NEUROSCIENCE

NEURAL LINEAGE DEVELOPMENT MARKERS

ATLAS ANTIBODIES

NEURAL LINEAGE DEVELOPMENT MARKERS

Lineages are the pathways of development and differentiation of neurons and glial cells in the central nervous system. They are defined by the temporal and spatial relationship between the progenitors, early neuronal precursors, and the mature neurons that result from them. Neuronal lineages can be studied in the context of cell fate determination and the processes of development, such as migration, axon guidance, and synaptogenesis.

A better comprehension of neuronal lineages is essential to our understanding of the nervous system and how it develops and functions in health and disease.

Atlas Antibodies manufactures primary polyclonal and monoclonal antibodies targeting relevant markers in the neural lineage development pathways.

In this white paper you can find our selections of PrecisA Monoclonals™ and TripleA Polyclonals™ validated in IHC, ICC-IF and WB for tissue and cell analysis. All antibodies are paired with their specific PrEST Antigens™.

CONTENT

FIGURES

Cover Image:
Radial glia in the developing brainstem of mouse embryo E14.
Anti-FABP7 (BLBP) monoclonal antibody (AMAb90595), green.
Anti-GLAST (SLC1A3) polyclonal antibody (HPA037467), red.

Introduction and Clinical Significance

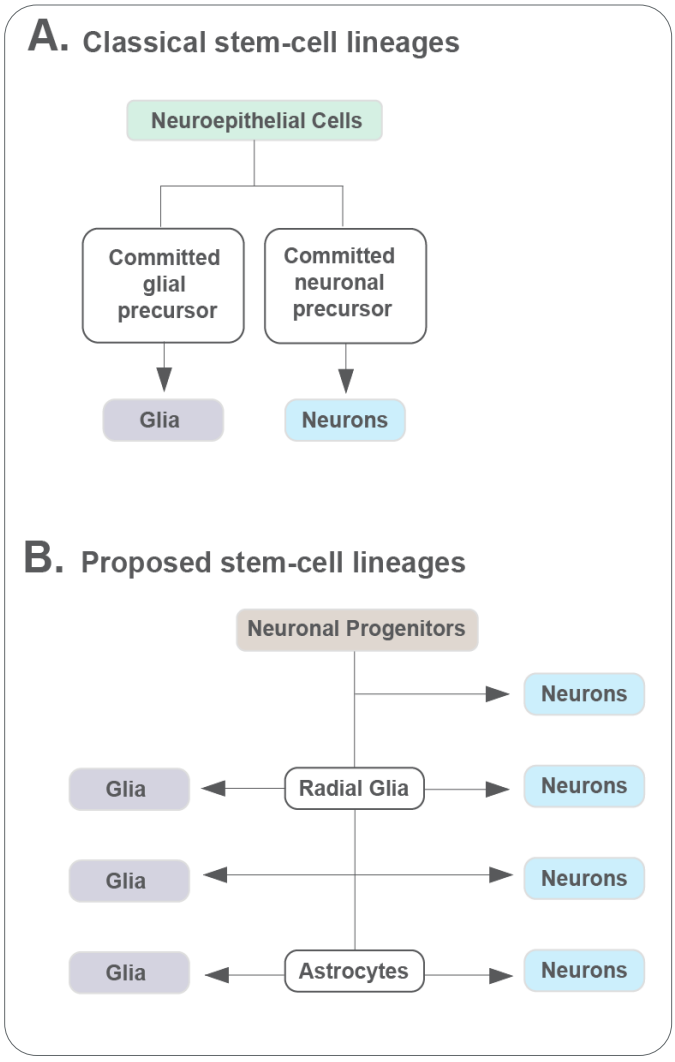
Brain function requires precise neural circuit assembly during development. Establishing a functional circuit involves multiple coordinated steps ranging from neural cell fate specification to proper matching between pre- and post-synaptic partners.

The principal cell types in the brain, neurons and glia, are generated in the proliferative zones that surrounds the ventricles, after which they migrate into the overlying cortical mantle.

Every neuron, oligodendrocyte, and astrocyte evolves from the differentiation of neural progenitor cells (NPCs). NPCs themselves are produced by multipotent neural stem cells (NSCs). Both NPCs and NSCs are termed neural precursor cells. Progenitors undergo a series of cell proliferation and differentiation events (lineage) generating postmitotic neurons.

The discovery of various proteins specific to certain cells in specific developmental stages led to the production of cell-type-specific antibodies used to identify cells using immunoassays such as immunostaining and western blot.

A lineage marker is an endogenous tag (either DNA, mRNA, RNA, or protein) expressed in different cells along neurogenesis and differentiated cells such as neurons and glial cells.



Neuronal lineage markers are used in research and clinical settings to examine the function of cells in normal conditions and during development and in clinical research to identify diseased cells and/or in the repair process.

NPCs are being explored alongside NSCs for their potential to treat diseases or injuries of the central nervous system. A deeper understanding of how these cells develop and function on a cellular and molecular basis is needed to progress from preclinical experimental research to therapeutic use.

Dopaminergic, GABAergic, and cholinergic markers of neuronal cell phenotype are of particular interest in understanding the pathology of clinical disease because the selective degeneration of these functional neurons is associated with the pathogenesis of neurodegenerative disorders.

For instance, Parkinson's disease is characterized by the degeneration of midbrain dopaminergic neurons in the substantia nigra of the brain. Alzheimer's disease involves a loss of forebrain cholinergic neurons; cortical GABAergic neurons degenerate in schizophrenia; choline acetyltransferase (ChAT) immunoreactivity is used to detect cognitive decline in several neurodegenerative disorders.

Elucidating the full potential of progenitor cells in the embryo and the adult and understanding the factors that guide the production of specific cell types will be essential for potential treatments of neurodegenerative diseases through cell replacement strategies.

Also, defects in proliferation produce cortical malformations that range from subtle, ectopic clusters of cortical neurons to the profound cortical disorganization observed in lissencephaly or anencephaly.

Figure 1 | Oak versus pine-tree models of neural stem-cell lineages.

A. Oak model: For many years, it was assumed that neurons and glia in the central nervous system were produced from two distinct precursor pools that diverged early during embryonic development

B. Pine tree model: Recent data support a different model in which NSCs develop into radial glia, which then develops into astrocytes. Radial glia can divide asymmetrically to produce neurons and glia and might produce these cells directly or through transit amplifying cells that are not shown in this figure. In mammals, radial cells disappear perinatally when they are thought to transform into astrocytes. In the adult subventricular zone, these astrocytes produce neurons, glia, and perhaps other cell types. In several non-mammalian species, radial glia persists into adulthood and generates new neurons.

Adapted from: Alvarez-Buylla A. et al, A unified hypothesis on the lineage of neural stem cells. Nat Rev Neurosci. 2001 Apr;2(4):287-93.

Insights into the Lineage Pathways that Govern Neurogenesis

The stochastic dynamics and regulatory mechanisms that govern the differentiation of individual human neural precursor cells into mature neurons still need to be fully understood. Also, the molecular patterns that switch on and off the pathways governing alternative neuronal fate choices and neurogenesis are still under investigation.

However, studies on neural lineage and adult neurogenesis have greatly expanded in the last decade due to improved detection and quantification tools. Further characterization of these cells should eventually provide a body of knowledge central to understanding brain development and disease.

Neural Stem Cells (NSCs)

Neural stem cells (NSCs) (or neuroepithelial progenitors) are primary progenitors that give rise to neurons and glia in the embryonic, neonatal, and adult brains. NSCs are self-regenerating multipotential cells found in the human brain which have the potential to differentiate into neurons, astrocytes and oligodendrocytes, and to self-renew sufficiently to provide adequate number of cells in the brain. In mammals, NSCs are the primary progenitors during embryogenesis, whereas intermediate progenitor cells are the secondary progenitors. **See Table 1 for neural stem cells markers.**

Radial Glial Cells (RGCs)

Radial glial cells (RGCs), or radial glial progenitor cells, are bipolar-shaped progenitor cells. During development, RGCs are the primary neural stem cells (NSCs) generating all neurons as well as astrocytes, oligodendrocytes, and ependymal cells.

RGCs are the key progenitor cells in the developing nervous system. During the late stages of neurogenesis, RGCs divide asymmetrically, generating a new radial glial cell and an intermediate progenitor (IPC) daughter cell. IPCs will then divide symmetrically to generate neurons.

RGCs differentiate from neuroepithelial progenitors at the beginning of neurogenesis and share with their ancestors the bipolar shape and the expression of some molecular markers. Radial glia, however, can be distinguished from neuroepithelial progenitors by the expression of astroglial markers.

When cortical neurogenesis is complete, radial glial cells transform into astrocytes and exit the ventricular zone, which thins to a single layer of ependymal cells in the postnatal cortex.

See Table 2 for radial glia cells (RGCs) markers.

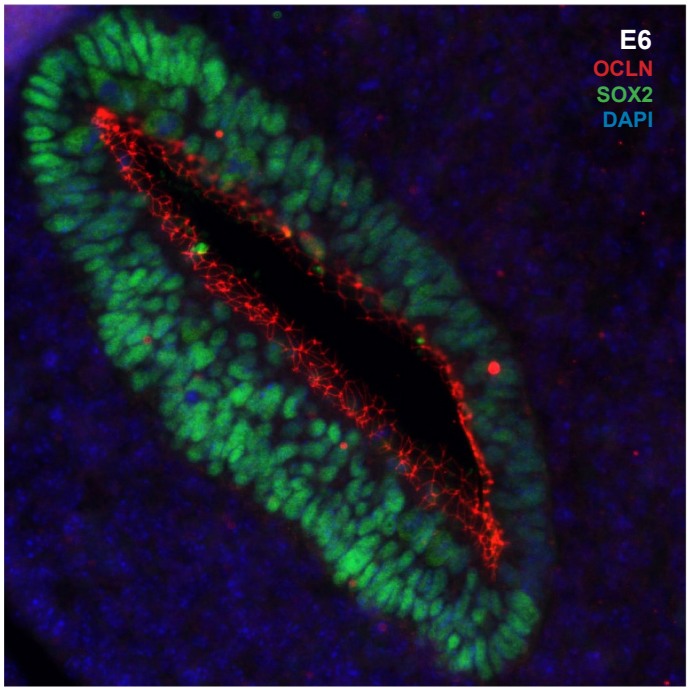


Figure 2 | Immunofluorescence of neuroepithelial cells in the neural tube.
Immunofluorescence staining of neuroepithelial cells in the neural tube of mouse embryo E6. The **anti-SOX2** monoclonal antibody (IgG1, AMAb91307) is visible in green; the **anti-OCLN** monoclonal antibody (IgG2a, AMAb90889) is visible in red. Nuclei are stained with DAPI, in blue.

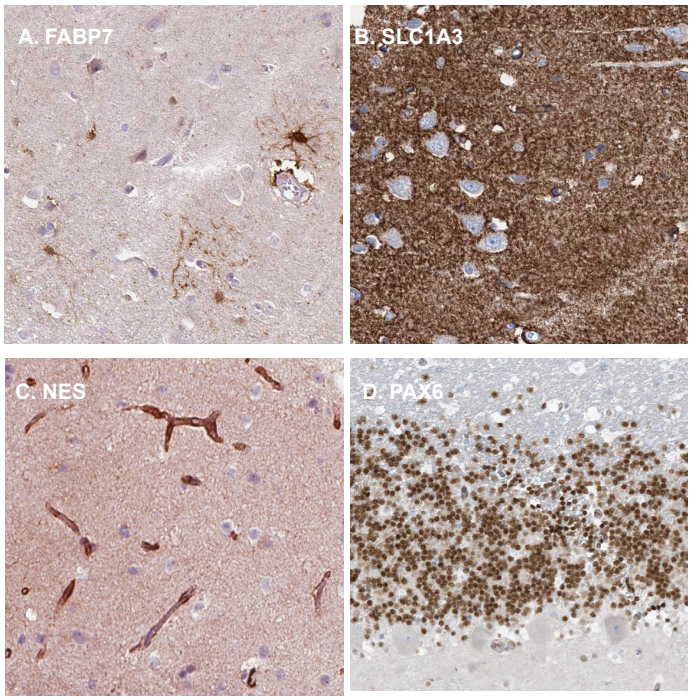


Figure 3 | Immunohistochemistry on human brain.
(A) Monoclonal **anti-FABP7** antibody (IgG1, AMAb90595) showing moderate to strong cytoplasmic positivity in glial cells.
(B) Polyclonal **anti-SLC1A3** antibody (HPA037468) showing strong cytoplasmic positivity in the neuropil (unmyelinated axons, dendrites, and glial cell processes).
(C) Monoclonal **anti-NES** antibody (IgG1, AMAb90556) showing strong immunoreactivity in the endothelial cells of the human cortex.
(D) Polyclonal **anti-PAX6** antibody (HPA030775) on human cerebellum showing moderate to strong nuclear positivity in cells in the granular layer.

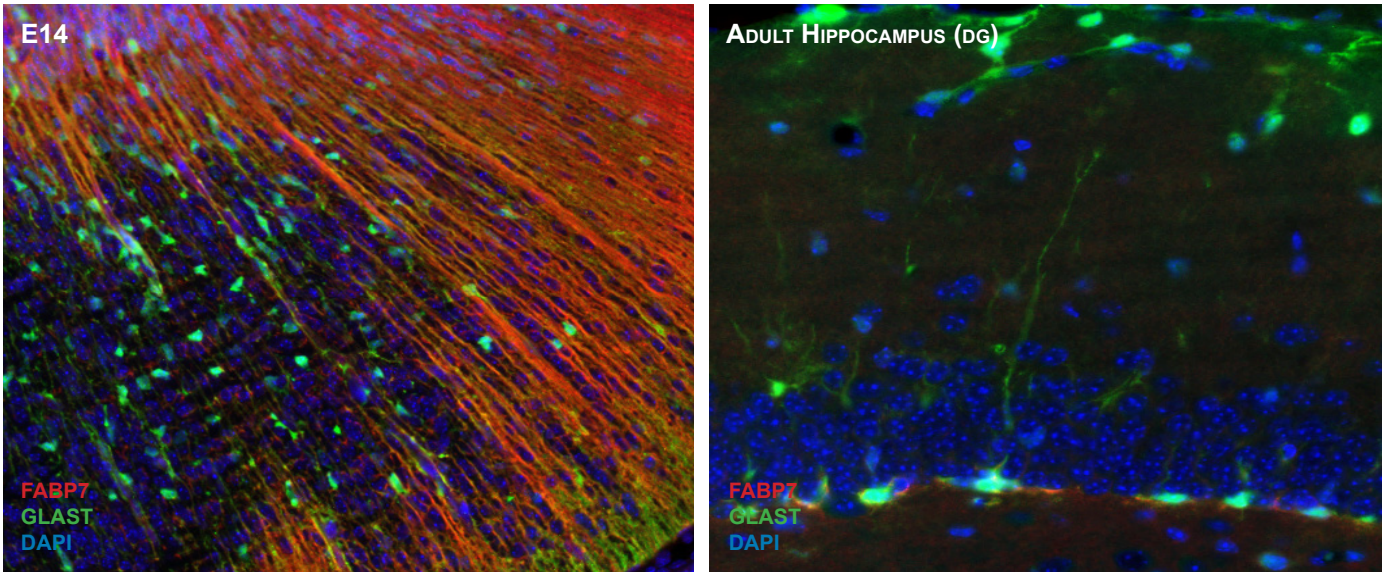


Figure 4 | Radial glia in developing brainstem
Immunofluorescence staining of radial glia in the developing brainstem of mouse embryo E14 and adult mouse dentate gyrus of hippocampus. The **anti-FABP7** (BLBP) monoclonal antibody (IgG1, AMAb90595) is visible in green; the **anti-GLAST** (SLC1A3) polyclonal antibody (HPA037467) is visible in red. Nuclei are stained with DAPI, in blue.

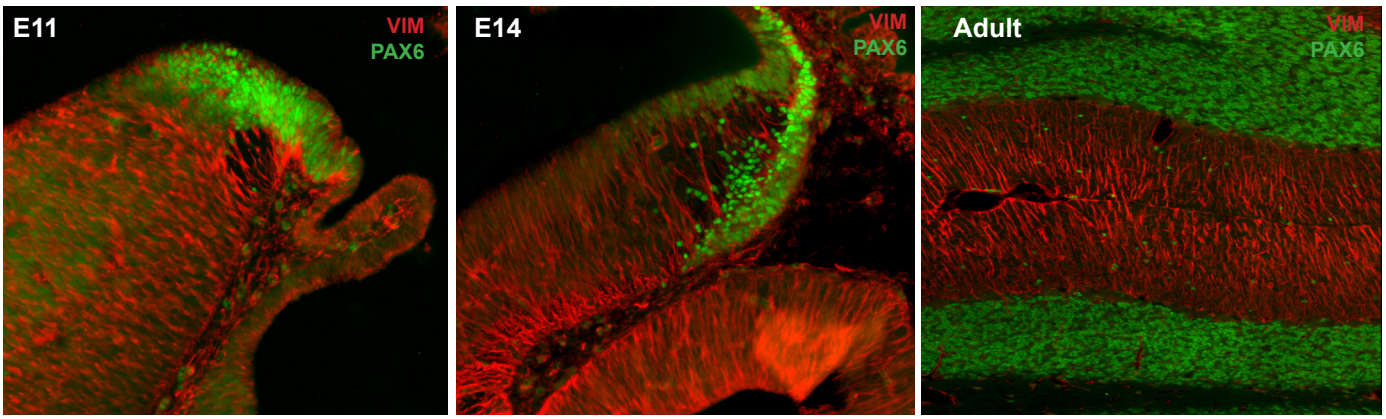


Figure 5 | Radial glia in developing cerebellum
Immunofluorescence of radial glia in mouse embryo E11-E14 and glial cells in adult mouse brain. The **anti-VIM** polyclonal antibody (HPA001762) is visualized in red; the **anti-PAX6** monoclonal antibody (IgG1, AMAb91372) is visible in green.

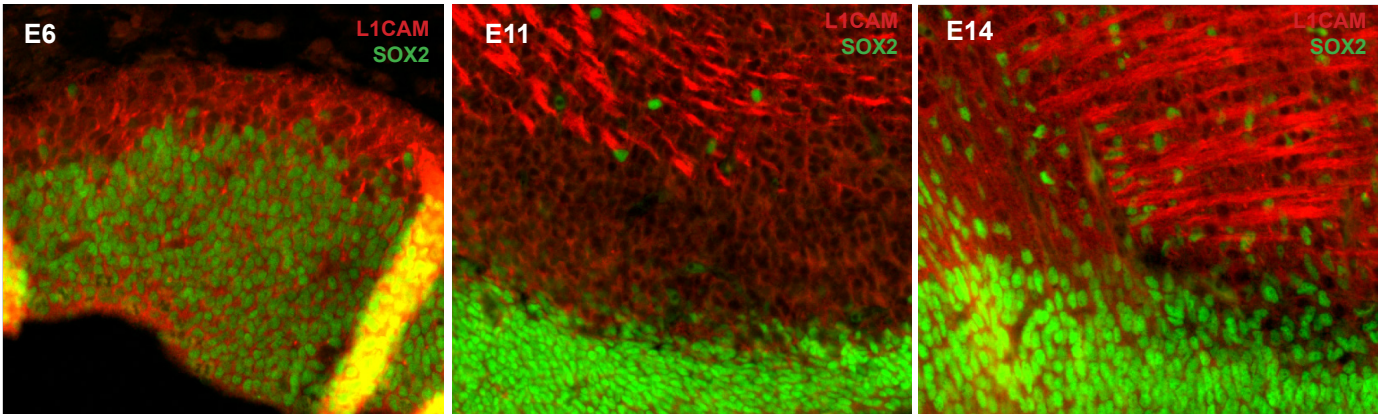


Figure 6 | Neuroepithelial cells in mouse developing hindbrain
Immunofluorescence of neuroepithelial cells in mouse embryos E6-E14. The **anti-SOX2** monoclonal antibody (IgG1, AMAb91307) is visible in green; the **anti-L1CAM** monoclonal antibody (IgG2a, AMAb91829) is visible in red.

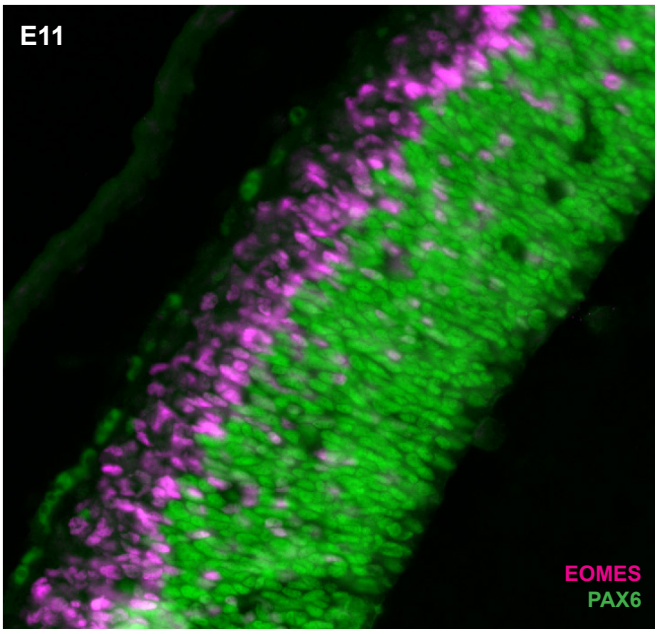
Intermediate Progenitor Cells (IPCs)

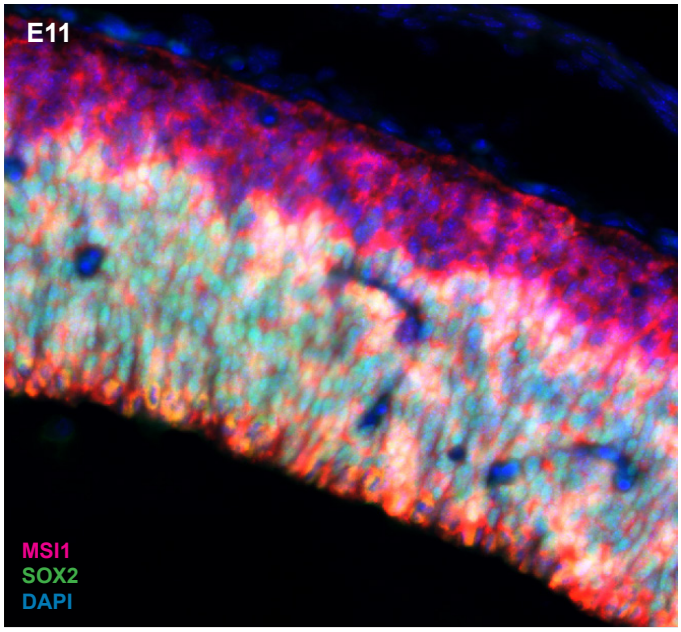
Intermediate progenitor cells (IPCs) are multipolar cells produced by RGCs that have undergone asymmetric division. IPCs are descendants of stem cells that will further differentiate to create specialized cell types. However, a neural progenitor cell is distinct from a neural stem cell since it is incapable of continuous self-renewal and usually can give rise to only one class of differentiated progeny.

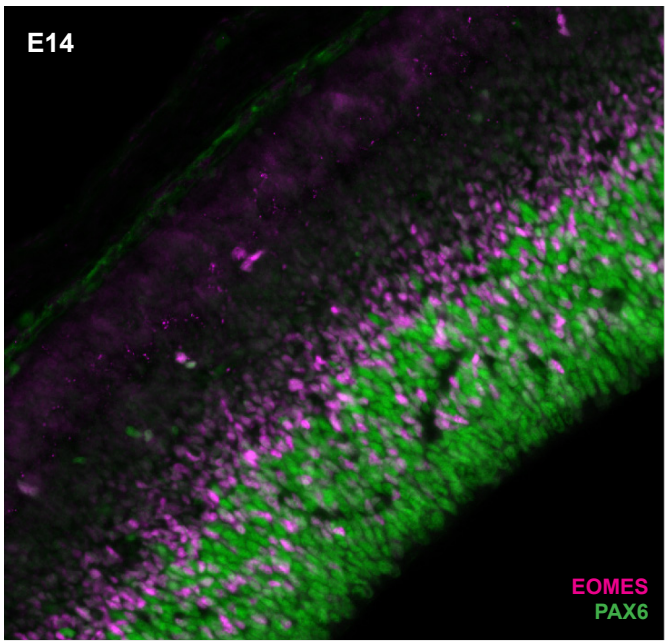
IPCs are tri-potent cells that can give rise to neurons, astrocytes, and oligodendrocytes. IPCs have a low proliferative capacity and single lineage commitment to producing only one type of neuron via neurogenesis. Each progenitor cell can only differentiate into cells belonging to the same tissue or organ.

After the neural tube closes, neuroepithelial cells begin expressing markers such as vimentin and nestin, marking the point at which radial glial cells appear in the cerebral cortex. At the onset of neurogenesis, radial glial cells begin generating both IPCs and cortical neurons, which migrate away from the ventricle.

See Tables 3 and 4 for intermediate progenitors and immature cells markers.







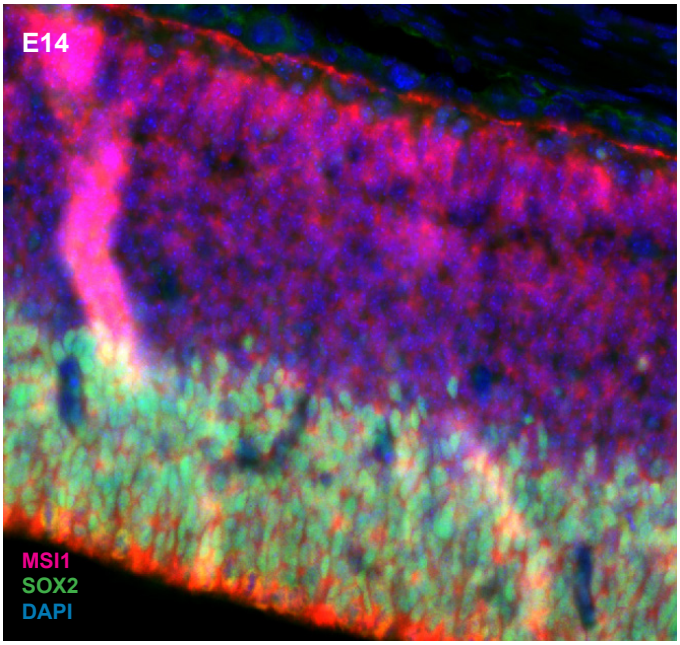


Figure 7 | Immunofluorescence staining of intermediate progenitors in the mouse brain cerebral cortex.
Intermediate progenitors in the developing mouse cerebral cortex. The **anti-PAX6** monoclonal antibody (IgG1, AMAb91372) is visible in green; the **anti-EOMES** (TBR2) polyclonal antibody (HPA028896) is visible in purple.

Figure 8 | Immunofluorescence staining of neural progenitors in the developing cerebral cortex of mouse embryos.
The **anti-SOX2** monoclonal antibody (IgG1, AMAb91307) is visible in green; the **anti-MSI1** (Musashi-1) polyclonal antibody (HPA074923) is visible in red. Nuclei are stained with DAPI, in blue.

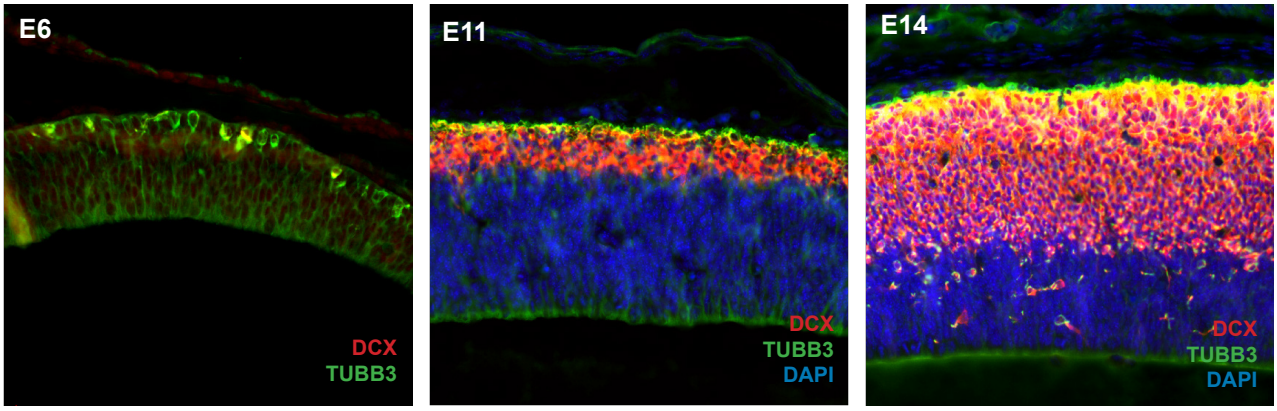


Figure 9 | Immunofluorescence staining of immature neurons in the developing telencephalon/cerebral cortex of mouse embryo E6- E14 The **anti-TUBB3** monoclonal antibody (IgG1, AMAb91394) is visible in green; the **anti-DCX** polyclonal antibody (HPA036121) is visible in red. Nuclei are stained with DAPI, in blue.

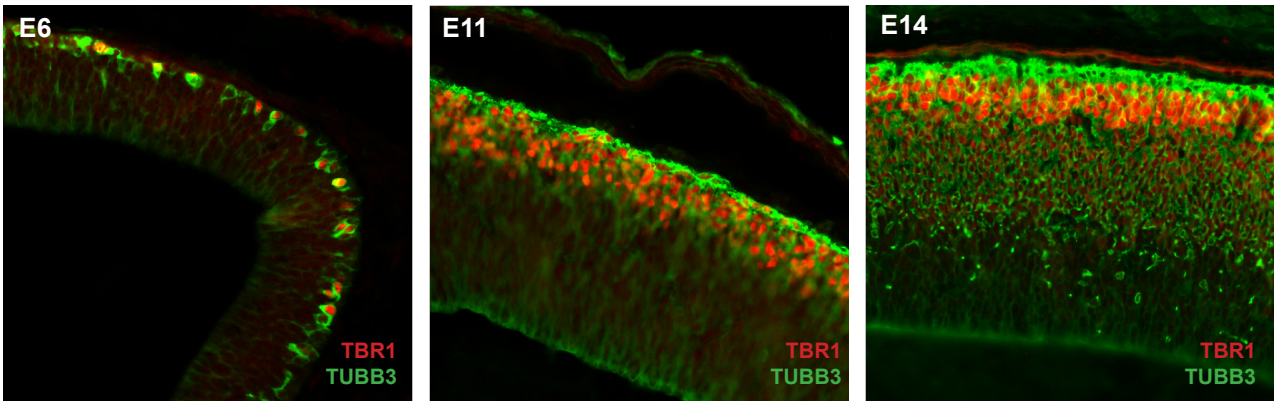


Figure 10 | Immunofluorescence staining of immature neurons in the developing telencephalon/cerebral cortex of mouse embryos E6-E14. The **anti-TUBB3** monoclonal antibody (IgG1, AMAb91394) is visible in green; the **anti-TBR1** polyclonal antibody (HPA078644) is visible in red.

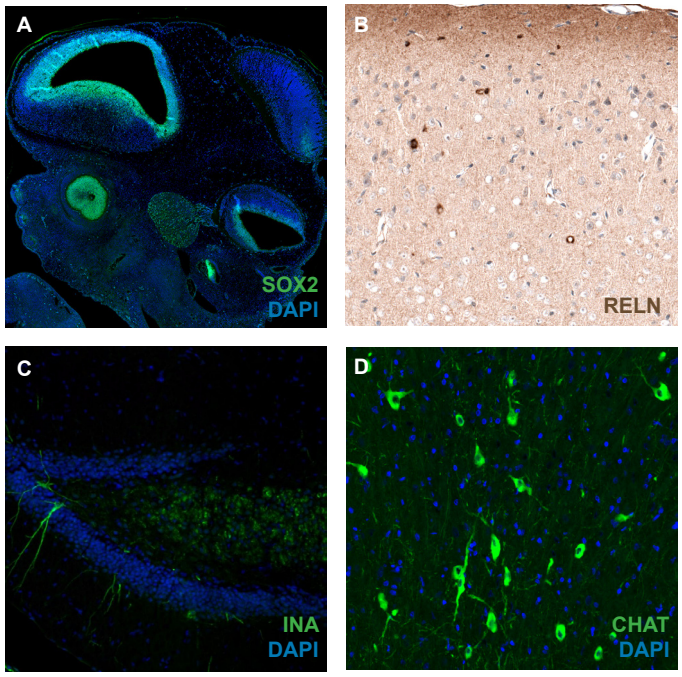


Figure 11 | IHC and ICC-IF staining of mouse brain.
(A) IHC-IF staining of mouse embryo E11 using the **anti-SOX2** monoclonal antibody (IgG1, AMAb91307) showing nuclear positivity in developing brain, eye and trigeminal ganglion, in green. Nuclei are stained with DAPI, in blue.

(B) IHC staining of mouse cerebral cortex using the **anti-RELN** monoclonal antibody (IgG1, AMAb91365) showing positivity in the neuropil of layer 1, as well as cytoplasmic positivity in a subset of neurons in various layers.

(C) ICC-IF using the polyclonal **anti-INA** antibody (HPA008057) shows moderate positivity in the mouse hippocampus, in green. Nuclei are stained with DAPI, in blue.

(D) ICC-IF using the **anti-CHAT** monoclonal antibody (IgG1, AMAb91129) showiing strong positivity in the mouse medial septum, in green. Nuclei are stained with DAPI, in blue.

Differentiated Neurons Markers

Mature neurons are terminally differentiated neurons that can no longer divide. They promote survival by employing multiple strategies to prevent cell death by apoptosis. This is a crucial mechanism. In fact, a cause of many neurodegenerative diseases affecting adult neuronal populations happens when the survival mechanisms in mature neurons are either reversed or circumvented.

Through differentiation, a given population of neurons gives rise to subpopulations that are specific to the various parts of the nervous system. During this stage, the neurons continue to proliferate and migrate to their final locations, where they will make specific connections with other neurons.

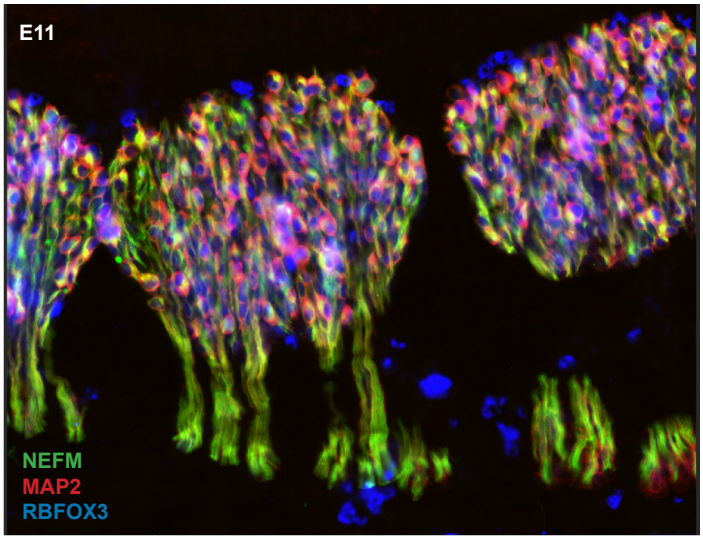
Neurons are terminally differentiated cells that do not utilize their microtubules for the formation of mitotic spindles. Instead, microtubules serve as architectural elements within axons and dendrites and also act as railways for the transport of organelles.

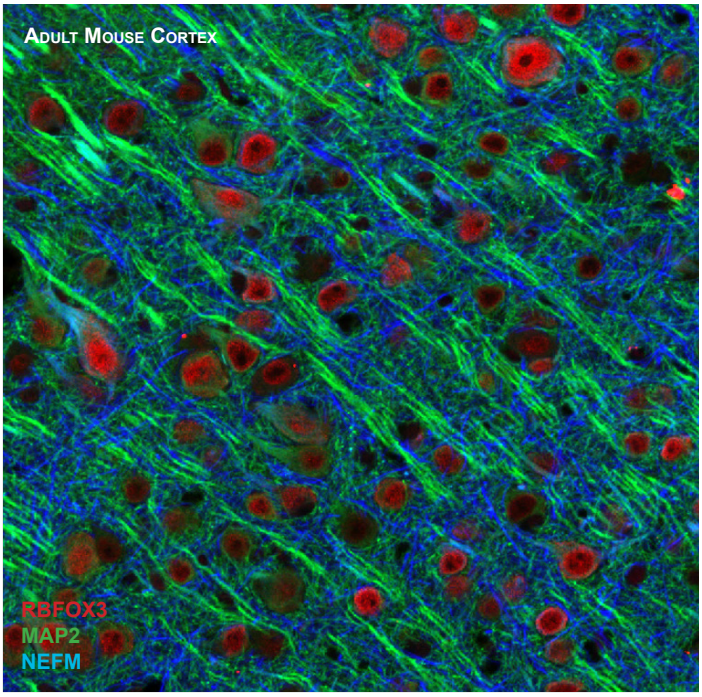
Markers can detect cholinergic, dopaminergic, serotonergic, GABAergic, or glutamatergic neurons in different stages of development from nuclear, cytoplasmic, membrane, or presynaptic products present in neurons.

Pan-neuronal markers, such as TH, ChAT, and TPH, have multiple targets (somatic, nuclear, dendritic, spine, and axonal proteins) and consequently label across all parts of the neuron. They are used to study neuronal morphology.

Motor neurons are located within the spinal cord and the brain. They come in two main subtypes: the upper motor neurons and the lower motor neurons. The upper motor neurons originate in the brain and travel downward to connect with the lower motor neurons.

Table 5. Differentiated Neuronal Markers
Table 6. Differentiated Glia Markers





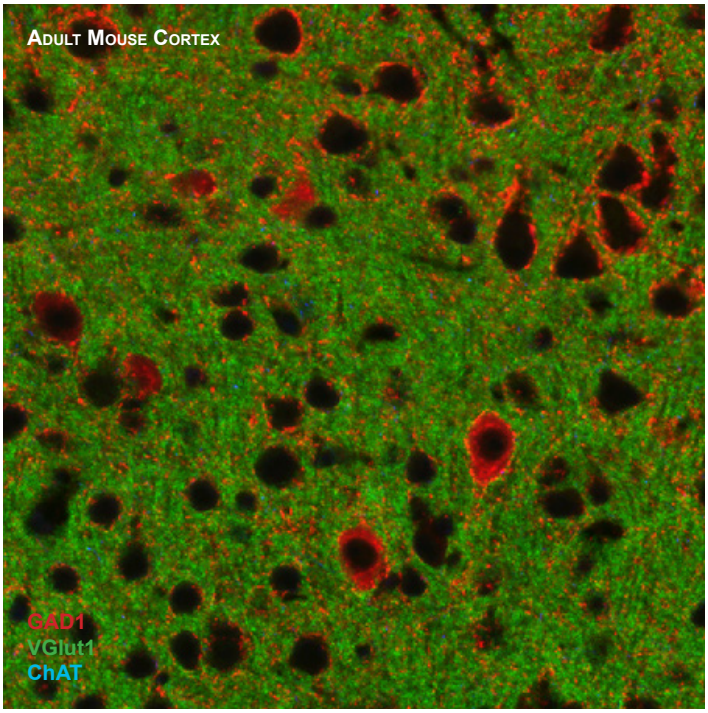


Figure 12 | *(Top)* Immunofluorescence staining of neurons in the developing dorsal root ganglia of the mouse embryo E11. The **anti-NEFM** monoclonal antibody (IgG1, AMAb91027) is visible in green; the **anti-MAP2** polyclonal (HPA012828) is visible in red, and the **anti-RBFOX3** polyclonal (IgG2b, AMAb91748) in blue.

Figure 13 | *(Middle)* Immunofluorescence staining of differentiated neurons in the adult mouse cerebral cortex. The **anti-MAP2** polyclonal antibody (HPA012828) is visible in green; the **anti-RBFOX3** monoclonal (IgG2b, AMAb91748) is visible in red, and the **anti-NEFM** monoclonal (IgG1, AMAb91027) in blue.

Figure 14 | *(Bottom)* Immunofluorescence staining of differentiated neurons in the adult mouse cerebral cortex. The **anti-VGluT1** monoclonal antibody (IgG2b, AMAb91041) is visible in green; the **anti-GAD1** monoclonal (IgG2a, AMAb91076) is visible in red, and the **anti-ChAT** monoclonal (IgG1, AMAb91129) in blue.

Suggested Readings

Alvarez-Buylla A. et al, ***A unified hypothesis on the lineage of neural stem cells.*** Nat Rev Neurosci. **2001** Apr;2(4):287-93

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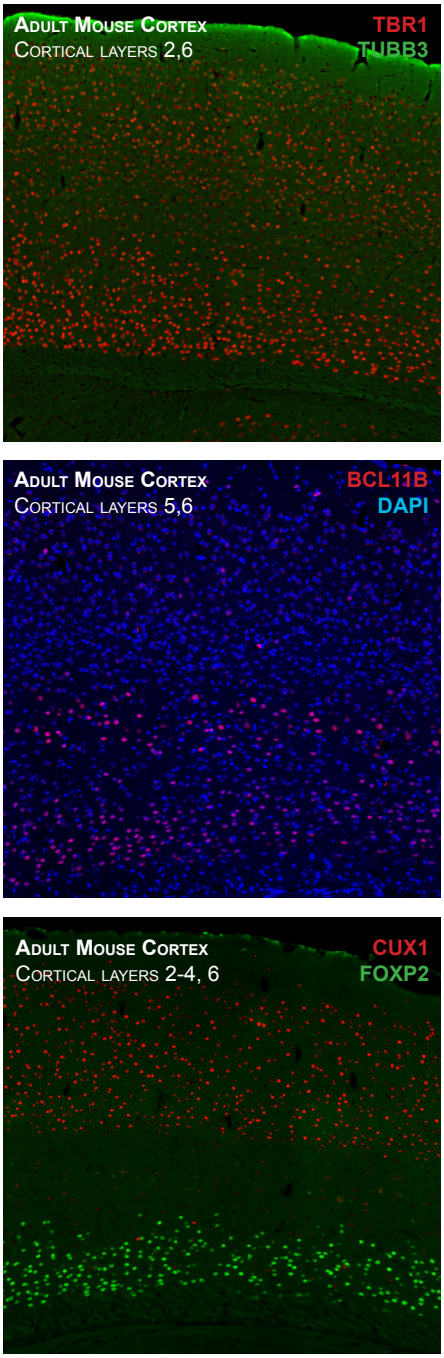

Figure 15 | Immunofluorescence staining with cortical layer markers in the adult mouse brain

(Top) Cortical layers 2,6: the **anti-TUBB3** monoclonal antibody (IgG1, AMAb91394) is visible in green; the **anti-TBR1** polyclonal (HPA078644) is visible in red.

(Middle) Cortical layers 5-6: the **anti-BCL11B** (CTIP2) polyclonal antibody (HPA049117) is visible in red. Nuclei are stained in blue with DAPI.

(Bottom) Cortical layers 2-4 and 6: the **anti-FOXP2** monoclonal antibody (IgG1, AMAb91361) is visible in green; the **anti-CUX1** polyclonal (HPA003277) is visible in red.

Table 1. Neural Stem Cells Markers

Product Name	Protein Name	Product ID	Validated Applications	Interspecies Sequence Homology	PrEST Control Antigen
Anti-BMI	BMI1 proto-oncogene, polycomb ring finger	HPA030472	IHC, WB*	Mouse 95% - Rat 95%	APrEST77904
Anti-CDH1	cadherin 1, type 1, E-cadherin (epithelial)	AMAb90862	IHC*, WB*, ICC-IF	Mouse 76% - Rat 80%	APrEST86781
		HPA004812	IHC*	Mouse 76% - Rat 80%	APrEST86781
Anti-C21orf33	chromosome 21 open reading frame 33	HPA018517	IHC, ICC-IF	Mouse 90% - Rat 88%	APrEST73887
Anti-EGFR/ERBB1	epidermal growth factor receptor	AMAb90819	WB	Mouse 90% - Rat 91%	APrEST78874
Anti-FABP7/BLBP	fatty acid binding protein 7, brain	AMAb90595	IHC*, WB	Mouse 89% - Rat 90%	APrEST72726
Anti-EGR1	early growth response 1	HPA029937	ICC-IF	Mouse 93% - Rat 94%	APrEST90701
Anti-NES	nestin	AMAb90556	IHC, WB*, ICC-IF	Mouse 47% - Rat 42%	APrEST70691
		HPA006286	ICC-IF	Mouse 47% - Rat 42%	APrEST70691
Anti-NOTCH1	notch 1	HPA067168	ICC-IF	Mouse 75% - Rat 75%	APrEST92698
Anti-NR2E1	nuclear receptor subfamily 2, group E, member 1	HPA055642	IHC*	Mouse 99% - Rat 99%	APrEST87723
Anti-OCLN	occludin	AMAb90889	IHC*, WB, ICC-IF	Mouse 85% - Rat 83%	APrEST83049
		HPA005933	IHC, WB*, ICC-IF	Mouse 85% - Rat 83%	APrEST83049
Anti-PCGF5	polycomb group ring finger 5	HPA038349	IHC, ICC-IF	Mouse 95% - Rat 93%	APrEST80382
Anti-PROML1/CD133	prominin 1	HPA004922	IHC*, WB*	Mouse 57% - Rat 60%	APrEST93420
		AMAb91494	IHC, WB	Mouse 45% - Rat 63%	-
Anti-RELN	reelin	HPA046512	ICC-IF	Mouse 90% - Rat 94%	APrEST91063
Anti-SOX2	SRY (sex determining region Y)-box 2	AMAb91307	IHC, WB*, ICC-IF	Mouse 99% - Rat 99%	APrEST89511
Anti-SOX10	SRY (sex determining region Y)-box 10	AMAb91297	IHC, ICC-IF	Mouse 98% - Rat 98%	APrEST92827

Table 2. Radial Glial Cells Markers

Product Name	Protein Name	Product ID	Validated Applications	Interspecies Sequence Homology	PrEST Control Antigen
Anti-CSF3R/CD114	colony stimulating factor 3 receptor (granulocyte)	HPA048086	IHC	Mouse 58% - Rat 60%	APrEST71845
Anti-C21orf33	chromosome 21 open reading frame 33	HPA018517	IHC, ICC-IF	Mouse 90% - Rat 88%	APrEST73887
Anti-GLI3	GLI family zinc finger 3	HPA005534	IHC	Mouse 74% - Rat 76%	APrEST77454
Anti-FABP7/BLBP	fatty acid binding protein 7, brain	AMAb90595	IHC*, WB	Mouse 89% - Rat 90%	APrEST72726
Anti-FGF2	fibroblast growth factor 2	HPA065502	IHC	Mouse 97% - Rat 97%	APrEST94915
Anti-GFAP	glial fibrillary acidic protein	AMAb91033	IHC*, WB*	Mouse 98% - Rat 100%	APrEST85954
		HPA056030	IHC*, WB, ICC-IF	Mouse 98% - Rat 100%	APrEST85954
Anti-HES5	hes family bHLH transcription factor 5	HPA076164	IHC	Mouse 96% - Rat 96%	APrEST92568
Anti-NOTCH1	notch 1	HPA067168	ICC-IF	Mouse 75% - Rat 75%	APrEST92698
Anti-PAX-6	paired box 6	AMAb91372	IHC, ICC-IF	Mouse 100% - Rat 100%	APrEST84701
		HPA030775	IHC, ICC-IF	Mouse 100% - Rat 100%	APrEST84701
Anti-PDGFD	platelet derived growth factor D	HPA066271	IHC	Mouse 86% - Rat 86%	APrEST91054
Anti-SLC1A3	solute carrier family 1 (glial high affinity glutamate transporter), member 3	HPA037467	IHC*, ICC-IF	Mouse 89% - Rat 95%	APrEST79992
Anti-SOX2	SRY (sex determining region Y)-box 2	AMAb91307	IHC, WB*, ICC-IF	Mouse 99% - Rat 99%	APrEST89511
Anti-SLC1A3/GLAST	solute carrier family 1 (glial high affinity glutamate transporter), member 3	HPA037467	IHC*, ICC-IF	Mouse 89% - Rat 95%	APrEST79992
Anti-VIM	vimentin	AMAb90516	IHC, WB*	Mouse 99% - Rat 99%	APrEST85020
		HPA001762	IHC*, WB*, ICC-IF	Mouse 99% - Rat 99%	APrEST85020

(AMAbxxx) Monoclonals
(HPAxxx) Polyclonals
**Enhanced Validation*

Table 3. Intermediate Progenitor Cells Markers

Product Name	Protein Name	Product ID	Validated Applications	Interspecies Sequence Homology	PrEST Control Antigen
Anti-AP2A2	adaptor-related protein complex 2, alpha 2 subunit	HPA043040	WB*, ICC-IF	Mouse 94% - Rat 94%	APrEST89460
Anti-ACVR2A	activin A receptor, type IIA	HPA046997	IHC	Mouse 100% - Rat 100%	APrEST84534
Anti-CD4	CD4 molecule	AMAb90754	IHC*, WB	Mouse 55% - Rat 57%	APrEST86770
		HPA004252	IHC*, WB	Mouse 55% - Rat 57%	APrEST86770
Anti-DCX	doublecortin	HPA036121	ICC-IF	Mouse 99% - Rat 94%	APrEST90823
Anti-EOMES	eomesodermin	HPA028896	IHC	Mouse 96% - Rat 96%	APrEST86712
Anti-FZD4	frizzled class receptor 4	HPA074833	ICC-IF	Mouse 95% - Rat 99%	APrEST90414
Anti-GAP43	Growth associated protein 43	AMAb91664	IHC*	Mouse 85% - Rat 85%	-
		AMAb91665	IHC*	Mouse 85% - Rat 85%	-
		HPA013392	IHC*, ICC-IF	Mouse 88% - Rat 86%	APrEST72531
Anti-GNL3	guanine nucleotide binding protein-like 3 (nucleolar)	HPA036742	IHC*, WB	Mouse 67% - Rat 69%	APrEST87203
		HPA036743	IHC*, WB, ICC-IF	Mouse 44% - Rat 48%	APrEST87204
Anti-HMMR	hyaluronan-mediated motility receptor (RHAMM)	HPA040025	IHC*, WB	Mouse 59% - Rat 62%	APrEST87348
		HPA061524	ICC-IF	Mouse 82% - Rat 69%	APrEST87348
Anti-INA	internexin neuronal intermed filament protein, alpha	HPA008057	IHC*, WB, ICC-IF	Mouse 83% - Rat 84%	APrEST70159
Anti-JAG1	jagged 1	HPA021555	IHC*	Mouse 94% - Rat 93%	APrEST76170
Anti-MLF2	myeloid leukemia factor 2	HPA010811	IHC*, ICC-IF	Mouse 95% - Rat 95%	APrEST71688
Anti-MSI1	musashi RNA-binding protein 1	HPA064401	ICC-IF	Mouse 98% - Rat 100%	APrEST92457
Anti-MSX1	msh homeobox 1	HPA063895	ICC-IF	Mouse 92% - Rat 71%	APrEST92415
		HPA073604	IHC*	Mouse 93% - Rat 93%	APrEST93156
Anti-NES	nestin	AMAb90556	IHC, WB*, ICC-IF	Mouse 47% - Rat 42%	APrEST70691
		HPA006286	ICC-IF	Mouse 47% - Rat 42%	APrEST70691
Anti-NTN1	netrin 1	HPA056419	IHC	Mouse 100% - Rat 100%	APrEST85934
Anti-NTN4	netrin 4	HPA049832	IHC	Mouse 90% - Rat 90%	APrEST85291
Anti-NEUROD1	neuronal differentiation 1	HPA003278	IHC, WB	Mouse 98% - Rat 97%	APrEST84787
Anti-NOTCH1	notch 1	HPA067168	ICC-IF	Mouse 75% - Rat 75%	APrEST92698
Anti-NOTCH2	notch 2	HPA048743	IHC, ICC-IF	Mouse 87% - Rat 86%	APrEST88601
Anti-NOTCH3	notch 3	HPA044392	ICC-IF	Mouse 83% - Rat 83%	APrEST76106
Anti-OTX2	orthodenticle homeobox 2	HPA000633	IHC	Mouse 100% - Rat 100%	APrEST70417
Anti-PAX3	paired box 3	HPA063659	IHC, ICC-IF	Mouse 92% - Rat 92%	APrEST86379
		HPA069000	ICC-IF	Mouse 98% - Rat 98%	APrEST92835
Anti-S100B	S100 calcium binding protein B	AMAb91038	IHC*, WB	Mouse 99% - Rat 98%	APrEST73328
		HPA015768	IHC*, WB, ICC-IF	Mouse 99% - Rat 98%	APrEST73328
Anti-SEMA6A	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6A	HPA031265	IHC	Mouse 99% - Rat 97%	APrEST78454
Anti-SEMA7A	semaphorin 7A, GPI membrane anchor (John Milton Hagen blood group)	HPA042273	IHC*	Mouse 85% - Rat 87%	APrEST71580
Anti-VIM	vimentin	AMAb90516	IHC, WB*	Mouse 99% - Rat 99%	APrEST85020
		HPA001762	IHC*, WB*, ICC-IF	Mouse 99% - Rat 99%	APrEST85020

(AMAbxxx) Monoclonals
(HPAxxx) Polyclonals
**Enhanced Validation*

Table 4. Immature Cells Markers

Product Name	Protein Name	Product ID	Validated Applications	Interspecies Sequence Homology	PrEST Control Antigen
Anti-ATOH1/MATH1	atonal bHLH transcription factor 1	HPA049400	ICC-IF	Mouse 90% - Rat 87%	APrEST94695
Anti-ASCL1	achaete-scute family bHLH transcription factor 1	HPA076307	ICC-IF	Mouse 97% - Rat 97%	APrEST95383
Anti-FGFR1	fibroblast growth factor receptor 1	HPA056402	IHC, WB	Mouse 94% - Rat 96%	APrEST86026
Anti-FOXA2	forkhead box A1	HPA050505	IHC*, ICC-IF	Mouse 96% - Rat 82%	APrEST87559
Anti-HES5	hes family bHLH transcription factor 5	HPA076164	IHC	Mouse 96% - Rat 96%	APrEST92568
Anti-INA	internexin neuronal intermed. filament protein, alpha	HPA008057	IHC*, WB, ICC-IF	Mouse 83% - Rat 84%	APrEST70159
Anti-L1CAM	L1 cell adhesion molecule	AMAb91829	IHC*	Mouse 96% - Rat 96%	-
		HPA005830	IHC*	Mouse 75% - Rat 75%	APrEST74285
Anti-LHX2	LIM homeobox 2	HPA000838	ICC-IF	Mouse 100% - Rat 100%	APrEST90527
		AMAb91404	IHC, WB	Mouse 100% - Rat 100%	-
Anti-MAP1B	microtubule-associated protein 1B	HPA022275	IHC*, WB*, ICC-IF	Mouse 85% - Rat 86%	APrEST86833
Anti-MAP2	microtubule-associated protein 2	AMAb91375	IHC, WB, ICC-IF	Mouse 91% - Rat 90%	APrEST71545
		HPA008273	IHC*, ICC-IF	Mouse 96% - Rat 96%	APrEST71546
Anti-NEFL	neurofilament, light polypeptide	AMAb91314	IHC, WB, ICC-IF	Mouse 97% - Rat 99%	APrEST88940
		HPA014850	IHC*, WB*	Mouse 97% - Rat 99%	APrEST88940
Anti-NES	nestin	AMAb90556	IHC, WB*, ICC-IF	Mouse 47% - Rat 42%	APrEST70691
		HPA006286	ICC-IF	Mouse 47% - Rat 42%	APrEST70691
Anti-NEUROD1	neuronal differentiation 1	HPA003278	IHC, WB	Mouse 98% - Rat 97%	APrEST84787
Anti-NGFR	nerve growth factor receptor	HPA004765	IHC*, WB, ICC-IF	Mouse 93% - Rat 93%	APrEST70014
Anti-NR4A2	nuclear receptor subfamily 4, group A, member 2	HPA000543	IHC, ICC-IF	Mouse 100% - Rat 100%	APrEST76146
Anti-RBFOX3	Rna binding protein, fox-1 homolog 3	AMAb91746	IHC*	Mouse 91% - Rat 91%	-
		HPA030790	IHC, ICC-IF	Mouse 93% - Rat 94%	APrEST75751
Anti-NKX2-2	NK2 homeobox 2	HPA003468	IHC, WB	Mouse 96% - Rat 97%	APrEST84761
		AMAb91708	IHC*, WB	Mouse 96% - Rat 97%	APrEST84761
Anti-NOG	noggin	HPA061318	IHC	Mouse 100% - Rat 100%	APrEST86333
Anti-PAX3	paired box 3	HPA069000	ICC-IF	Mouse 98% - Rat 98%	APrEST92835
Anti-PAX6	paired box 6	AMAb91372	IHC, ICC-IF	Mouse 100% - Rat 100%	APrEST84701
		HPA030775	IHC, ICC-IF	Mouse 100% - Rat 100%	APrEST84701
Anti-PDGFRA	platelet-derived growth factor receptor, alpha polypept.	HPA004947	ICC-IF	-	APrEST93915
Anti-PDGFRB	platelet-derived growth factor receptor, beta polypept.	HPA028499	WB, ICC-IF	Mouse 76% - Rat 76%	APrEST77984
Anti-POU3F2	POU class 3 homeobox 2	AMAb91406	IHC, WB*, ICC-IF	Mouse 100% - Rat 100%	APrEST91088
		HPA056261	ICC-IF	Mouse 100% - Rat 100%	APrEST91088
Anti-SOX4	Sry-box 4	AMAb91378	IHC, ICC-IF	Mouse 78% - Rat 78%	-
		HPA029901	IHC, ICC-IF	Mouse 100% - Rat 39%	APrEST77513
Anti-SOX21	Sry-box 21	AMAb91309	IHC, WB	Mouse 100% - Rat 100%	-
		HPA064084	ICC-IF	Mouse 96% - Rat 37%	APrEST92430
Anti-S100B	S100 calcium binding protein B	AMAb91038	IHC*, WB	Mouse 99% - Rat 98%	APrEST73328
Anti-TBR1	T-box, brain 1	HPA078644	IHC*	Mouse 100% - Rat 100%	APrEST91310
Anti-TBR2/EOMES	T-box, brain 2/eomesodermin	HPA028896	IHC	Mouse 96% - Rat 96%	APrEST86712
Anti-TH	tyrosine hydroxylase	AMAb91112	IHC	Mouse 88% - Rat 88%	APrEST87899
		HPA014010	ICC-IF	Mouse 91% - Rat 89%	APrEST94048
Anti-TUBB3	Tubulin beta 3 class iii	AMAb91394	IHC, WB, ICC-IF	Mouse 93% - Rat 86%	-
		AMAb91395	IHC, WB, ICC-IF	Mouse 93% - Rat 86%	-

(AMAbxxx) Monoclonals
(HPAxxx) Polyclonals
**Enhanced Validation*

Table 5. Differentiated Neuronal Markers

Product Name	Protein Name	Product ID	Validated Applications	Interspecies Sequence Homology	PrEST Control Antigen
Neuronal PAN markers					
Anti-DLG4/PSD-95	discs, large homolog 4 (Drosophila)	HPA010122	IHC*	Mouse 99% - Rat 99%	APrEST71165
Anti-MAP2	microtubule-associated protein 2	AMAb91375	IHC, WB, ICC-IF	Mouse 91% - Rat 90%	APrEST71545
		HPA008273	IHC*, ICC-IF	Mouse 96% - Rat 96%	APrEST71546
Anti-NEFL	neurofilament, light polypeptide	AMAb91314	IHC, WB, ICC-IF	Mouse 97% - Rat 99%	APrEST88940
		HPA014850	IHC*, WB*	Mouse 97% - Rat 99%	APrEST88940
Anti-NEFM	neurofilament, medium polypeptide	AMAb91027	IHC, WB	Mouse 98% - Rat 98%	APrEST76207
		HPA023138	IHC*, WB*, ICC-IF	Mouse 98% - Rat 98%	APrEST76207
Anti-RBFOX3/NeuN	Rna binding protein, fox-1 homolog3	AMAb91746	IHC*	Mouse 91% - Rat 91%	-
		HPA030790	IHC*, ICC-IF	Mouse 93% - Rat 94%	APrEST75751
Anti-SYP	synaptophysin	HPA002858	IHC*, WB	Mouse 83% - Rat 37%	APrEST74355
Glutamatergic neurons					
Anti-GLS	glutaminase	HPA036223	IHC*, WB, ICC-IF	Mouse 6% - Rat 98%	APrEST78979
Anti-GRIN1/NMDAR1	glutamate ionotropic receptor NMDA type subunit 1	HPA067773	IHC	Mouse 99% - Rat 99%	APrEST94967
Anti-GRIN2B/NMDAR2B	glutamate receptor, ionotropic, N-methyl D-aspartate 2B	HPA069762	IHC	Mouse 100% - Rat 100%	APrEST88269
Anti-VGLuT2 (SLC17A6)	solute carrier family 17 member 6	AMAb91081	IHC*	Mouse 85% - Rat 85%	APrEST80507
		AMAb91086	IHC*	Mouse 85% - Rat 85%	APrEST80507
Anti-VGluT1 (SLC17A7)	solute carrier family 17 member 7	HPA063679	IHC*	Mouse 94% - Rat 94%	APrEST88047
		AMAb91041	IHC*, WB	Mouse 94% - Rat 94%	APrEST88047
GABAergic neurons					
Anti-GABBR1	gamma-aminobutyric acid B receptor, 1	HPA050483	IHC	Mouse 97% - Rat 97%	APrEST83906
Anti-GABBR2	gamma-aminobutyric acid B receptor, 2	HPA013820	IHC*	Mouse 99% - Rat 99%	APrEST72751
Anti-GAD1/GAD67	glutamate decarboxylase 1	HPA048871	ICC-IF	Mouse 97% - Rat 97%	APrEST94691
		AMAb91079	IHC, WB	Mouse 94% - Rat 94%	APrEST79051
Anti-GAD2/GAD65	glutamate decarboxylase 2 (pancreatic islets and brain, 65kDa)	AMAb91048	IHC*, WB	Mouse 84% - Rat 88%	APrEST80257
Anti-SLC6A1/GAT1	solute carrier family 6 (neurotransmitter transporter), member 1	HPA013341	IHC, WB	Mouse 98% - Rat 98%	APrEST86858
Dopaminergic neurons					
Anti-DAT (SLC6A3)	solute carrier family 6 member 3	AMAb91125	IHC	Mouse 85% - Rat 85%	APrEST72519
		HPA012763	IHC	Mouse 86% - Rat 86%	APrEST94046
Anti-FOXA2	forkhead box A1	HPA050505	IHC*, ICC-IF	Mouse 96% - Rat 82%	APrEST87559
Anti-LMX1B	LIM homeobox transcription factor 1B	HPA073716	ICC-IF	Mouse 67% - Rat 100%	APrEST93163
Anti-NR4A2/Nurr1	nuclear receptor subfamily 4, A2	HPA000543	IHC, ICC-IF	Mouse 100% - Rat 100%	APrEST76146
Anti-NET (SLC6A2)	Solute carrier family 6 member 2	AMAb91116	IHC	Mouse 93% - Rat 93%	APrEST86811
		HPA076311	IHC*	Mouse 85% - Rat 32%	APrEST94017
Anti-TH	tyrosine hydroxylase	AMAb91112	IHC	Mouse 88% - Rat 88%	APrEST87899
		HPA014010	ICC-IF	Mouse 91% - Rat 89%	APrEST94048
Serotonergic neurons					
Anti-SLC6A4/SERT1	solute carrier family 6, member 4	HPA074728	ICC-IF	Mouse 90% - Rat 88%	APrEST93243
Anti-TPH1	tryptophan hydroxylase 1	HPA022483	IHC*	Mouse 85% - Rat 86%	APrEST70062
Anti-TPH2	tryptophan hydroxylase 2	AMAb91108	IHC	Mouse 100% - Rat 100%	APrEST81951
Cholinergic neurons					
Anti-CHAT	choline O-acetyltransferase	AMAb91129	IHC*	Mouse 96% - Rat 96%	APrEST86792
		HPA048547	IHC	Mouse 96% - Rat 96%	APrEST86792
Anti-ACHE	acetylcholinesterase (Yt blood group)	HPA027098	ICC-IF	Mouse 91% - Rat 89%	APrEST90648
Motor neurons					
Anti-Isl1	Isl lim homeobox 1	AMAb91729	ICC-IF	Mouse 100% - Rat 100%	-
Anti-Isl2	Isl lim homeobox 2	HPA075192	ICC-IF	Mouse 100% - Rat 100%	APrEST9327
Anti-Olig2	oligod. lineage transcription factor 2	HPA003254	IHC*, WB	Mouse 93% - Rat 94%	APrEST84779

Table 6. Differentiated Glia Markers

Product Name	Protein Name	Product ID	Validated Applications	Interspecies Sequence Homology	PrEST Control Antigen
Astrocytes type 2					
Anti-ALDH1L1	aldehyde dehydrogenase1 family1	HPA036900	IHC*, WB	Mouse 83% - Rat 84%	APrEST79397
Anti-AQP4	aquaporin 4	AMAb90537	IHC*, WB	Mouse 93% - Rat 92%	APrEST73067
		HPA014784	IHC*, WB*, ICC-IF	Mouse 93% - Rat 92%	APrEST73067
Anti-GFAP	glial fibrillary acidic protein	AMAb91033	IHC*, WB*	Mouse 98% - Rat 100%	APrEST85954
		HPA056030	IHC*, WB, ICC-IF	Mouse 98% - Rat 100%	APrEST85954
Anti-SLC1A2/GLT-1	solute carrier family 1 (glial high affinity glutamate transporter), member 2	HPA009172	IHC*	Mouse 87% - Rat 48%	APrEST71560
Anti-SLC1A3/GLAST	solute carrier family 1 (glial high affinity glutamate transporter), member 3	HPA037467	IHC*, ICC-IF	Mouse 89% - Rat 95%	APrEST79992
Anti-S100B	S100 calcium binding protein B	AMAb91038	IHC*, WB	Mouse 99% - Rat 98%	APrEST73328
Anti-VIM	vimentin	AMAb90516	IHC, WB*	Mouse 99% - Rat 99%	APrEST85020
		HPA001762	IHC*, WB*, ICC-IF	Mouse 99% - Rat 99%	APrEST85020
Oligodendrocytes					
Anti-MBP	myelin basic protein	AMAb91062	IHC, WB, ICC-IF	Mouse 97% - Rat 97%	APrEST78641
		HPA049222	IHC, WB	Mouse 97% - Rat 97%	APrEST78641
Anti-MOG	myelin oligodendrocyte glycoprotein	AMAb91066	IHC, WB	Mouse 91% - Rat 89%	APrEST72887
		AMAb91067	IHC, WB	Mouse 91% - Rat 89%	APrEST72887
Anti-Olig 2	oligodendrocyte transcription factor 2	HPA003254	IHC*, WB	Mouse 93% - Rat 94%	APrEST84779
Anti-Olig 3	oligodendrocyte transcription factor 3	HPA018303	IHC	Mouse 98% - Rat 98%	APrEST73755
Anti-SOX10	SRY (sex determining region Y)-box 10	AMAb91297	IHC, ICC-IF	Mouse 98% - Rat 98%	APrEST92827
		HPA068898	IHC*, ICC-IF	Mouse 98% - Rat 98%	APrEST92827

(AMAbxxx) Monoclonals
(HPAxxx) Polyclonals
**Enhanced Validation*

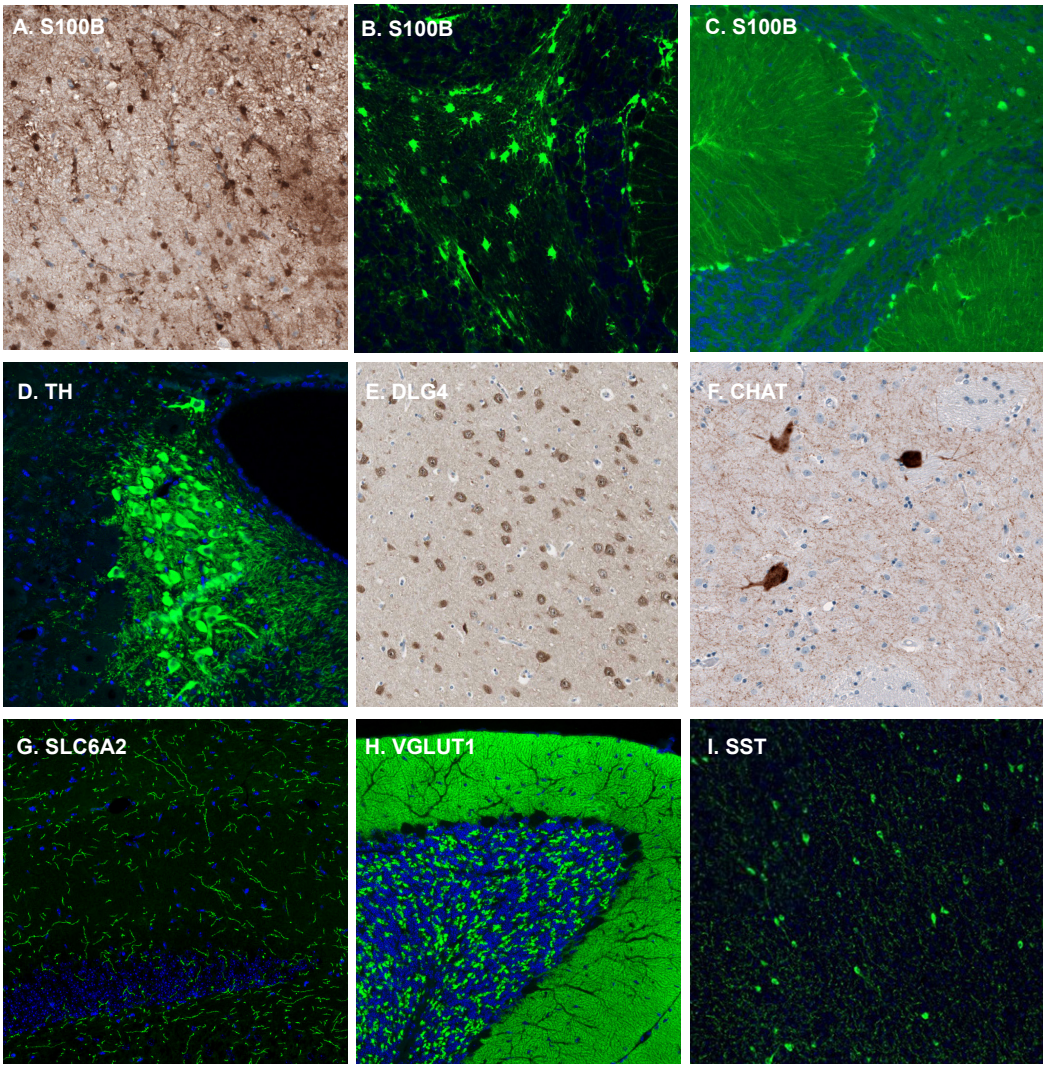

Figure 16 | IHC and ICC-IF staining on human and rodent brains.

(A) IHC staining of glial cells using the **anti-S100B** monoclonal antibody (IgG1, AMAb91038) on human cerebral cortex shows moderate nuclear positivity in astrocytes.

(B,C) The immunofluorescence staining of rat (B) and mouse (C) cerebellum using the **anti-S100B** monoclonal antibody (cAMAb91038) shows strong positivity in glial cells.

(D) Immunofluorescence staining of rat locus coeruleus using the monoclonal **anti-TH** antibody (IgG1, AMAb91112) shows strong positivity in noradrenergic neurons.

(E) IHC staining using the **anti-DLG4** polyclonal antibody (HPA010122) shows high expression in human hippocampal neurons.

(F) IHC staining of human caudate nucleus using the **anti-CHAT** polyclonal antibody (HPA048547) shows strong cytoplasmic positivity in large neurons.

(G) IHC staining of the mouse hippocampus using the **anti-SLC6A2** monoclonal antibody (IgG1, AMAb91116) showing strong positivity in noradrenergic fibers.

(H) IHC staining of mouse cerebellum using the **anti-VGLUT1** monoclonal antibody (IgG1, AMAb91041) showing strong positivity in glutamatergic fibers in the molecular and granular layers.

(I) IHC staining of mouse brain using the **anti-SST** polyclonal antibody (HPA019472) showing strong positivity in a subset of neurons in the cerebral cortex.

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