DYRK inhibitor that sustains embryonic stem cell (ESC) self-renewal and pluripotency.
HY-10936	S 18986	A selective, orally active, brain penetrant AMPA positive allosteric modulator that enhances cognitive properties.
HY-108628	SU16f	A selective PDGFRβ inhibitor that blocks the promoting role of GC-MSCs in gastric cancer cell proliferation and migration.
HY-N0204	Pulchinenoside A	A natural triterpenoid saponin. AMPAR and NMDAR modulator.

Compound Screening Library

Cat. No. : HY-L039

Reprogramming Compound Library

A unique collection of compounds that act on reprogramming signaling pathways.

Chemical Cocktails

HY-10585 Valproic acid	HY-10182 CHIR99021	HY-13012 RepSox		

A combination of small molecules that induces reprogramming of mouse fibroblasts and human urinary cells into neural progenitor cell [3].

HY-10585 Valproic acid	HY-10182 CHIR99021	HY-10432 A 83-01	HY-10587 BIX-01294	HY-13642 RG108
HY-B0166 Vitamin C	HY-10254 Mirdametinib			

A combination of small molecules that induces reprogramming of mouse fibroblasts into neural stem cell[4].

HY-10182 CHIR99021	HY-10432 A 83-01	HY-124899 Hh-Ag1.5	HY-100200 SMER28	HY-12071 LDN193189
HY-B1496 Tranylcypromine	HY-13642 RG108			

A combination of small molecules that induces reprogramming of mouse fibroblasts into neural stem cell-like cells (ciNSLCs)[5].

HY-10432 A 83-01	HY-13257 Thiazovivin	HY-15108 Purmorphamine	HY-10585 Valproic acid

A combination of small molecules that induces reprogramming of mouse fibroblasts into neural stem cell[6].

HY-10585 Valproic acid	HY-10182 CHIR99021	HY-12071 LDN193189	HY-10431 SB-431542	HY-15682 TTNPB
HY-13257 Thiazovivin	HY-13027 DAPT	HY-12848 SAG	HY-15108 Purmorphamine	

A combination of small molecules can reprogram human astrocytes into fully functional neurons[7].

Neurodegenerative Diseases

Neurodegenerative diseases are a series of diseases caused by tremendous neuronal dysfunction and death including Parkinson's Disease (PD), Alzheimer's Disease (AD), Huntington's Disease (HD), Amyotrophic Lateral Sclerosis (ALS), and Prion Diseases, etc. It is reported that oxidative stress, environmental factors, aging and protein dysfunction are the major risk factors for neurodegeneration.

Protein misfolding, accumulation and aggregation are common characteristics in many neurodegenerative diseases. Protein aggregates formed by proteins such as α-synuclein, tau, and β-amyloid (Aβ) peptides will trigger unfolded protein response (UPR), ER stress, and autophagy of neurons. The dysfunction of mitochondrial may lead to the induction of apoptosis. What's more, the reports about the function of non-neuronal cells (glia) and neuroinflammation in neurodegeneration are growing.

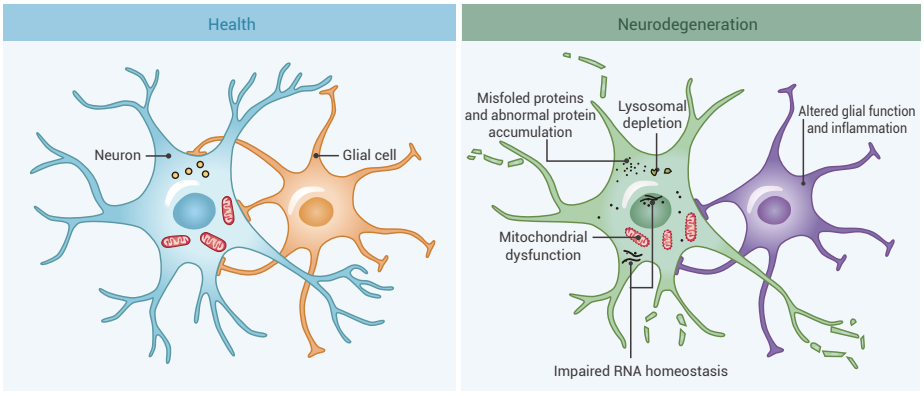

Figure 3. Major risk factors contribute to neurodegeneration [8]

Compounds

Cat. No.	Product Name	Description
HY-115038	ELN484228	A blocker of α-synuclein which is a key protein in Parkinson's Disease.
HY-124876	SynuClean-D	A potent α-synuclein aggregation inhibitor for the treatment of Parkinson's Disease.
HY-N2099	Onjisaponin B	Accelerates the degradation of mutant α-synuclein, and exhibits potential therapeutic effects on Parkinson's Disease and Huntington's Disease.
HY-50882	ELN318463	An amyloid precursor protein (APP) selective γ-secretase inhibitor.
HY-W010041	Scyllo-Inositol	An amyloid inhibitor that lowers amyloid plaques in an Alzheimer's Disease mouse model.
HY-103374	Phenserine	An AChE inhibitor that inhibits β-amyloid peptide formation. Improves cognitive performance and attenuates the progression of Alzheimer's Disease.

Cat. No.	Product Name	Description
HY-N0064	Macelignan	Possesses therapeutic potentials against neurodegenerative diseases with oxidative stress and neuroinflammation.
HY-101860	GIBH-130	An effective inhibitor of neuroinflammation and significantly suppresses the IL-1β secretion by activating microglia.
HY-125999	EPI-589	A quinone derivative, which has the potential for the treatment of amyotrophic lateral sclerosis (ALS).
HY-122607	DPA-714	Evaluates for the specific imaging of inflammation in various models of neuroinflammation and in a brain tumor model.
HY-135749	BN201	Activates pathways associated with the response to stress and neuron survival. Neuroprotective effects.
HY-124293	AA147	An endoplasmic reticulum (ER) proteostasis regulator.
HY-15976	P7C3	An orally available and CNS penetrant aminopropyl carbazole, with neuroprotective effects.
HY-P1061A	Colivelin TFA	A brain penetrant neuroprotective peptide that has the potential for the treatment of Alzheimer's Disease and ischemic brain injury.
HY-17646	Verdiperstat	A selective, irreversible and orally active MPO inhibitor that can be used in the research of neurodegenerative brain disorders.
HY-105285	Piromelatine	A melatonin MT1/MT2 receptor agonist that possesses anti-neurodegenerative, anxiolytic and antidepressant potentials.

Compound Screening Libraries

Cat. No. : HY-L054

Endoplasmic Reticulum Stress Compound Library

A unique collection of endoplasmic reticulum stress-related compounds that acts a useful tool for researching ER related diseases.

Cat. No. : HY-L069

Anti- Alzheimer's Disease Compound Library

A unique collection of compounds with anti-Alzheimer's Disease activities or targeting the unique targets of AD.

Cat. No. : HY-L070

Neuroprotective Compopund Library

A unique collection of compounds with potential neuroprotective activities.

Blood Brain Barrier

The blood-brain barrier (BBB) protects the central nervous system (CNS) from the peripheral blood circulation and supplies the brain with the required nutrients for normal function. It is a multicellular vascular structure that mainly composed of brain microvascular endothelial cells (ECs), pericytes, astrocytes and the basement membrane (Figure 4). ECs cells contribute to the barrier property by forming tight junctions (TJs) and limiting transcytosis. Pericytes are cells that cover capillaries and play important roles in the formation, maturation and maintenance of BBB. Astrocytes participate in BBB maintenance and ion/water transport by interacting with ECs and pericytes.

For the important roles in maintaining the homeostasis of CNS, BBB disruption has been found in a variety of neurological disorders. Meanwhile, BBB is also an obstacle to deliver beneficial drugs to treat CNS diseases or brain tumors, as it has the least permeable capillaries in the entire body. Therefore, it is crucial to discover drugs which can regulate this barrier for the treatment of brain-based diseases, such as Alzheimer's Disease (AD), Parkinson's Disease (PD) and Epilepsy.

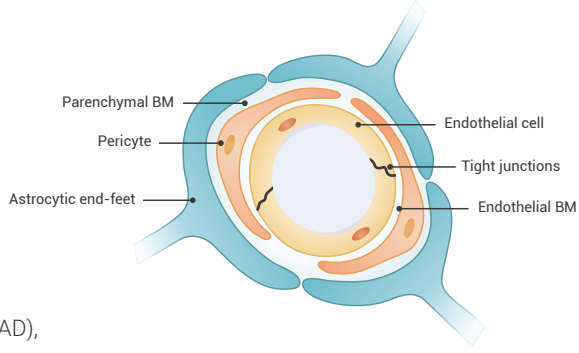

Figure 4. Schematic of blood-brain barrier [9]

Compounds & Compound Screening Libraries

Cat. No.	Product Name	Description
HY-114426	AT-1002	A tight junction regulator and absorption enhancer.
HY-15204	Tonabersat (SB-220453)	A gap-junction modulator that prevents inflammatory damage in the central nervous system.
HY-P0139	Gap 27	A synthetic Cx43 mimetic peptide. A gap junction inhibitor.
HY-10913	Danegaptide (GAP-134)	An orally active gap-junction modifier with an antiarrhythmic effect.
HY-13779	J-147	A CNS penetrant neuroprotective agent for cognitive enhancement.
HY-136341	7,8-Dihydroneopterin	Induces cellular apoptosis in astrocytes and neurons and can be used in the research of neurodegenerative diseases.
HY-107661	Arundic Acid	An astrocyte-modulating agent, which has the potential for stroke and Alzheimer's Disease research.
HY-10052	Aprepitant (MK-0869)	A neurokinin 1 receptor antagonist. Approved by FDA for the treatment of chemotherapy-induced nausea.
HY-100740	Lanabecestat (AZD3293)	A CNS penetrating BACE1 inhibitor for the treatment of Alzheimer's Disease.

Cat. No.	Product Name	Description
HY-104003	S 38093	A CNS penetrating antagonist of H3 receptor that enhances hippocampal neurogenesis.
HY-108295	Pivagabine (CXB-722)	A hydrophobic 4-aminobutyric acid derivative with neuromodulatory activity.
HY-108710	VU0650786	A CNS penetrant negative allosteric modulator of mGlu3 NAM.
HY-114153	PLX5622	A highly selective brain penetrant and oral active CSF1R inhibitor for extended and specific microglial elimination.
HY-N0304	L-DOPA	An orally active and CNS permeant metabolic precursor of neurotransmitter dopamine for Parkinson's Disease.
HY-110256	N-Acetylcysteine amide	A blood brain barrier permeant thiol antioxidant and a neuroprotective agent, reduces ROS production.
HY-15608	MPTP hydrochloride	A brain penetrant dopamine neurotoxin, inducing Parkinson's Disease.
HY-12599	URMC-099	An orally bioavailable and potent MLK3 inhibitor that has excellent blood-brain barrier penetration properties.
HY-15976	P7C3	An orally bioavailable and blood-brain barrier penetrant aminopropyl carbazole, with neuroprotective effects.

Compound Screening Library

Cat. No. : HY-L028

CNS-Penetrant Compound Library

A unique collection of bioactive CNS-penetrant compounds for the discovery of drugs used for brain diseases.

Refenences:

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[2]. Yuewen Tang, et al. Current progress in the derivation and therapeutic application of neural stem cells. Cell Death Dis. 2017 Oct 12;8(10):e3108.
[3]. Lin Cheng, et al. Generation of neural progenitor cells by chemical cocktails and hypoxia. Cell Res. 2014 Jun;24(6):665-79.
[4]. Yan-Chuang Han, et al. Direct Reprogramming of Mouse Fibroblasts to Neural Stem Cells by Small Molecules. Stem Cells Int. 2016;2016:4304916.
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[8]. Alla Katsnelson, et al. Neurodegeneration: From cellular concepts to clinical applications. Sci Transl Med. 2016 Nov 9;8(364):364ps18.
[9]. Lingling Xu, et al. Basement membrane and blood-brain barrier. Stroke Vasc Neurol. 2018 Dec 5;4(2):78-82.

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Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA

MedChemExpress Europe

Tel: + 46 86500910 **E-mail:** eu.sales@MedChemExpress.com
Address: Bergkällavägen 37C, 192 79 Sollentuna, SWEDEN

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