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Introduction

Neurons and their precursors express unique sets of transcription factors, enzymes, cytoskeletal proteins and receptors. These can be labeled using antibodies, allowing particular cell types to be distinguished from the surrounding tissue. In this booklet, we present the most widely used markers so you can label neurons at every stage of their developmental journey, from neural stem cell to mature neuron.

Neuroepithelial cells

Neuroepithelial cells are the stem cells of the central nervous system and give rise to the spinal cord, brain and retina. Their origin is ectodermal and they line the cerebral ventricles during early embryonic development. The following markers are commonly used to stain neuroepithelial cells:

Pax6

Pax6 is a transcriptional regulator that is important for cortical progenitor proliferation, eye development and early forebrain dorsoventral patterning.

Notch1

Notch1 is a transmembrane receptor that plays a role in intercellular signaling between adjacent cells. Upon ligand binding, its intracellular domain goes to the nucleus where it modifies gene expression.

PCNA

PCNA is a DNA clamp that act as a cofactor of DNA polymerase delta. It is important for DNA synthesis and is widely expressed during S phase.

HES5

HES5 is a transcriptional repressor that acts downstream of the Notch signaling pathway to regulate differentiation of neuroepithelial cells.

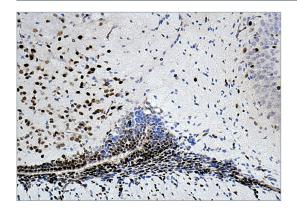
SOX:

SOX1 is a transcription factor whose expression is limited to neuroepithelial cells. It suppresses neurogenic cell divisions by blocking cell cycle exit, leading to neuronal differentiation.

SOX3

SOX3 is a transcription factor with a high sequence similarity to SOX1. It is required for development of the dorsal telencephalon and hypothalamus.

Anti-SOX1 Antibody (ab87775)



Description: Rabbit polyclonal to SOX1

Tested applications: ICC/IF, WB, IHC-P

Species reactivity: Mouse, rat, human

Image:

Subventricular zone of the lateral ventricle of a P5 mouse brain stained with ab87775.

Radial glia

Radial glia cells are the product of asymmetric division of neuroepithelial cells. They are progenitor cells capable of producing both neurons and glia. During development they provide a scaffold for migrating neurons. Markers for radial glia include the following:

Vimentin

Vimentin is a type III intermediate filament protein that acts as a cytoskeletal component of mesenchymal cells. Due to its involvement in cell migration it is used as an epithelial to mesenchymal transition (EMT) marker.

Nestin

Nestin is a type VI intermediate filament that is widely expressed in neural stem cells. It does not play a major role in the cytoskeleton but its loss is positively correlated with increased apoptotic rates and reduced self-renewal ability.

N cadherin

Neural cadherin is a calcium-dependent transmembrane protein that plays a vital role in the formation of adherens junctions.

SOX2

SOX2 is a transcription factor with a critical role in the maintenance of self-renewal and pluripotency.

Musashi 1

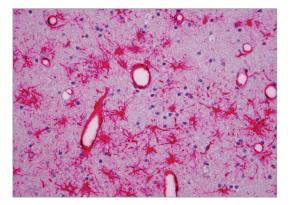
Musashi 1 is a mRNA-binding protein that acts as a translational regulator. It promotes Notch signaling by binding to the mRNA of the Notch inhibitor, Numb.

Olig2

Olig2 is a transcription factor that plays a role in the differentiation of motor neuron progenitors early in development by promoting cell cycle exit and subsequent differentiation. In later stages it directs the formation of oligodendrocytes.

Anti-Vimentin Antibody (EPR3776) (ab92547)





Description

Rabbit monoclonal (EPR3776) to vimentin

Tested applications: ICC/IF, WB, flow cyt, IHC-P

Species reactivity:
Mouse, rat, human, rhesus monkey

Image:

Rhesus monkey brain sections stained with ab92547.

Immature neurons

Immature neurons do not undergo further cell divisions. They migrate to their final destinations in the nervous system, extend neurites and integrate into the neuronal network. At this stage, they can be identified using the following markers:

Doublecortin

Doublecortin is a microtubule-associated phosphoprotein that promotes neurite extension and cell migration by regulating the organization and stability of microtubules.

NeuroD1

NeuroD1 is a transcription factor that promotes neuronal differentiation and is essential for the development of the central nervous system. It is specific for post-mitotic cells and is not expressed in radial glia or neuronal progenitors.

TBR1

TBR1 is a member of the T-box family of transcription factors. It exerts both positive and negative control over regional and laminar identity. Proteins whose expression is regulated by TBR1 include BCL6, cadherin 9 and SOX5.

PSA-NCAM

PSA-NCAM is required for cell migration, neurite extension and synaptogenesis. The negative charge of polysialic acid (PSA) attenuates adhesion forces between neighboring cells, therefore facilitating cell motility.

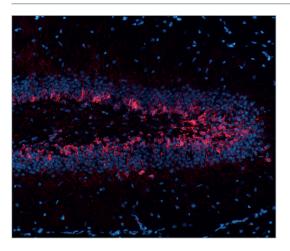
MASH1

Mash1 is a transcription factor whose expression is controlled by the Hedgehog signaling pathway and in turn affects the Notch signaling pathway by controlling expression of Delta-like proteins 1 and 2.

Reelin

Reelin is a glycoprotein that is secreted in the developing cortex and affects immature projection neurons migrating from the germinal zone. It binds to Src family kinases and their substrate, Dab1.

Anti-Doublecortin Antibody (ab18723)



Description:

Rabbit polyclonal to doublecortin

Tested applications:

WB, ICC, ICC/IF, IHC-FrFI, IHC-FoFr, IHC-Fr, IHC-P

Species reactivity:

Mouse, rat, chicken, cat, human, cynomolgus monkey, quail, rhesus monkey

Image:

Doublecortin staining of adult mouse dentate gyrus sections using ab18723 (red)

Mature neurons

Mature neurons are terminally differentiated and are no longer able to divide. They can be identified by staining with the following markers:

NeuN

NeuN (neuronal nuclei), otherwise known as Fox3, is a RNA binding protein and is specifically expressed in post-mitotic neurons. Please note, the following cell types do not express NeuN: Golgi cells, Purkinje cells, olfactory bulb mitral cells, retinal photoreceptor cells, inferior olivary and dentate nucleus neurons and sympathetic ganglion cells.

MAP2

MAP2 (microtubule-associated protein 2) is a neuron-specific protein whose main function is to interact with tubulin, promote its assembly into microtubules and stabilize the microtubule network.

Beta III tubulin

Class III beta tubulin is one of the five families of tubulin molecules. Its expression is limited to neurons where it plays a vital role in neurite extension and vesicle trafficking.

160 kD neurofilament medium/200 kD neurofilament heavy

Neurofilaments are the major intermediate filaments found in neurons. As major components of the cytoskeleton they are involved in axonal structural support and transport.

NSE

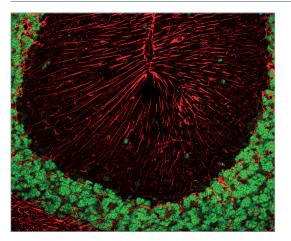
Neuron specific enolase (NSE), also known as gamma-enolase or enolase 2 is a phosphopyruvate hydratase occurring exclusively in neurons.

PSD93/PSD95

Both PSD93 and PSD95 are components of the post-synaptic density (PSD), which is a protein accumulation attached to the postsynaptic membrane. The PSD is involved in signal transmission and neurotransmitter receptor organization.

Anti- NeuN Antibody (EPR12763) (ab177487)





Description:

Rabbit monoclonal (EPR12763) to NeuN

Tested applications:

Flow cyt, IHC-FoFr, IHC-Fr, IHC-P, WB, ICC/IF

Species reactivity:

Mouse, rat, sheep, goat, cat, dog, human, zebrafish, marmoset (common)

Image:

NeuN (green) and GFAP (red) staining of mouse cerebellum sections using ab 177487 and ab 4674 respectively.

Glutamatergic neurons

Glutamatergic neurons produce glutamate, which is one of the most common excitatory neurotransmitters in the central nervous system (CNS). Glutamatergic neurons can be identified by expression of the following markers:

VGIuT1

VGLuT1 is a vesicular glutamate transporter mainly expressed in layers I-III of the neocortex, entorhinal and piriform cortex, hippocampus, amygdala, subiculum as well as parallel fibers of the cerebellum.

VGIuT2

vGLuT2 is a vesicular glutamate transporter found in the olfactory bulb, layer IV of the cerebral cortex, granular layer of the dentate gyrus, thalamus, hypothalamus, brain stem as well as cerebellar climbing fibers and Purkinje cell dendrites.

Glutaminase

Glutaminase is an enzyme that produces glutamate from glutamine. There are two isomorphs of the enzyme, kidney glutaminase (K-glutaminase or GLS1) and liver glutaminase (L-glutaminase or GLS2), both of which are expressed in the brain.

Glutamine synthetase

Glutamine synthetase catalyzes the conversion of glutamate to glutamine. When staining for glutamine synthetase, we recommend also using a mature neuron marker, such as NeuN.

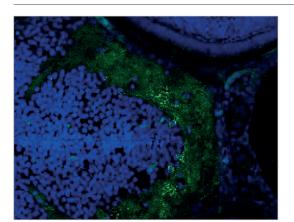
NMDAR1

NMDA receptor subunit 1 (NMDAR1, NR1 or GluN1) is a subunit of the NMDA receptor, a glutamate receptor and ion channel found in neurons.

NMDAR2B

NMDA receptor subunit 2B (NMDAR2B or NR2B or GluN2B) is a subunit of the NMDA receptor that forms the glutamate binding site.

Anti-VGluT1 Antibody (ab77822)



Description:
Rabbit polyclonal to VGluT1

Tested applications: IHC-Fr, WB

Species reactivity: Rat, zebrafish (predicted in mouse, cow, pigeon, human)

Image: VGIuT1 staining of zebrafish retina sections

using ab77822 (green).

GABAergic neurons

GABAergic neurons generate gamma aminobutyric acid (GABA), one of the two inhibitory neurotransmitters in the central nervous system. Some of the most commonly used markers for identifying GABAergic neurons are below:

GABA transporter 1

GABA transporter 1 (GAT1) is localized on the cell membrane and mediates translocation of GABA from the extracellular to the intracellular space.

GABA_R Receptor 1

GABA $_B$ receptor 1(GABA $_{B1}$) is the B1 subunit of the metabotrophic G protein-coupled GABA $_B$ receptor. GABA $_{B1}$ comprises seven transmembrane helices and is responsible for ligand binding.

GABA_B Receptor 2

GABA_B receptor 2 (GABA_{B2}) is the B2 subunit of the metabotrophic G protein-coupled GABA_B receptor. GABA_{B2} is responsible for coupling to G proteins via its intracellular loops.

GAD65

GAD65 (also known as GAD2) is the 65 kDa isomorph of the enzyme glutamate decarboxylase, which catalyzes the formation of GABA from glutamate.

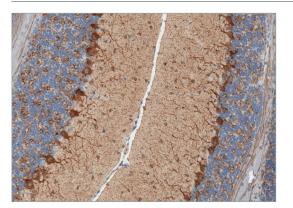
GAD67

GAD67 (also known as GAD1) is the 67 kDa isomorph of glutamate decarboxylase. Unlike GAD65, which is also expressed in the pancreas, GAD67 is CNS-specific.

ABAT

4-Aminobutyrate aminotransferase (ABAT, also known as GABA transaminase) is an enzyme that catalyzes the formation of L-glutamate using GABA as a substrate.

Anti-GAD67 Antibody (K-87) (ab26116)



Description:

Mouse monoclonal (K-87) to GAD67

Tested applications:

Flow cyt, IHC-Fr, IHC-P, WB, ICC/IF

Species reactivity: Mouse, rat, human

Image:

GAD67 staining of mouse cerebellum sections using ab26116.

Dopaminergic neurons

Dopaminergic neurons produce dopamine, a neurotransmitter with roles in neurological functions such as mood and reward. Progressive loss of dopaminergic neurons is the cause of many of the motor symptoms associated with Parkinson's disease. The following markers are commonly used:

Tyrosine hydroxylase

Tyrosine hydroxylase is an enzyme that converts L-tyrosine to L-3,4-dihydroxyphelylalanine (L-DOPA). L-DOPA is the precursor for dopamine.

Nurr1

Nurr1 is a transcriptional activator that induces tyrosine hydroxylase expression, leading to differentiation into dopaminergic neurons.

Dopamine transporter

The dopamine transporter (also known as DAT) is a transmembrane, sodium-dependent protein that controls reuptake of extracellular dopamine into presynaptic neurons.

FOXA2

Forkhead box protein A2 (FOXA2, also known as hepatocyte nuclear factor 3-beta or HNF-3B) is a transcriptional activator that regulates specification and differentiation of dopaminergic neurons and retains expression in the adult brain.

GIRK2

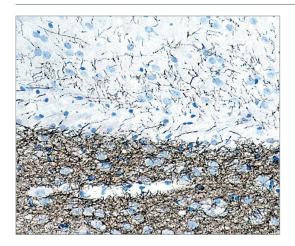
GIRK2 is a potassium channel with greater tendency for influx rather than efflux of potassium ions. It is important for resting potential maintenance, duration of action potential and cell-excitability modulation.

LMX1B

LMX1B is a transcription factor involved in a number of processes during dopaminergic neuron development, such as neuronal migration, axonal guidance and Wnt signaling. It may also bind the Nurr1 transcriptional activator complex.

Anti-Tyrosine Hydroxylase Antibody (EP1533Y) (ab75875)





Description:

Rabbit monoclonal (EP1533Y) to tyrosine hydroxylase

Tested applications:

WB, ICC, flow cyt, IHC-P

Species reactivity:

Mouse, rat, human, pig

Image:

Tyrosine hydroxylase staining of rat brain sections (striatum-frontal cortex border) using ab75875.

Serotonergic neurons

Serotonergic neurons synthesize the neurotransmitter serotonin (5-HT), which is found in the gastrointestinal tract, blood platelets and the central nervous system (CNS). Markers for serotonergic neurons include:

Tryptophan hydroxylase

Tryptophan hydroxylase (TPH) is an enzyme involved in serotonin synthesis. There are two isoforms of tryptophan hydroxylase, TPH1 and TPH2. TPH2 is the isoform predominantly found in the brain.

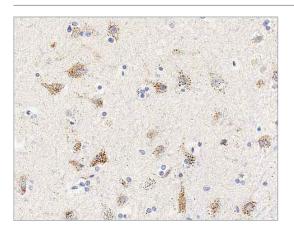
Serotonin transporter

The serotonin transporter (SERT or 5-HTT) is a transmembrane protein that is responsible for the re-uptake of serotonin from the synaptic cleft into the presynaptic neuron.

Pet1

Pet1 is a transcription factor that drives the transcription of genes essential for the metabolism as well as re-uptake of serotonin.

Anti-Serotonin Transporter Antibody (ab174770)



Description:

Rabbit polyclonal to serotonin transporter antibody

Tested applications: IHC-P

Species reactivity: Human

Image:

Serotonin transporter staining of human cerebral cortex sections using ab 174770.

Cholinergic neurons

Cholinergic neurons use the neurotransmitter acetylcholine. Their progressive loss is one of the hallmarks of neurodegenerative diseases with cognitive deficits such as Alzheimer's disease. The most important cholinergic neuron markers are the following:

Choline acetyltransferase

Choline acetyltransferase (ChAT) catalyzes the synthesis of acetylcholine. ChAT is expressed in neurons of both the central and peripheral nervous system and is arguably the most common cholinergic neuron marker.

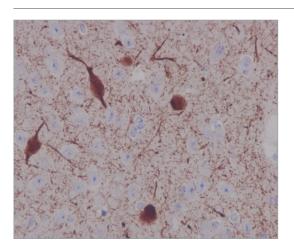
Vesicular acetylcholine transporter

The vesicular acetylcholine transporter (VAChT) uses a proton gradient established by the vacuolar ATPase to transport acetylcholine into secretory vesicles.

Acetylcholinesterase

Acetylcholinesterase catalyzes the breakdown of acetylcholine into acetate and choline. It terminates cholinergic synaptic transmission by clearing acetylcholine from the synaptic cleft.

Anti-Choline Acetyltransferase Antibody (EPR16590) (ab178850) RabMAb®



Description:

Rabbit monoclonal (EPR16590) to choline acetyltransferase

Tested applications: WB, IHC-P

Species reactivity: Mouse, rat, rabbit, guinea pig

Image:

Choline acetyltransferase staining of guinea pig cerebral cortex sections using ab178850.

