

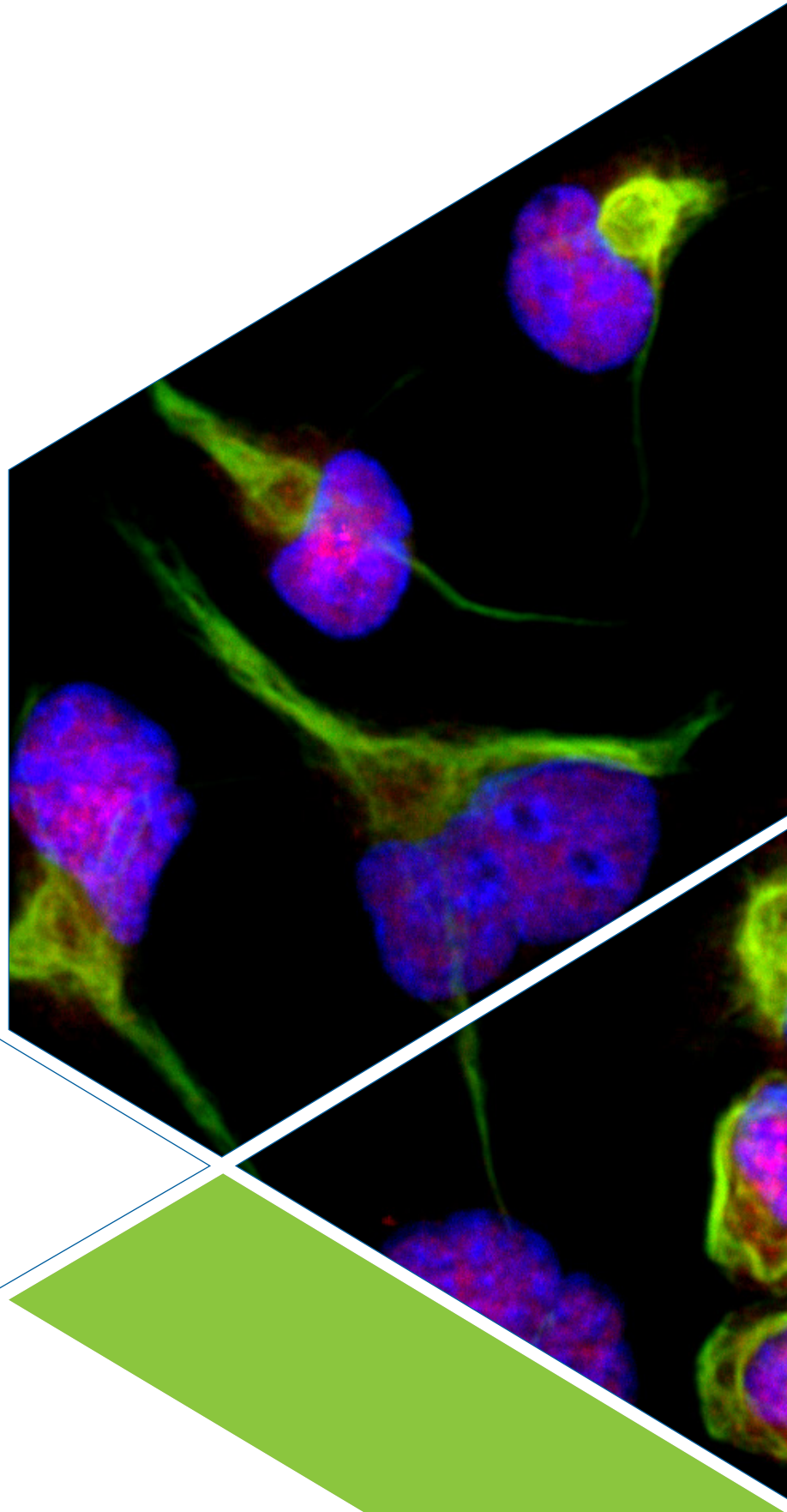
# Neural Stem Cells

ISOLATE & CULTURE

VERIFY

DIFFERENTIATE

INVESTIGATE



# ISOLATE AND CULTURE

Neural Stem cells (NSCs) require specialized media and growth factors to ensure efficient expansion. In addition to multipotent mouse and rat primary cortical stem cells, Bio-Techne offers a variety of serum-free neural media supplements, growth factors, and small molecules to maintain and expand NSCs.

## Primary Cortical Stem Cells

- **Ready-to-Use:** cells are highly pure and are contamination-free
- **Guaranteed Multipotency:** confirmed differentiation into neurons, astrocytes, and oligodendrocytes
- **Cost-Effective:** use a homogeneous cell population to reduce experimental variation

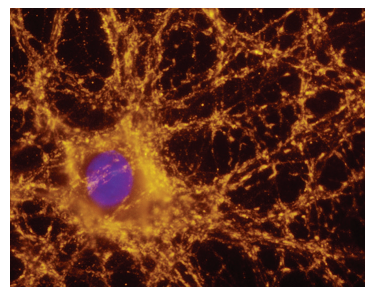
Product	Description	Catalog #
Rat Primary Cortical Stem Cells	Isolated from E14.5 Sprague-Dawley rats; $3 \times 10^6$ cells/vial	NSC001
Mouse Primary Cortical Stem Cells	Isolated from E14.5 CD-1 mice; $2 \times 10^6$ cells/vial	NSC002

## Cell Culture Supplements and Substrates

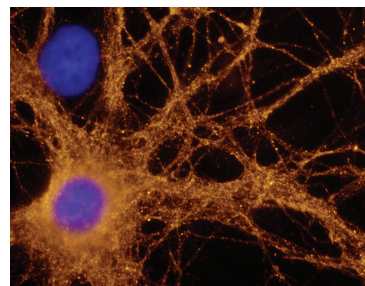
- **Improved Cell Health:** high-quality culture reagents to ensure better growth and differentiation
- **Efficient Growth:** optimized to enhance neural cell growth in culture

Product	Catalog #
N-2 Plus Media Supplement	AR003
N-2 MAX Media Supplement	AR009
N21-MAX Media Supplement	AR008
N21-MAX Insulin Free Media Supplement	AR010
N21-MAX Vitamin A Free Media Supplement	AR012
Holo-Transferrin	2914-HT
StemXVivo® Culture Matrix	CCM013
Human Fibronectin, CF	1918-FN
Bovine Fibronectin, CF	1030-FN
Recombinant Human Fibronectin Full, CF	4305-FN
Recombinant Human Fibronectin Fragment 2	3225-FN
Recombinant Human Fibronectin Fragment 3	3938-FN
Recombinant Human Fibronectin Fragment 4	3624-FN
Recombinant Human Fibronectin, GMP	4305-GMP
Recombinant Human Fibronectin, ACFP	ACFP4305
Cultrex® Poly-L-Lysine	3438-100-01

N21-MAX



Competitor



**Increased Synaptic Puncta and Neurite Outgrowth of Primary Neurons Cultured in N21-MAX.** E18 rat hippocampal neurons were grown for 21 days *in vitro* in media supplemented with either N21-MAX Media Supplement (Catalog # AR008) or the neural media supplement from the most widely-used competitor. Staining for Synaptotagmin (yellow) showed more robust synaptic puncta and increased neurite outgrowth in neurons cultured in N21-MAX compared to those cultured in competitor media. Cells were stained with a Mouse Anti-Rat Synaptotagmin-1 Monoclonal Antibody (Catalog # MAB4364) followed by the NorthernLights™ (NL)557-conjugated Donkey Anti-Mouse IgG Secondary Antibody (Catalog # NL007). Nuclei were counterstained with DAPI (blue).

## Individual Growth Factors for NSC Expansion

- **Clean Results:** high purity and the lowest endotoxin levels on the market
- **Consistent Performance:** biological activity is equivalent across lots

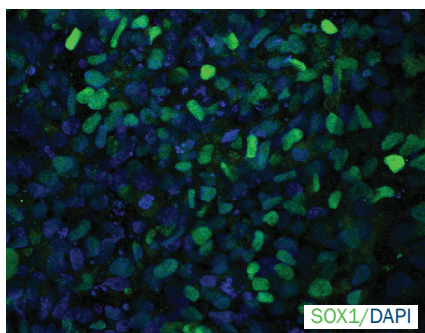
Protein	Catalog #
Recombinant Human $\beta$ -NGF	256-GF
Recombinant Human EGF	236-EG
Recombinant Human FGF basic	233-FB
Recombinant Human PDGF-AA	221-AA
Recombinant Human PDGF-BB	220-BB
Recombinant Human VEGF 165	293-VE
Recombinant Mouse $\beta$ -NGF	1156-NG
Recombinant Mouse EGF	2028-EG

Protein	Catalog #
Recombinant Mouse FGF basic	3139-FB
Recombinant Mouse VEGF 164	493-MV
Recombinant Rat $\beta$ -NGF	556-NG
Recombinant Rat EGF	3214-EG
Recombinant Rat FGF basic	3339-FB
Recombinant Rat PDGF-AA	1055-AA
Recombinant Rat PDGF-BB	520-BB
Recombinant Rat VEGF 164	564-RV

# Tocris® Small Molecules for NSC Expansion

Use small molecules alone or in combination with growth factors to enhance your control of NSC maintenance and expansion.

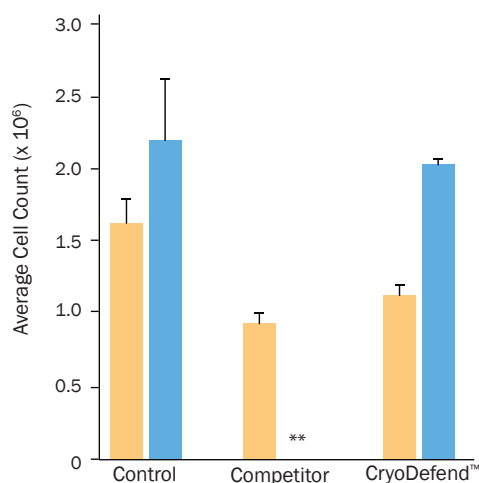
Product	Description	Catalog #
17-AAG	Selective Hsp90 inhibitor; protects neural progenitors from naturally occurring apoptosis	1515
Amiodarone hydrochloride	Ion channel blocker; selectively inhibits NSC proliferation in hESC-derived cell populations	4095
CHIR 99021	Selective GSK-3 inhibitor; enhances ESC self-renewal in combination with PD 0325901 (Catalog # 4192)	4423
Cyclopamine	Hedgehog signaling inhibitor; suppresses the proliferation of Ptch1 <sup>-/-</sup> medulloblastoma precursor cells	1623
DMH-1	Selective ALK2 receptor inhibitor; promotes iPSC neurogenesis in combination with SB 431542 (Catalog # 1614)	4126
INDY	Dyrk1A/B inhibitor; impairs the self-renewal capacity of NSCs	4997
P7C3	Neuroprotective and proneurogenic compound; orally available	4076
SB 431542	Induces proliferation, differentiation and sheet formation of ESC-derived endothelial cells	1614
Y-27632 dihydrochloride	Selective p160ROCK inhibitor; enhances survival of hES cells undergoing cryopreservation	1254



**SB 431542 Promotes the Differentiation of Pluripotent Stem Cells into NSCs.** BG01V human embryonic stem cells were grown to confluence then switched into differentiation media containing SB 431542 and Dorsomorphin. Differentiation into NSCs was confirmed at day 9 of differentiation by staining for SOX1 using a Goat Anti-Human SOX1 Affinity-Purified Polyclonal Antibody (Catalog # AF3369) and the NorthernLights™ (NL)493-Conjugated Donkey Anti-Goat IgG Secondary Antibody (Catalog #NL003).

## CryoDefend®-Stem Cells Media

- **Superior Recovery:** high yields of viable NSCs compared to competitor media
- **Reduced Variability:** fully defined to ensure functionally consistent cells
- **Better Control:** protein-free formulation eliminates undefined factors commonly found in traditional cryopreservation media



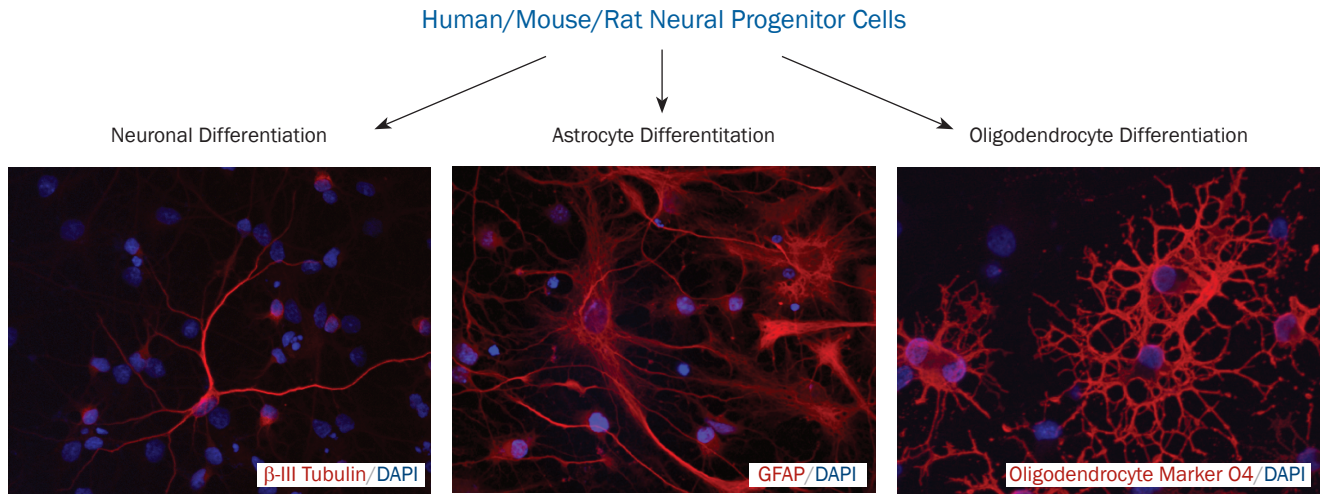
**Superior Recovery of Rat NSCs from CryoDefend®-Stem Cells Media Compared to Competitor Cryopreservation Media.** Rat cortical stem cells (Catalog # NSC001) were frozen ( $2 \times 10^6$  cells/vial) in control (10% BSA/10% DMSO), competitor, or CryoDefend®-Stem Cells media (Catalog # CCM018). Cell viability was assessed at the time of thaw (yellow bars) and after 5 days of culture (blue bars) in DMEM/F12 media supplemented with N-2 MAX (Catalog # ARO09) and Recombinant Human FGF basic (20 ng/mL; Catalog # 4114-TC). After 5 days in culture the number of viable cells recovered from cryopreservation in CryoDefend®-Stem Cells was significantly increased compared to competitor ( $p < 0.001$ ) media but not control ( $p = 0.637$ ) media. Error bars indicate the standard deviation of duplicate samples. The asterisks (\*\*) indicate low recovery yield.

# VERIFY

Validating the multipotency of a NPC population prior to their expansion, differentiation, and experimentation will ensure confidence when analyzing the data from downstream experiments. Using suboptimal, unverified NPC populations puts the investigator at risk for inconsistent results, thus wasting time and reagents. Bio-Techne offers a variety of solutions to quickly and confidently assess NPC multipotency.

## Neural Lineage Functional Identification Kit

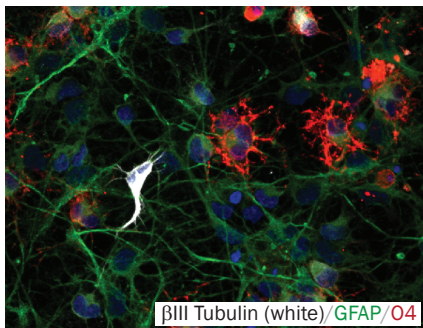
- **Definitively Verifies Multipotency:** uses optimized growth factors for unquestionable differentiation into neurons, astrocytes, and oligodendrocytes
- **Time-Saving:** differentiates NPCs in 7–10 days
- **Cost-Efficient:** differentiation supplements and cell-specific marker antibodies packaged together
- **Flexible:** for human, mouse, and rat NPCs



**Functional Verification of NSC Multipotency.** Rat cortical stem cells were maintained in culture and differentiated towards neural lineages using the Human/Mouse/Rat Neural Lineage Functional Identification Kit (Catalog # SC028). NSC differentiation into neurons, astrocytes, and oligodendrocytes was validated using the cell-specific marker antibodies supplied in the kit.

## Neural 3-Color Immunocytochemistry Kit

- **Comprehensive Characterization:** includes antibodies for neurons, astrocytes, and oligodendrocytes
- **Time-Efficient:** simultaneous 3-color staining with fluorochrome-conjugated primary antibodies



**Differentiation of Rat NSCs Confirmed with the Neural 3-Color Immunocytochemistry Kit.** Rat cortical stem cells were differentiated into neurons, astrocytes, and oligodendrocytes using the Human/Mouse/Rat Neural Lineage Functional Identification Kit (Catalog # SC028). Differentiated cells were stained with cell-specific antibodies from the Human/Mouse/Rat Neural 3-Color Immunocytochemistry Kit (Catalog # SC024). The images show NSC cells differentiated into neurons (pseudocolored white; βIII Tubulin), astrocytes (green; GFAP), and oligodendrocytes (red; O4). Nuclei were counterstained with DAPI (blue).



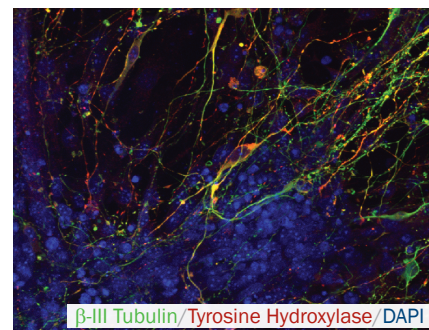
# DIFFERENTIATE

Efficient and consistent NSC differentiation is essential for maximizing research productivity, increasing data reliability, and reducing the cost and labor associated with lengthy differentiation protocols. Bio-Techne remedies these challenges by providing all-in-one kits specifically designed to differentiate embryonic stem (ES)/induced pluripotent stem (iPS) cells into neuronal cell-types, including kits for the directed differentiation of dopaminergic neurons or oligodendrocytes. In addition, Bio-Techne offers a wide selection of small molecules to enhance NSC differentiation.

## Differentiation Kits

- **Reproducible Differentiation:** includes optimized growth factors for the consistent differentiation of ES/iPS cells into dopaminergic neurons or oligodendrocytes
- **Eliminates Variation:** reliable differentiation for confidence during downstream data interpretation
- **Consistent Quality:** Each kit validated to generate high quality dopaminergic neurons

Product	Species	Catalog #
Dopaminergic Differentiation Kit	Human, Mouse	SC0018
Oligodendrocytes Differentiation Kit	Mouse	SC004



**Dopaminergic Neurons Generated from ES Cells Using the Dopaminergic Neuron Differentiation Kit.** D3 mouse ES cells were differentiated into dopaminergic neurons using the Dopaminergic Neuron Differentiation Kit (Catalog # SC001B). A dopaminergic phenotype was confirmed using the Mouse Anti-Human Tyrosine Hydroxylase Monoclonal Antibody (red; Catalog # MAB7566) followed by the NL557-Conjugated Donkey Anti-Mouse IgG Secondary Antibody (Catalog # NLO07). Cells were counterstained with the NL637-Conjugated Mouse Anti-Neuron-Specific  $\beta$ -III Tubulin (Clone Tuj-1) Monoclonal Antibody (green; Catalog #NL1195V). The nuclei were counterstained with DAPI (blue).

## Individual Proteins for NSC Differentiation

Protein	Catalog #			GMP Grade, Catalog #		
	Human	Mouse	Rat	Human	Mouse	Rat
Recombinant BMP-2	355-BM	355-BM	355-BM			
Recombinant BMP-4	314-BP	5020-BP		314-GMP		
Recombinant CNTF	257-NT		557-NT			
Recombinant FGF-10	345-FG	6224-FG	7804-FG			
Recombinant GDNF	212-GD		512-GF	212-GMP		
Recombinant IGF-I	291-G1	791-MG	4326-RG	291-GMP		
Recombinant NT-3	267-N3	267-N3	267-N3	267-GMP		
Recombinant NT-4	268-N4	3236-N4		268-GMP		
Recombinant Sonic Hedgehog/Shh	1845-SH, 1314-SH	464-SH, 461-SH		1314-GMP		
Recombinant FGF-8b	423-F8	423-F8				
Recombinant BDNF	248-BD	248-BD	248-BD	248-GMP	248-GMP	248-GMP

## Tocris® Small Molecules for NSC Differentiation

Use small molecules to gain temporal control of differentiation pathways and to modulate cell fate by targeting specific signaling pathways.

Product	Description	Catalog #
DAPT	$\gamma$ -secretase inhibitor; induces neuronal differentiation of neural cells	2634
Fluoxetine hydrochloride	5-HT re-uptake inhibitor; induces differentiation of neuronal precursors	0927
Forskolin	Adenylyl cyclase activator; induces neuronal differentiation in NSCs	1099
ISX 9	Induces neuronal differentiation of SVZ progenitors	4439
KHS 101 hydrochloride	Selective inducer of neuronal differentiation in hippocampal neural progenitors	4888
Metformin hydrochloride	Antidiabetic agent; promotes neurogenesis	2864
Neuropathiazol	Selective inducer of neuronal differentiation in hippocampal neural progenitors	5186
1-Oleoyl lysophosphatidic acid sodium salt	Endogenous agonist of LPA <sub>1</sub> and LPA <sub>2</sub> ; inhibits differentiation of NSCs into neurons	3854
Retinoic acid	Retinoic acid receptor agonist; promotes differentiation of ESCs into neurons, glia and adipocytes	0695
SAG	Smo agonist; enhances differentiation of iPSCs into dopaminergic neurons	4366
SU 5402	FGFR and VEGFR inhibitor; attenuates integrin B4-induced differentiation of ESCs	3300
TWS 119	GSK-3 $\beta$ inhibitor; induces neuronal differentiation in ESCs	3835
Valproic acid, sodium salt	Histone deacetylase inhibitor; promotes neuronal differentiation	2815

# INVESTIGATE

After carefully validating NSC multipotency, expanding your NSC starting population, and driving cell differentiation, it is important to investigate the biology of newly formed cells. Bio-Techne offers a variety of tools to investigate neural function including Tocris small molecule agonists, antagonists, modulators, and blockers to functionally characterize the receptors and ion channels expressed by NSC-derived cells. In addition, explore synaptic development and function with our vast selection of neuroscience-related antibodies.

## Tocris® Small Molecules to Investigate Synapse Function

- Modulate neuronal function by targeting specific receptors and ion channels
- Utilize our highly bioactive agonists, antagonists, modulators, and blockers

Product	Description	Catalog #
A803467	Selective Na <sub>v</sub> 1.8 channel blocker	2976
α, β-Methylene adenosine 5' triphosphate	P2 agonist	3209
DL-AP5	Potent, selective NMDA antagonist	0105
(+)-Bicuculline	Potent GABA <sub>A</sub> antagonist	0130
nor-Binaltorphimine dihydrochloride	Standard selective κ opioid receptor antagonist	0347
CGP 35348	Brain penetrant, selective GABA <sub>B</sub> antagonist	1245
(+)-MK 801 maleate	Non-competitive NMDA antagonist, acts at ion channel site	0924
MPEP hydrochloride	mGlu <sub>5</sub> antagonist and positive allosteric modulator at mGlu <sub>4</sub>	1212
RS 127445 hydrochloride	Selective, high affinity 5-HT <sub>2B</sub> antagonist	2993
SCH 23390 hydrochloride	Standard selective D <sub>1</sub> -like antagonist; also 5-HT <sub>2C</sub> agonist	0925
Tetrodotoxin	Na <sup>+</sup> channel blocker	1078
(±)-U-50488 hydrochloride	Standard selective κ opioid receptor agonist	0495
Varenicline tartrate	Orally active, subtype-selective α4β2 partial agonist	3754
Xanomeline oxalate	Functionally selective M <sub>1</sub> agonist	3569

## Caged Compounds for Neural Cell Cultures

Product	Description	Catalog #
DPNI-caged-GABA	Nitroindoline-caged GABA	2991
MNI-caged-D-aspartate	Caged D-aspartate	2277
MNI-caged-L-glutamate	Stable photoreleaser of L-glutamate	1490
MNI-caged-NMDA	Caged NMDA	2224
NPEC-caged-(S)-AMPA	Caged (S)-AMPA	3840
NPEC-caged-D-AP5	Caged D-AP5 (Cat.No. 0106)	4230
NPEC-caged-dopamine	Caged dopamine	3992
RuBi GABA trimethylphosphine	Caged GABA; inhibits neural activity	4709
RuBi-Dopa	Caged dopamine; exhibits two-photon sensitivity	4932
RuBi-Glutamate	Caged glutamate; excited by visible wavelengths	3574
RuBi-Nicotine	Caged nicotine; rapidly excitable by visible light	3855

## Photoswitchable Ligands

Product	Description	Catalog #
AAQ	Photoswitchable K <sub>v</sub> channel blocker	5462
PA1	Photoswitchable ENa C blocker	5463
QAQ	Photoswitchable Na <sub>v</sub> , K <sub>v</sub> , and Ca <sub>v</sub> channel blocker	5470

## Fluorescent Probes for Neuroscience Research

Target Molecule	Description	Catalog #
Calcein AM	Cell permeable compound; hydrolyzed to become fluorescent in living cells	5119
Dansyl-NECA	Potent and selective fluorescent adenosine A1 agonist	5122
FFN 102 mesylate	Selective fluorescent substrate of DAT and VMAT2	5200
FFN 206 dihydrochloride	Fluorescent VMAT2 substrate	5043
FFN 511	Fluorescent substrate for VMAT2	3878
FURA-2AM	Fluorescent Ca <sup>2+</sup> indicator	2220
K 114	Amyloid fibril-specific fluorescent dye	3144
L 012 sodium salt	Chemiluminescent ROS and RNS indicator	5085
Methoxy-X04	Fluorescent amyloid $\beta$ detector; brain penetrant	4920
SynaptoRed™ C2	Fluorescent dye; stains synaptic vesicles	5118
Tocrifluor T1117	Novel fluorescent cannabinoid ligand; fluorescent form of AM 251 (Cat. No. 1117)	2540

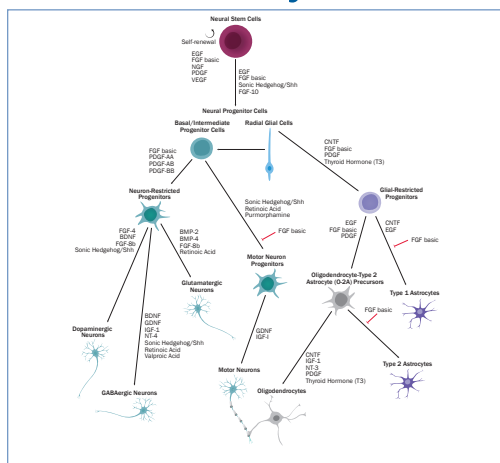
## Antibodies to Investigate Synapse Development

Target Molecule	Description	Applications	Species Reactivity	Catalog #	Brand
$\alpha$ -Synuclein	Pre-synaptic protein	WB, FC, ICC, IHC	Human, Mouse	NBP1-26380	Novus
CaMKII $\alpha$	Concentrated at the postsynaptic density	WB, ELISA, ICC, IHC	Human, Mouse, Rat, +	NB100-1983	Novus
EAAT1/GLAST-1	Glutamate transporter	WB, IHC	Human	AF6048	R&D Systems
GFAP	Astrocyte marker	WB, IHC, SW	Human	AF2594	R&D Systems
Homer1	Concentrated at the postsynaptic density	WB, ICC	Human, Mouse	NBP1-44999	Novus
MOG	Identifies myelinating oligodendrocytes	IHC, WB	Mouse	AF2439	R&D Systems
Myelin basic protein	Myelin sheath protein	WB, ELISA, FC, ICC, IHC	Human	NBP2-22121	Novus
Neurologin 1/NLGN1	Post-synaptic protein	WB, IHC	Human, Rat	AF4340	R&D Systems
NMDAR2B	NMDA receptor subunit	WB, FC, ICC, IHC, IP	Human, Mouse, Rat	NB300-106	Novus
PSD95	Post-synaptic protein	WB	Human, Mouse, Rat	PPS059	R&D Systems
SHANK3	Concentrated at the postsynaptic density	WB, IHC	Human, Mouse, Rat	NBP1-20197	Novus
Synapsin I	Pre-synaptic protein	WB, ICC, IHC, IP	Human, Mouse, Rat, +	PPS035	R&D Systems
Synaptophysin	Neuronal secretory vesicle-associated protein	WB, IHC	Human	AF5555	R&D Systems
Synaptotagmin	Synaptic vesicle protein	WB, ICC, IHC, IP	Rat	MAB4364	R&D Systems
Tyrosine Hydroxylase	Dopaminergic neuron marker	WB, ICC, IHC, SW	Human, Mouse, Rat, +	NB300-109	Novus
Glut1	Glutamate transport into synaptic vesicles	WB, CHIP, FC, ICC, IHC	Human, Mouse	NB110-39113	Novus

Species Key: + Additional Species

Applications Key: **WB** Western blot, **CHIP** Chromatin Immunoprecipitation, **FC** Flow Cytometry, **ICC** Immunocytochemistry, **IHC** Immunohistochemistry, **IP** Immunoprecipitation, **SW** Simple Western™

## View Pathway



[rndsystems.com/pathways\\_nsc](http://rndsystems.com/pathways_nsc)

## Neural Stem Cells

Neural stem cells (NSCs) are undifferentiated precursor cells defined by their capacity for self-renewal and multipotency. During central nervous system development, NSCs proliferate and divide to generate clonally related progeny that differentiate into neurons, astrocytes, oligodendrocytes, and ventricular ependymal cells. The symmetric division of NSCs underlies their ability to self-renew and serves to maintain the NSC population. In contrast, asymmetric mitosis produces one NSC and one neural progenitor cell (NPC), daughter cells with differentiation capacity restricted to neuronal or glial lineages. Asymmetric division generates two NPCs, but does not contribute to maintaining the NSC pool. NSC self-renewal and differentiation is regulated by a precise temporal sequence of growth factor presentation, intracellular signaling, and transcription factor expression. Bio-Techne presents tools to optimize NSC experimentation, from expansion and differentiation to verification and investigation. Using reagents that ensure a reliable workflow will reduce experimental variability, improve data consistency, and prevent wasted effort and reagents.

R&D SYSTEMS

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Global info@bio-techne.com bio-techne.com/find-us/distributors TEL +1 612 379 2956  
North America TEL 800 343 7475 Europe | Middle East | Africa TEL +44 (0)1235 529449  
China info.cn@bio-techne.com TEL +86 (21) 52380373

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