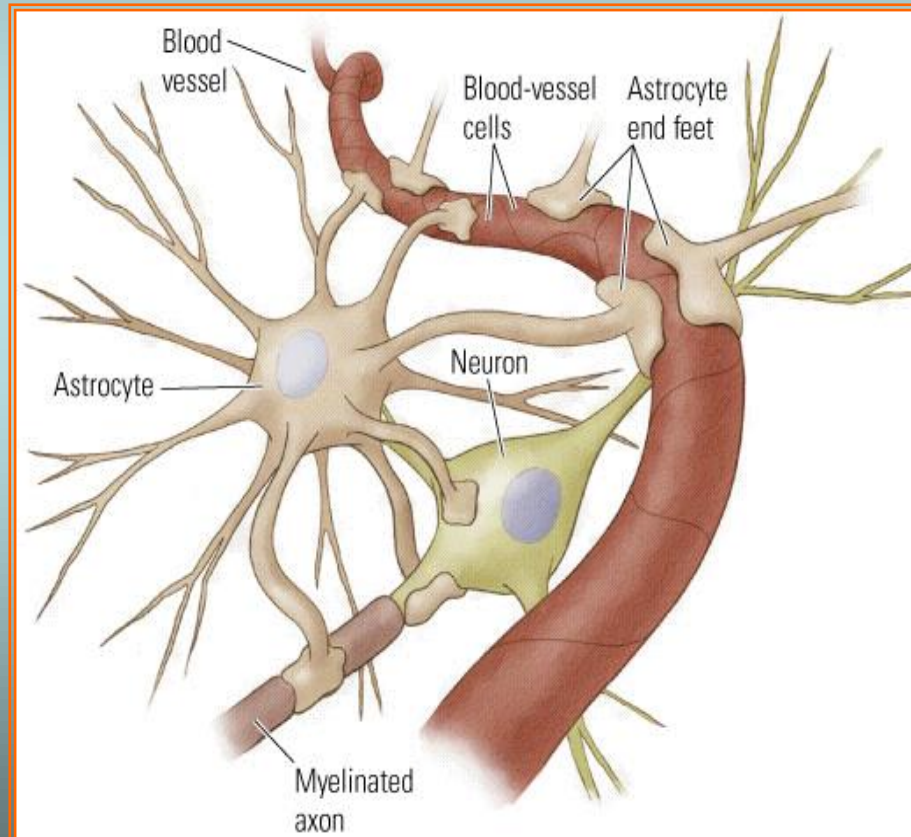


Lineage astrocita- oligodendrocita



I molteplici ruoli degli astrociti

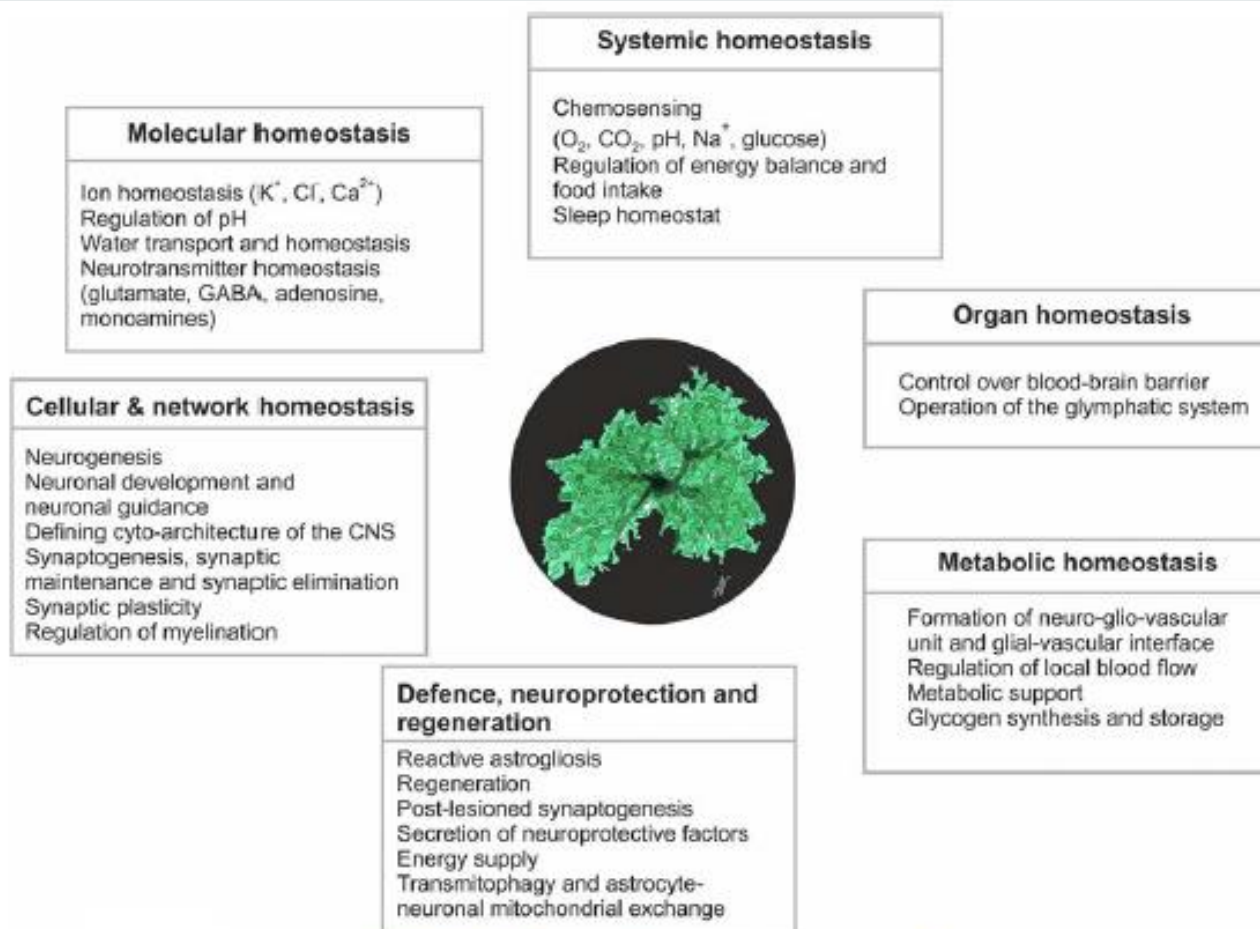
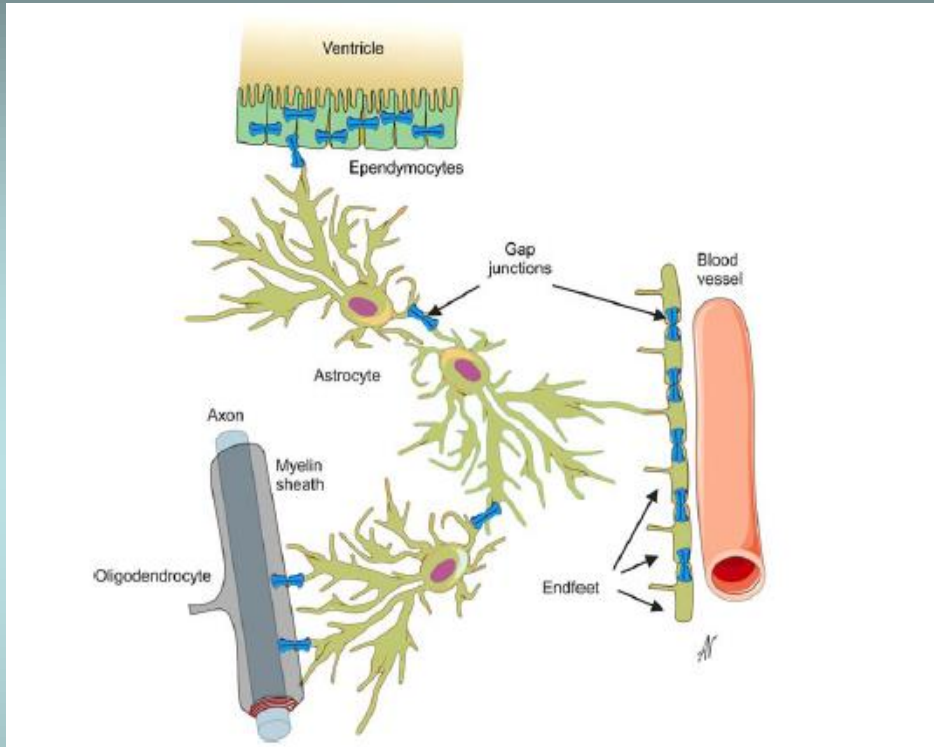
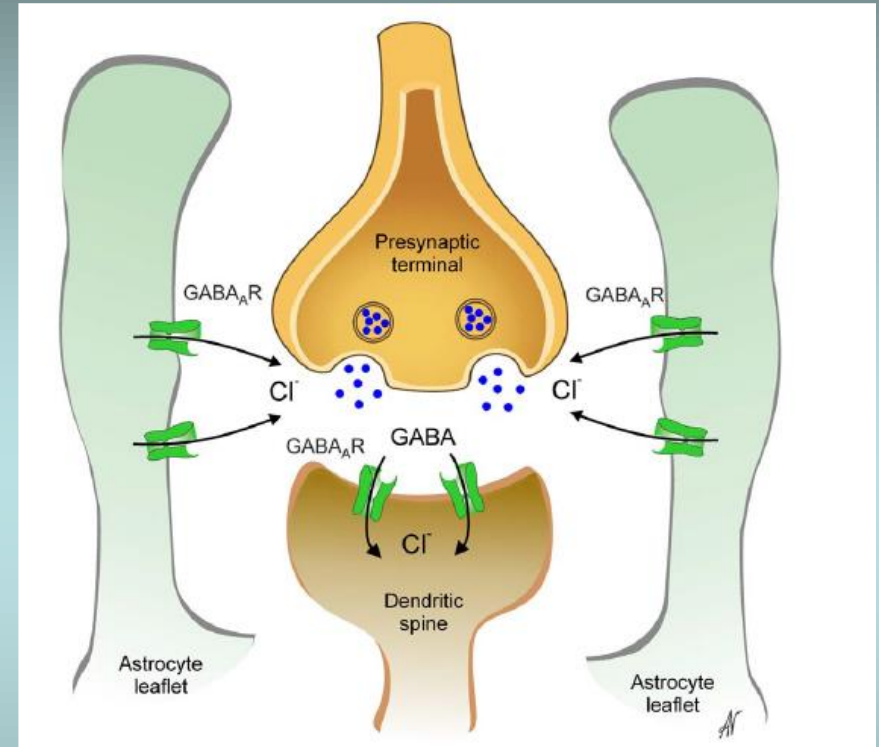


FIGURE 3.1 Homeostatic and defensive functions of astroglial.



↑

Astrociiti mediano il dialogo delle cellule del sistema nervoso con i vasi



↑

Astrociiti aiutano la formazione e la funzionalità delle sinapsi nel SNC

Astroglia

(20 - 40% of all glial cells in human CNS)

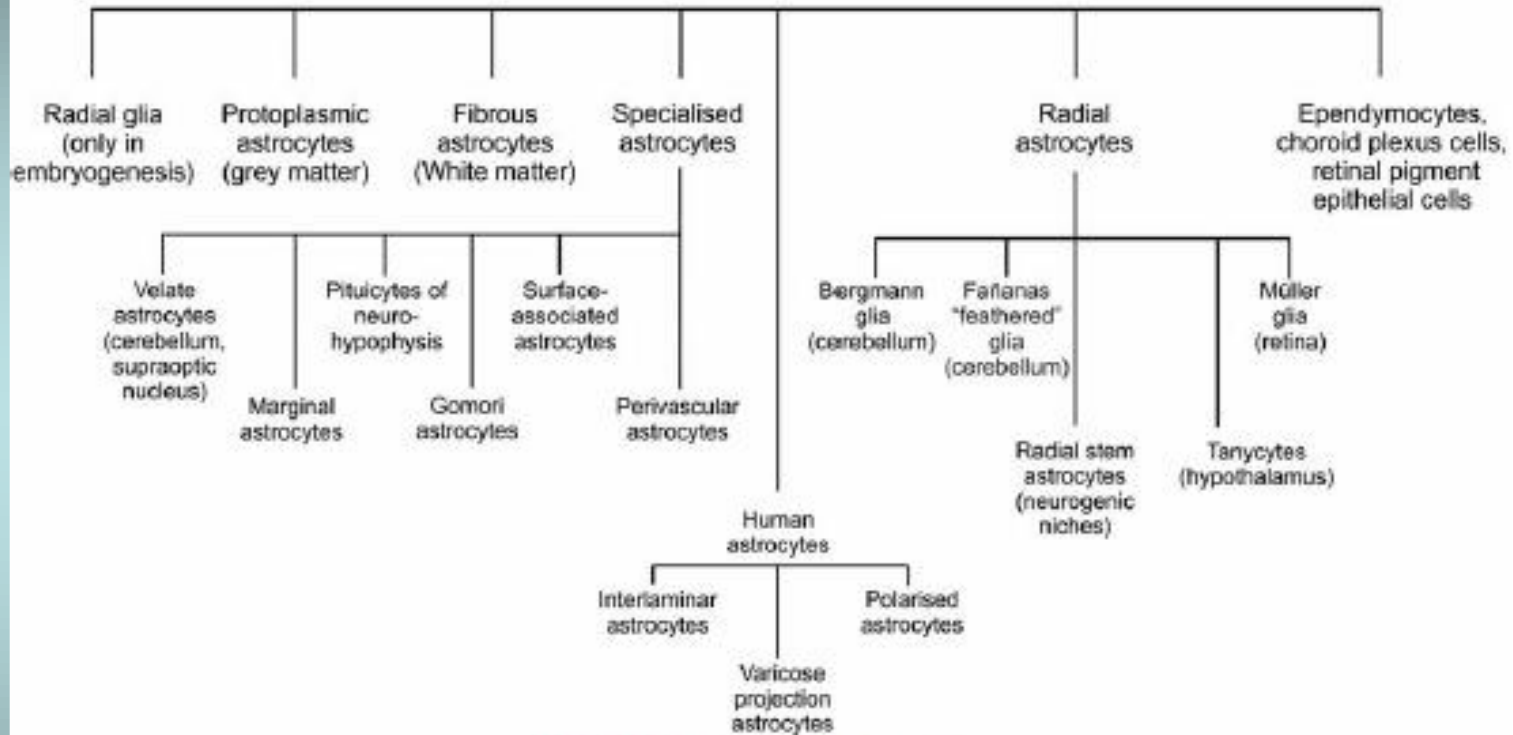
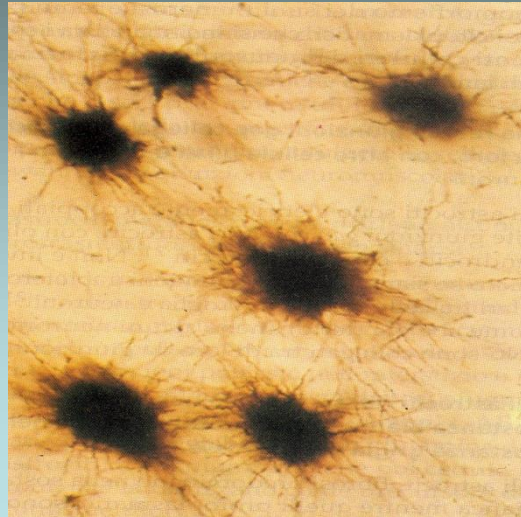
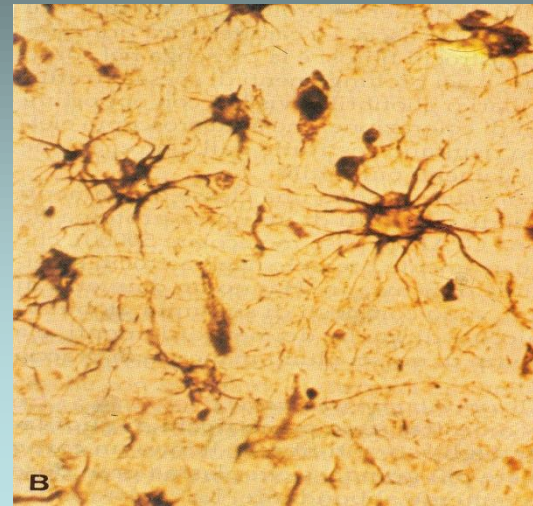


FIGURE 3.2 Classification of astroglia.

Astrociti fibrosi

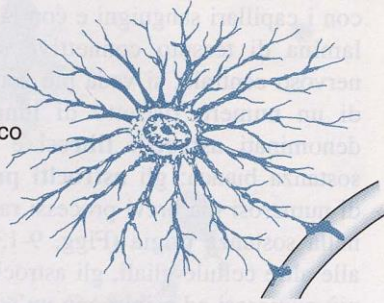


Astrociti protoplasmatici

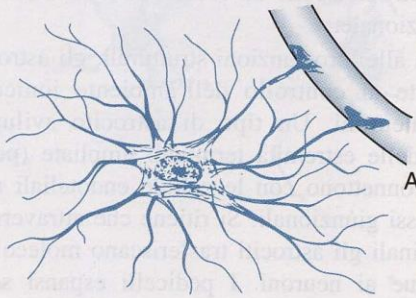


1. Fibrosi: lunghi processi. Presenti nella sostanza bianca
2. Protoplasmatici: processi più brevi. Presenti nella sostanza grigia

Astrocito protoplasmatico



Astrocito fibroso



ASTROCYTES

A

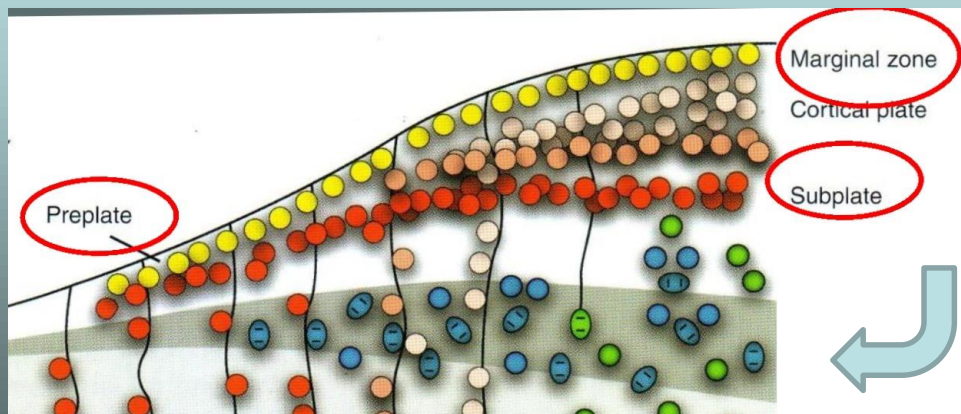
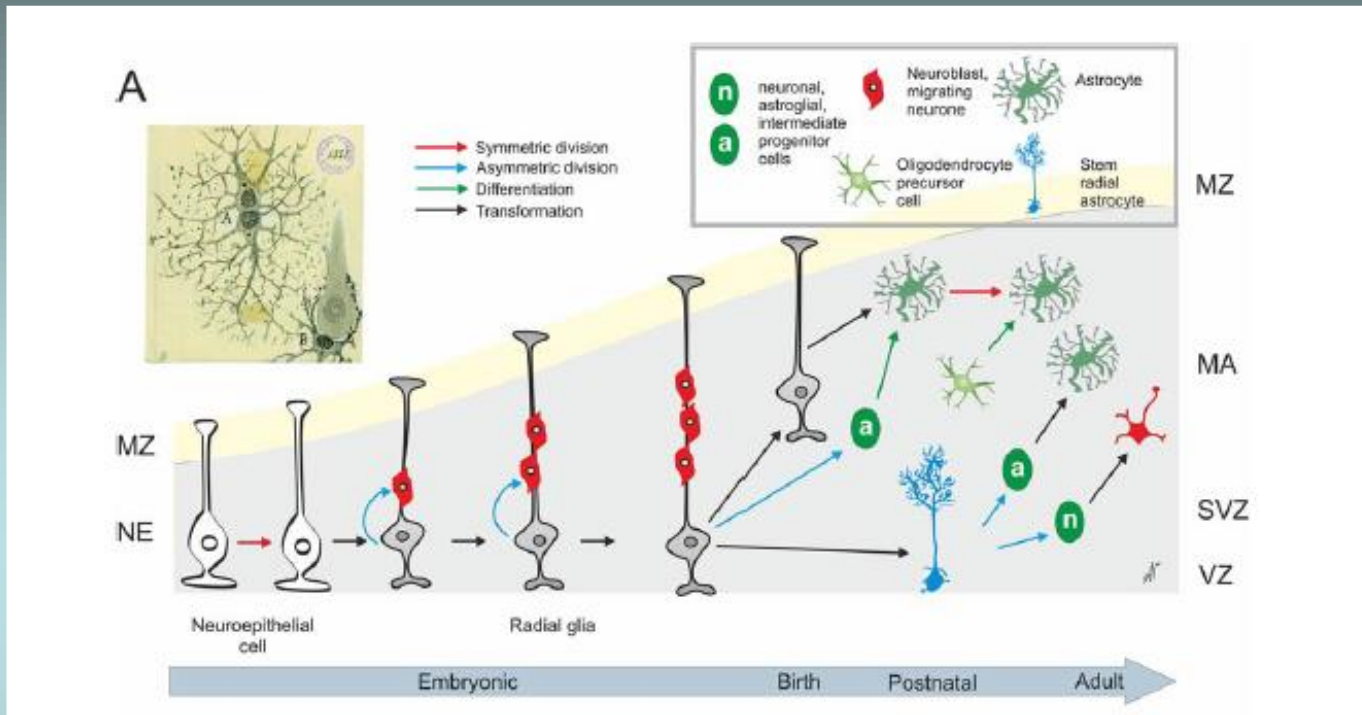


WM

Astroцити

1. Tipo I: da glia radiale
2. Tipo II: da altri progenitori

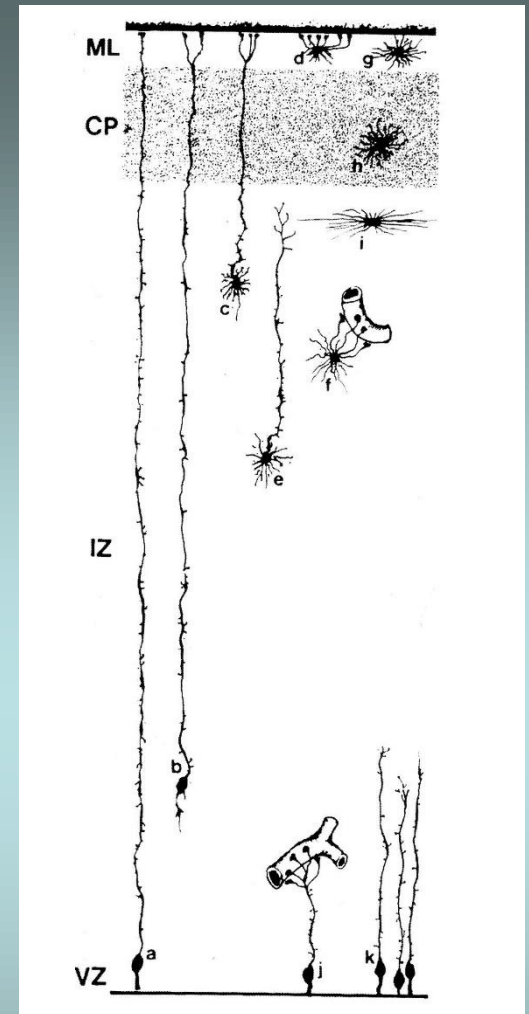
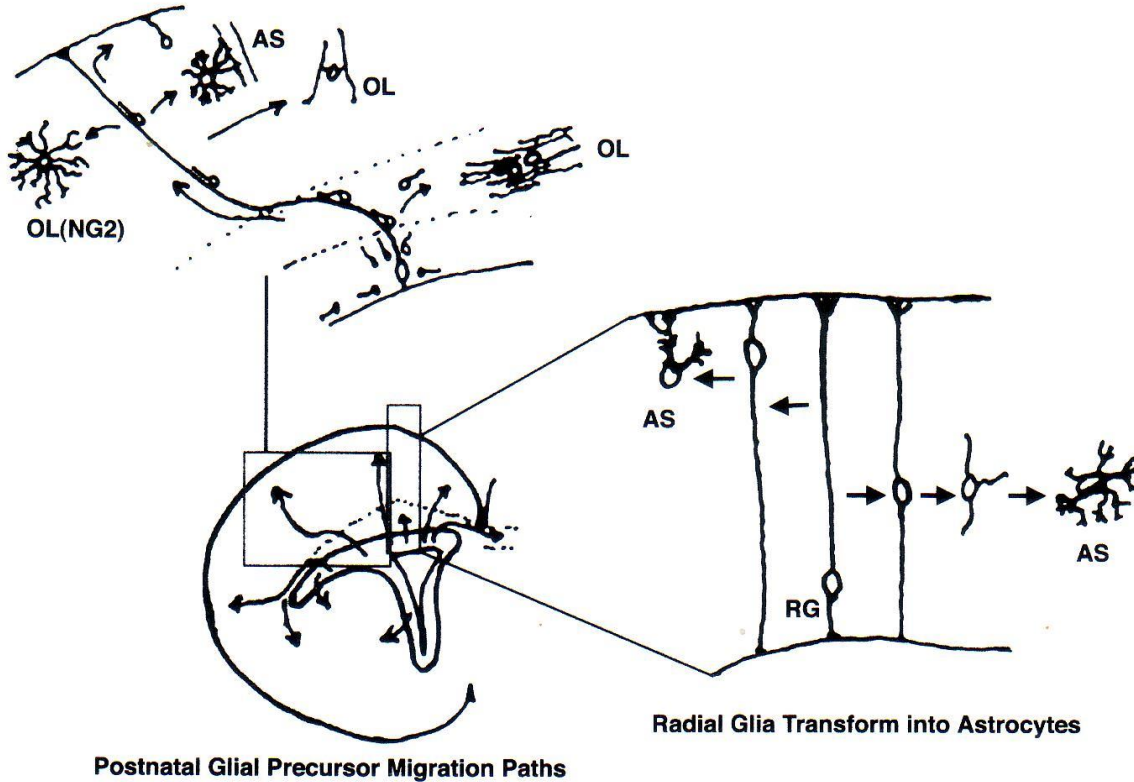
La glia radiale è il primo progenitore neurale in grado di formare astrociti o direttamente o tramite la formazione di altri progenitori



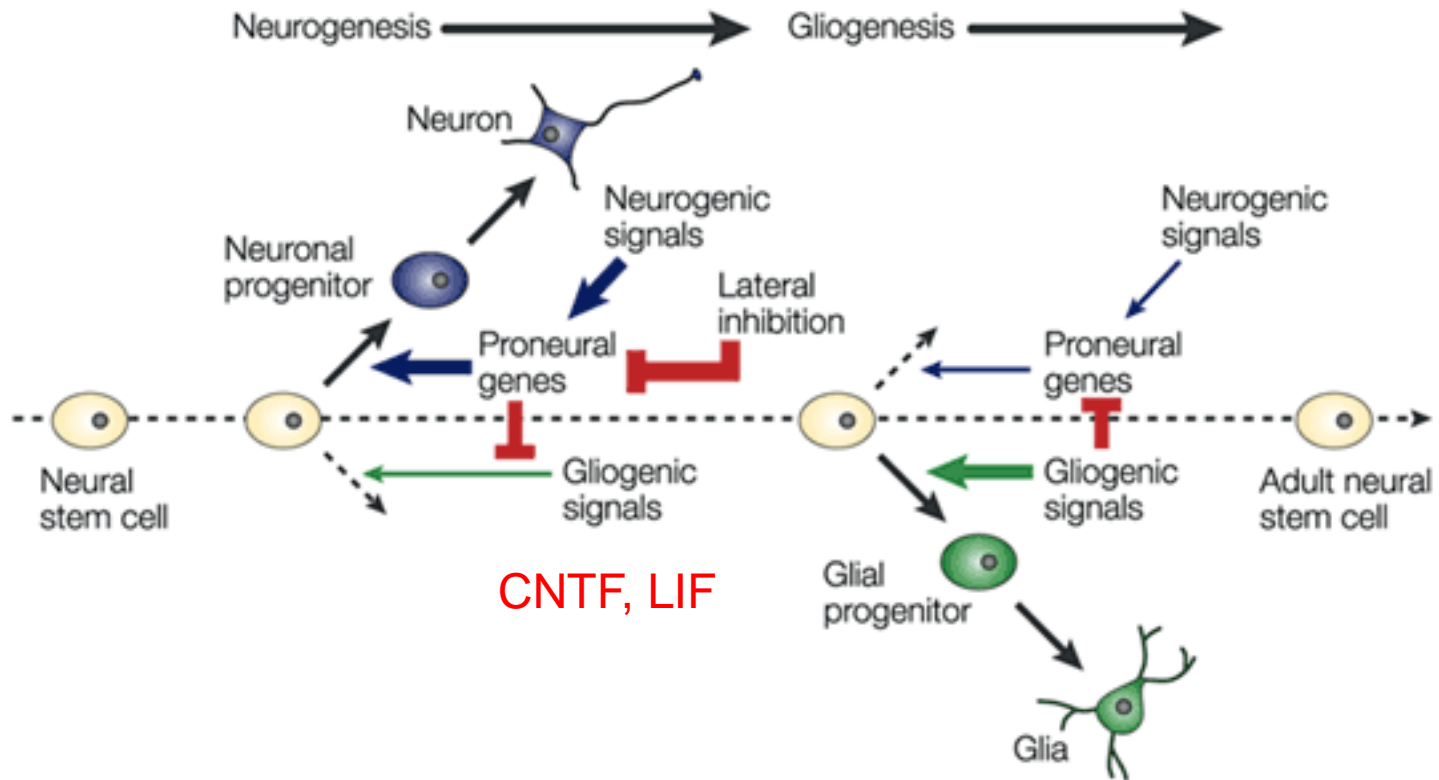
Altri progenitori gliali rimangono nelle zone di nicchia al termine della migrazione radiale

Ventricular zone

Glial Precursor Migration and Differentiation in Forebrain



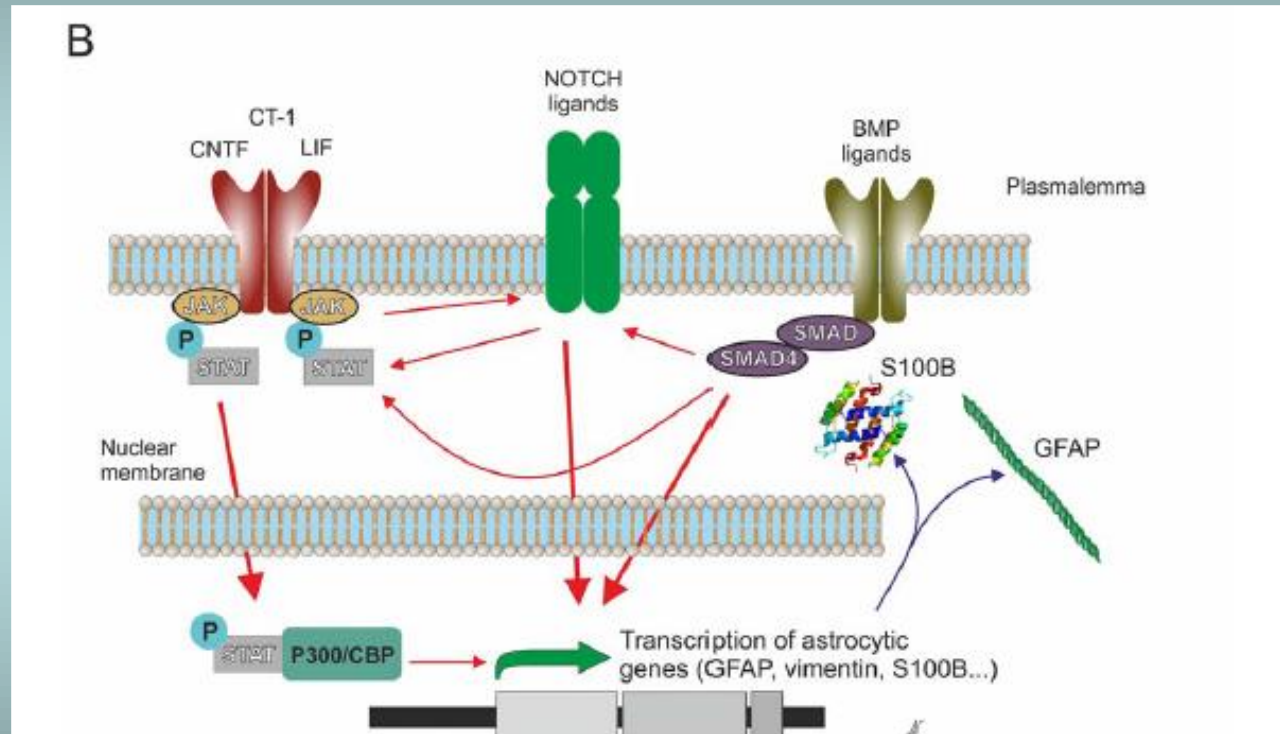
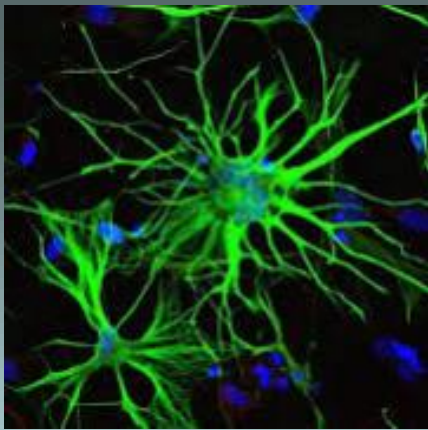
1. La glia radiale forma astrociti: espressione di marcatori specifici (GLAST, BLBP, GFAP)
2. Dalla glia radiale si formano sia gli astrociti fibrosi che quelli protoplasmatici
3. Astrociti di tipo II da altri progenitori (O2A)



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Partendo da progenitori comuni, quando i lineages neuronale e gliale divergono?

Sviluppo del lineage astrocitario



Oltre al sistema Delta-Notch, partecipano alla definizione della via astrocitaria diversi fattori di crescita (IL-6/LIF, CNTF, BMP).

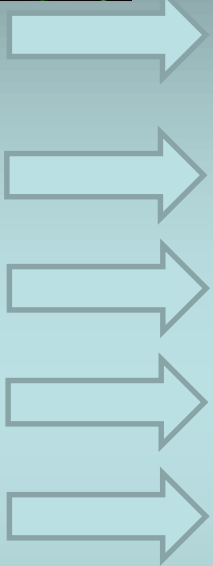
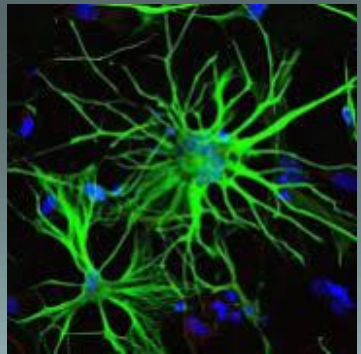
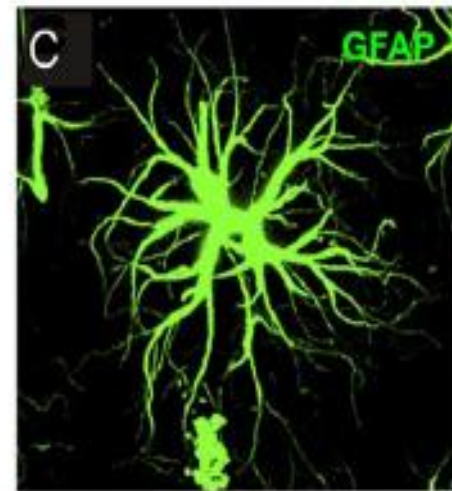
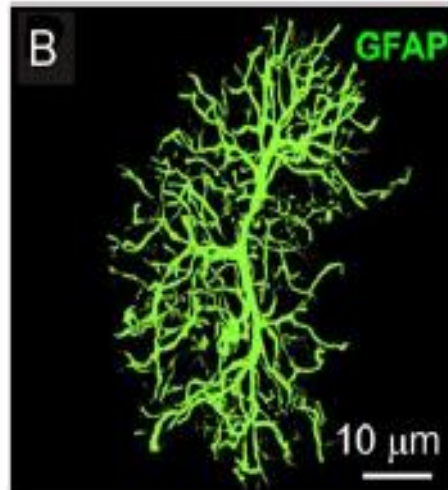
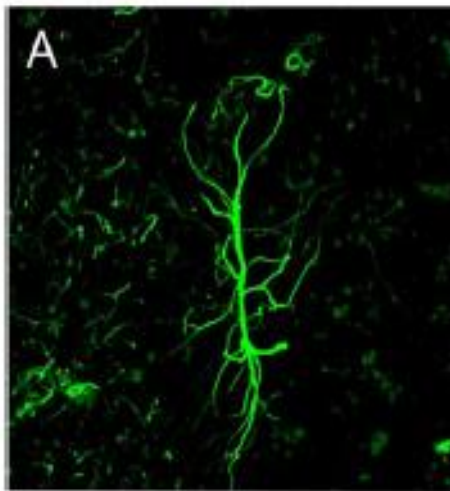


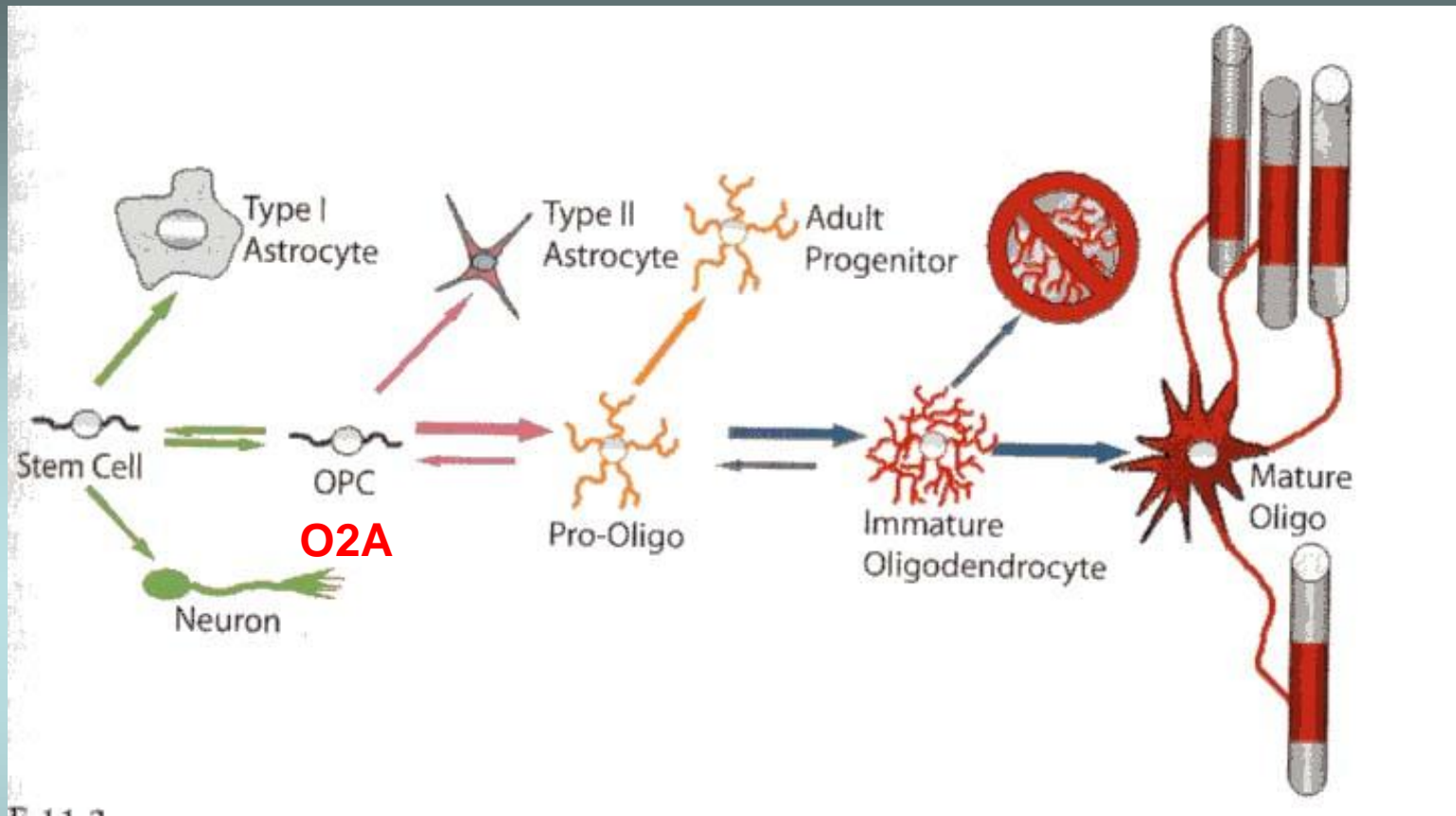
TABLE 3.1 Astrocyte markers (antibodies) used for immunolabelling.

Molecule/antigen	Properties and functional relevance
Glial fibrillary acidic protein, GFAP	Intermediate filament protein, expressed in many cells outside the nervous system; in the CNS, expressed in a sub-population of astrocytes with substantial regional variability. Generally, GFAP expression is up-regulated in reactive astroglia, although it may also increase during physiological adaptive responses.
Vimentin	Intermediate filament protein, expressed in immature astrocytes, in sub-populations of protoplasmic and fibrous astrocytes, Bergmann glia, tanyocytes and ependymocytes. Vimentin expression is up-regulated in reactive astrocytes.
S100B protein	Ca ²⁺ -binding protein, which acts as a Ca ²⁺ buffer as well as Ca ²⁺ sensor. Antibodies against S100B stain more astrocytes than GFAP in the grey as well as in the white matter.
Glutamate transporters: EAAT-1 (GLAST) EAAT-2 (GLT-1)	Astroglial glutamate transporters; show regional variability: EAAT1 is predominantly expressed in the cerebellum; in other regions, EAAT2 is the main transporter type.
Glutamine synthetase	Astroglial enzyme converting ammonia and glutamate into glutamine. Expressed in the majority of astrocytes. Immunostaining reveals full structure of the cell due to cytosolic localisation of the enzyme.
Aldehyde dehydrogenase 1 family, member L1 (ALDH1L1)	ALDH1L1 is a key enzyme in folate metabolism contributing to nucleotide biosynthesis and cell division. Proposed as a specific astroglial marker with a reach substantially broader than GFAP. ALDH1L1 expression however changes with age, and it was also detected in a subpopulation of oligodendrocytes.
Connexins Cx43 Cx30	Both Cx43 and Cx30 are expressed exclusively in astrocytes; the Cx30 is expressed mostly in the grey matter (being particularly concentrated in astroglial endfeet) and is absent in astrocytes from white matter.
Aquaporin AQP4	AQP4 in the CNS is expressed exclusively in astrocytes and ependymocytes. In healthy astrocytes, AQP4 is preferentially located in the endfeet and hence stains this structure.
CD44 (plasma membrane protein and extracellular matrix receptor)	Label interlaminar astrocytes and some (possibly age-modified) protoplasmic astrocytes in the human brain.
Transcriptional factor SOX9	Specifically labels nuclei of astrocytes outside the neurogenic niches.

Marcatura per GFAP

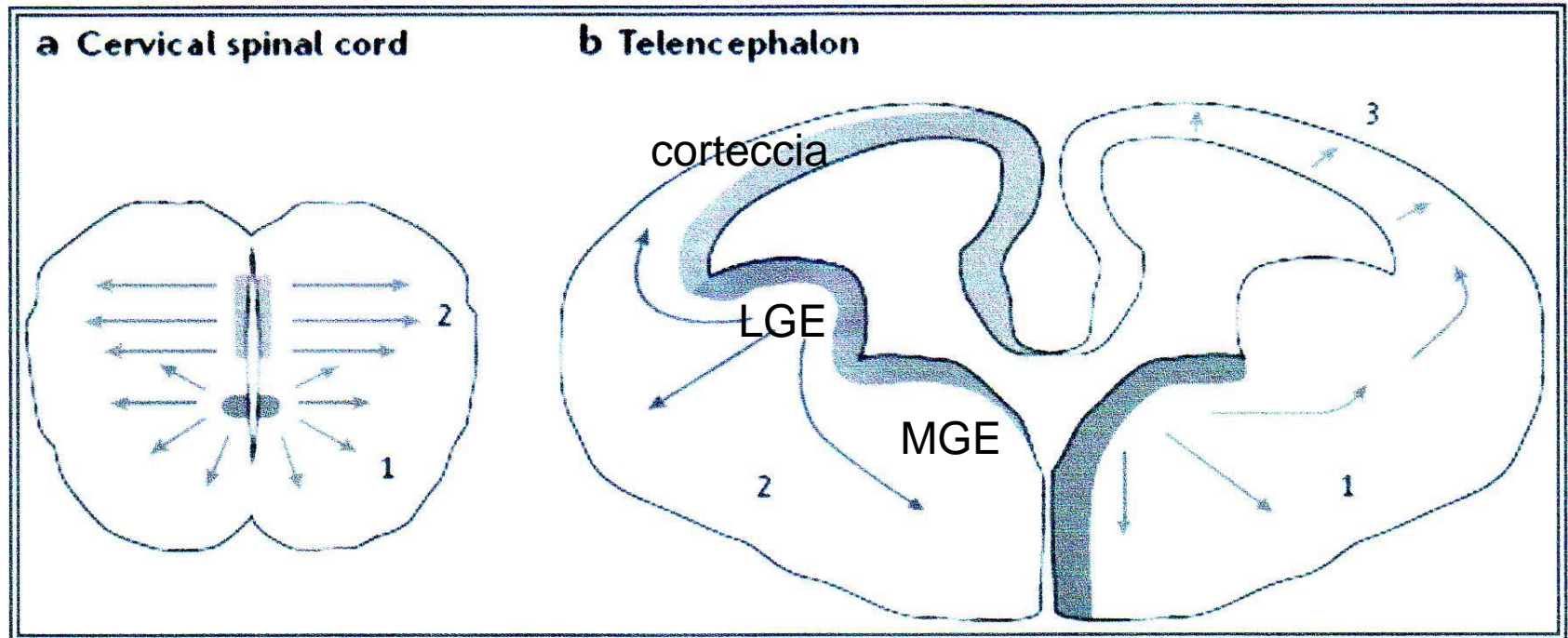


Caratteristiche dei progenitori O2A



1. I progenitori (O2-A) originano, da diverse aree: nervo ottico, zona ventricolare, midollo spinale, cervelletto
2. O2-A si dividono lentamente nell'adulto, altri sono quiescenti e si attivano solo in seguito a traumi o a eventi demielinizzanti

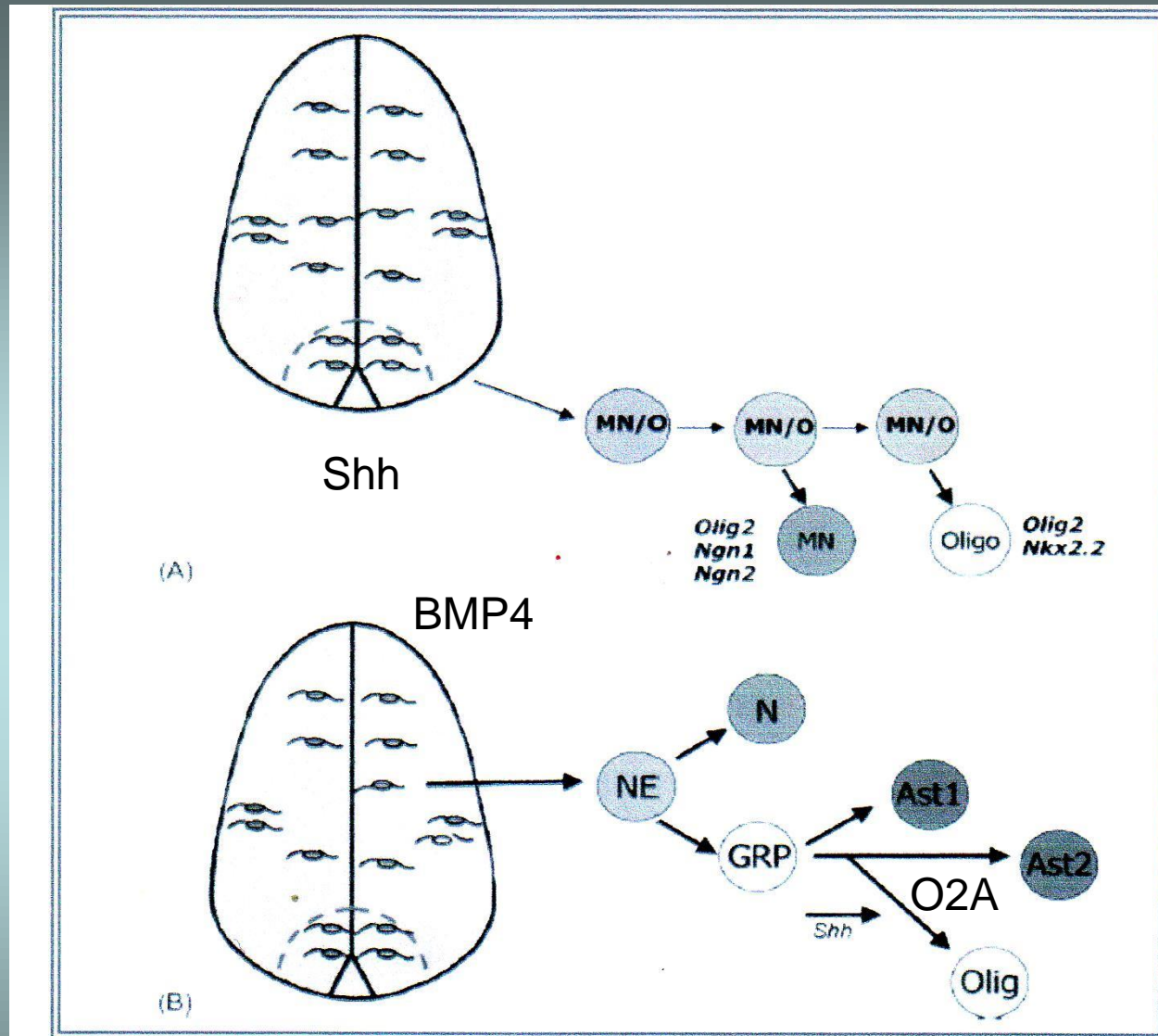
Origine e migrazione dei precursori oligodendrocitari



Zona 1: parte ventrale (E12.5 in topo)

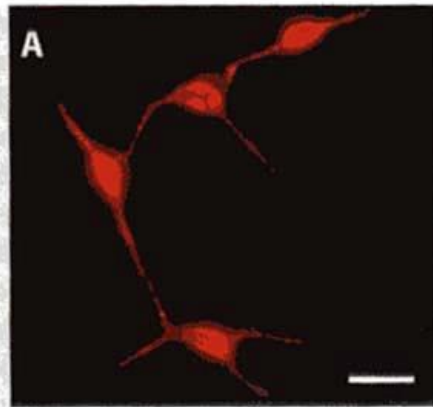
Zona II: parte dorsale (E15)

Zona III: regione corticale (solo nel periodo post natale)



- Il gradiente di Shh è richiesto per la specificazione verso la via di motoneuroni e oligodendrociti
- La via BMP4 favorisce la via astrocitaria

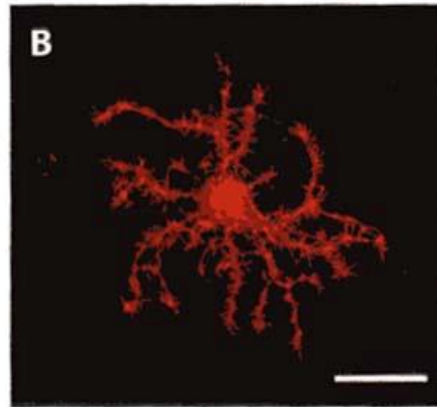
Stadi maturativi e markers di superficie



0 1 1 1

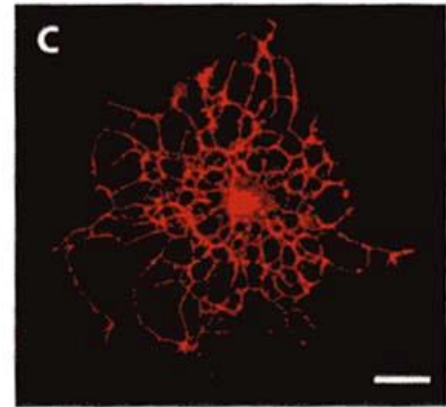
Progenitore O2A

A2B5+



Pro-oligo

O4+/GC+



Oligo maturo

O4+/GC+

MBP+

PLP+



Neural stem cell

Nestin
PSA-NCAM



Oligodendrocyte precursor cell, OPC

NG2
PDGF α R
GRP17



Immature oligodendrocyte

MBP positive
or negative
GALC
O4
CNP

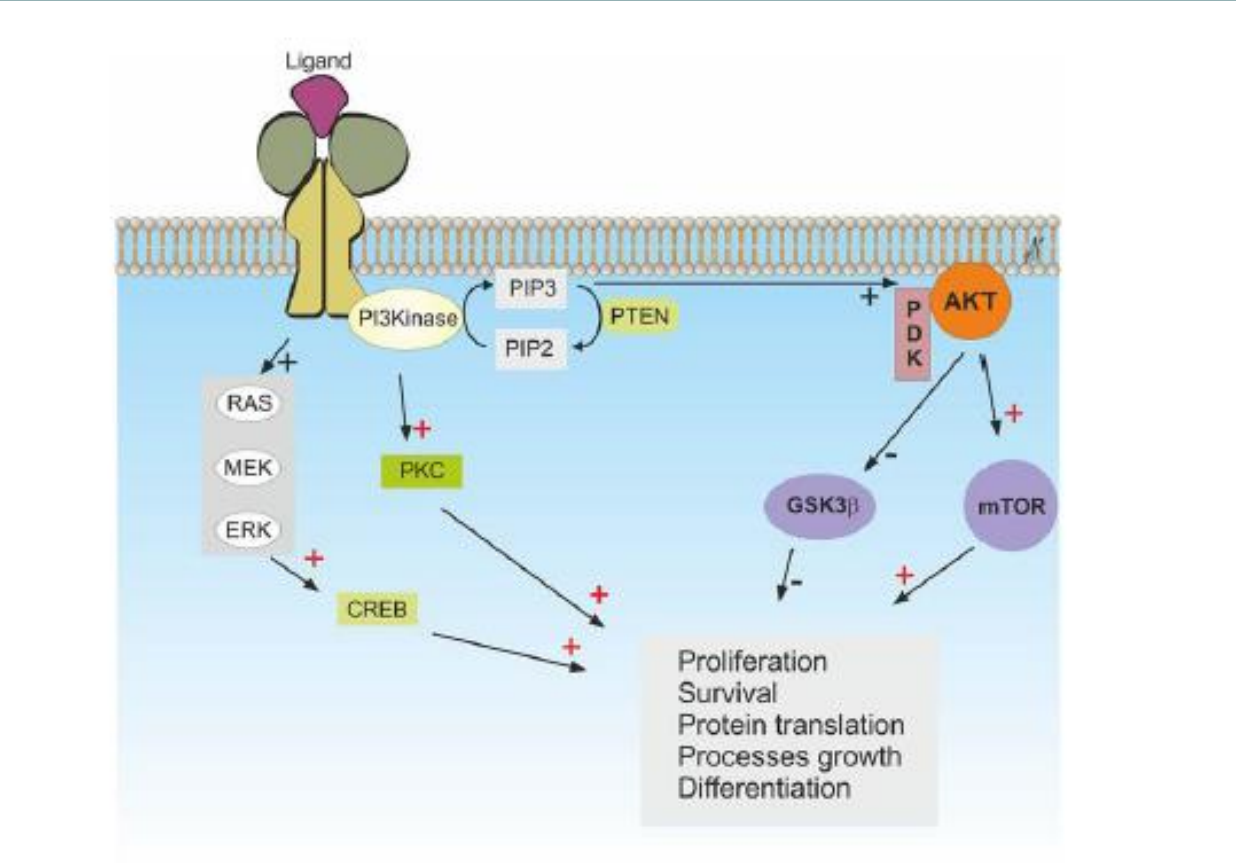


Mature oligodendrocyte

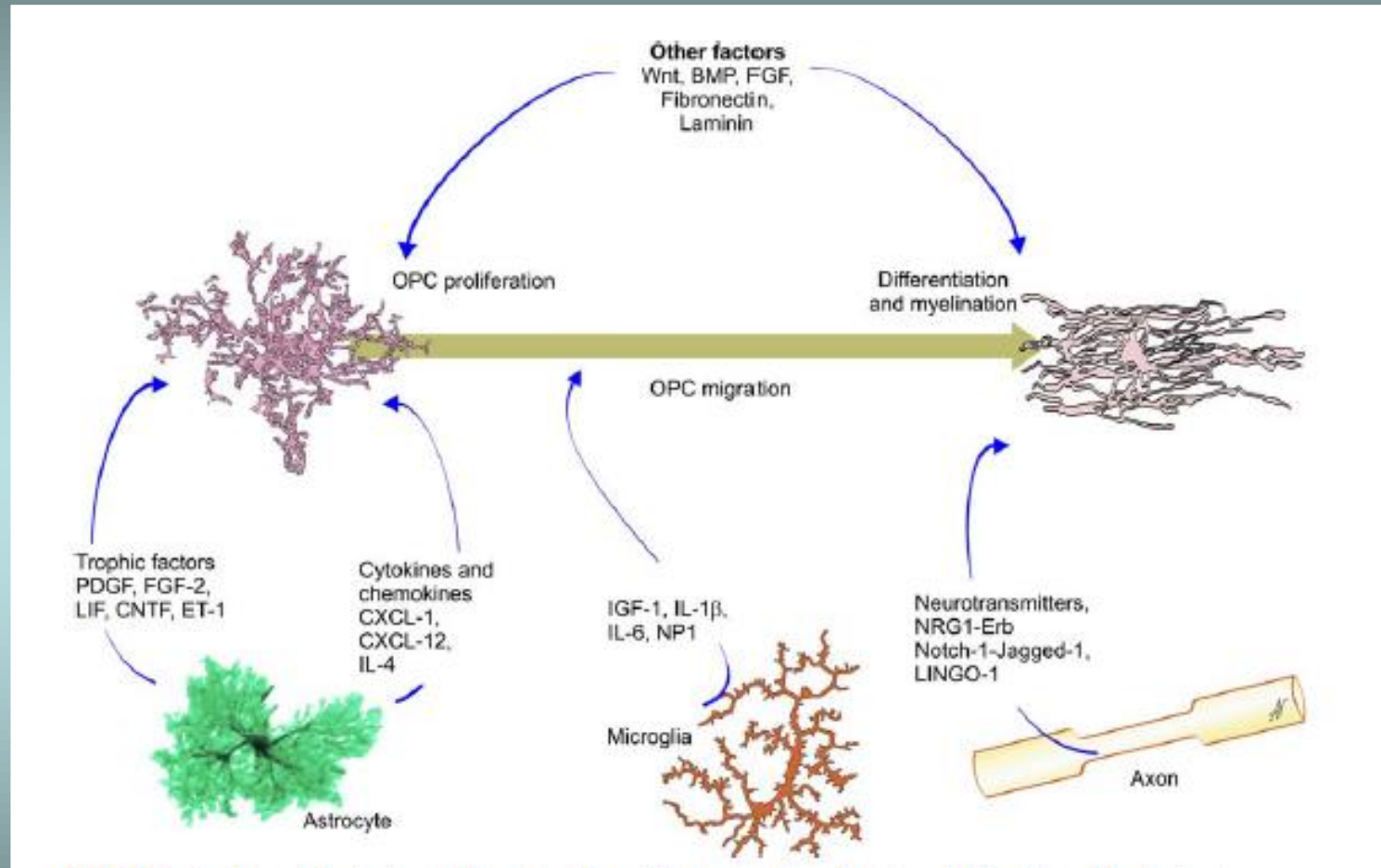
APC
MBP
PLP
MAG
MOG
GALC
O4
CNP

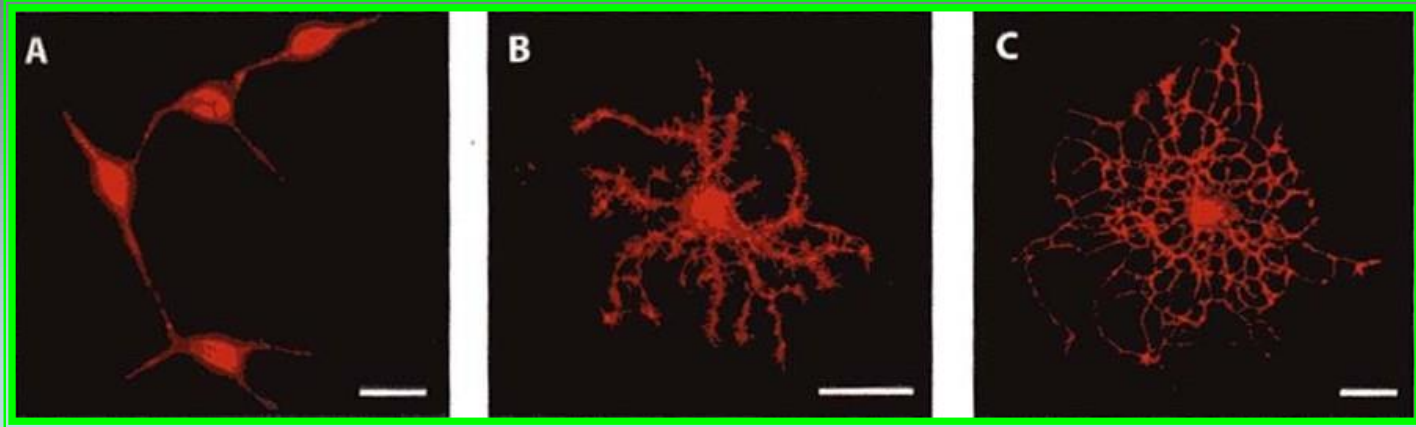
1. I fattori di crescita FGF, PDGF, NRG1 regolano la fase proliferativa
2. La NRG1 e gli ormoni tiroidei T3 e T4 modulano la fase di differenziamento e di mielinizzazione.

Vie di trasduzione attivate a valle di recettori PDGF

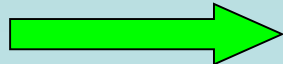


Segnali regolatori per sviluppo e differenziamento degli oligodendrociti





Olig 2
Nkx 2.2



NRG-1/erbB2-3

Olig1
Sox 10



FGF/PDGF

NRG-1/ErbB3-4 e ormoni tiroidei



Regolano l'espressione delle
proteine della mielina

MBP

Olig 1 e 2: fattori di trascrizione HLH
SOX 10: Fattore di trascrizione HMG

I neurotrasmettitori possono condizionare lo sviluppo degli OL

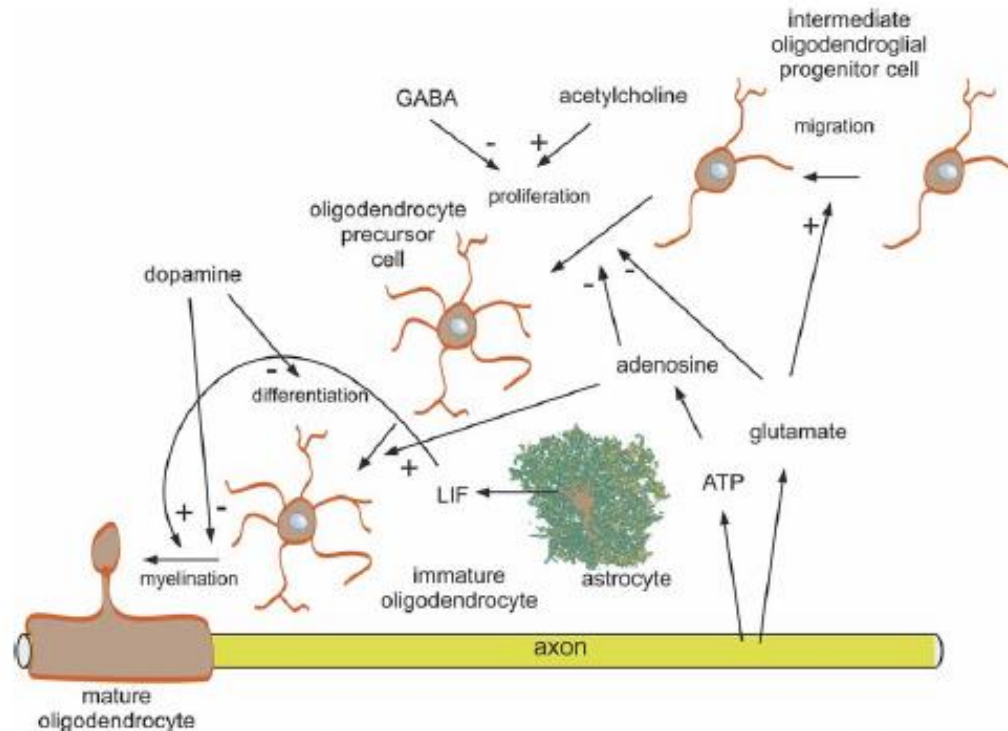
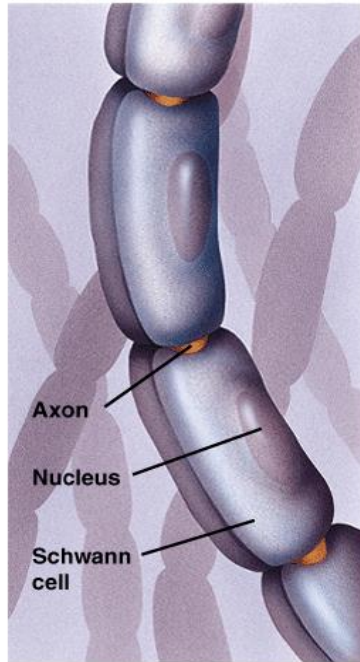


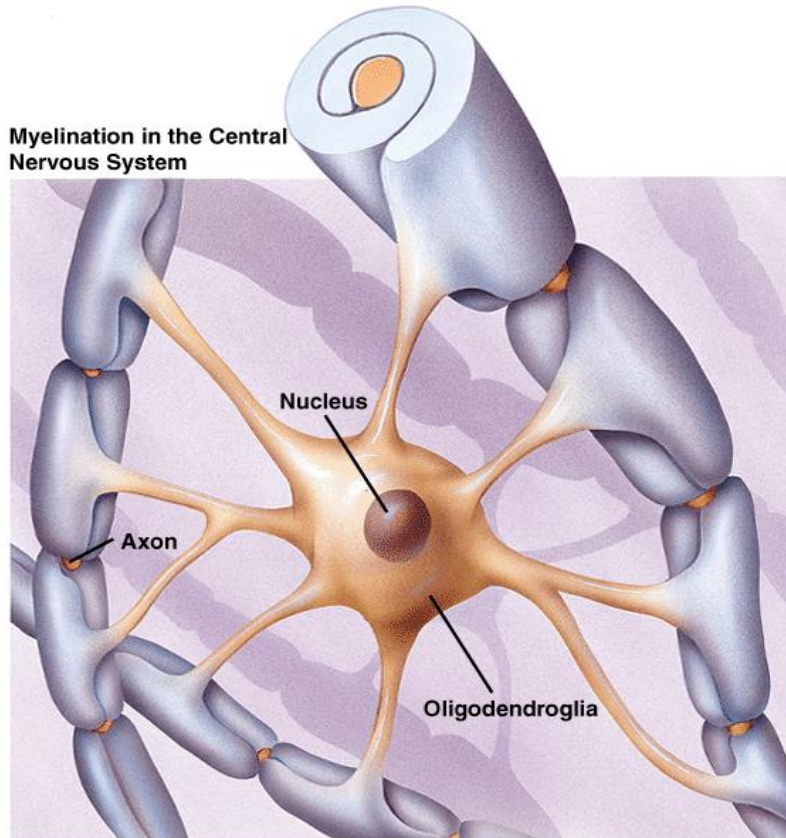
FIGURE 5.20 Neurotransmitter signalling in oligodendrocytes. Oligodendrocytes express a wide range of neurotransmitter receptors that mediate axoglial interactions and regulate differentiation and myelination. Glutamate and ATP, together with its breakdown product adenosine, stimulate oligodendrocyte precursor cell migration. Glutamate also inhibits their proliferation and differentiation, whereas adenosine inhibits proliferation and stimulates differentiation and myelination. ATP stimulates astrocytes to release leukemia inhibitory factor (LIF), which stimulates oligodendrocyte differentiation. Oligodendrocyte precursor cell proliferation and differentiation are also altered by GABA and dopamine, which are inhibitory, and ACh, which is generally stimulatory. (See text for further details).

► Myelination of PNS and CNS Axons

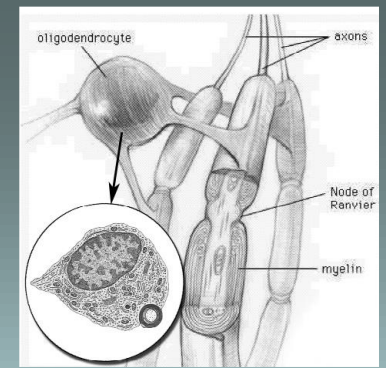
Myelination in the Peripheral Nervous System



Myelination in the Central Nervous System



Mielinizzazione



► Formation of Myelin

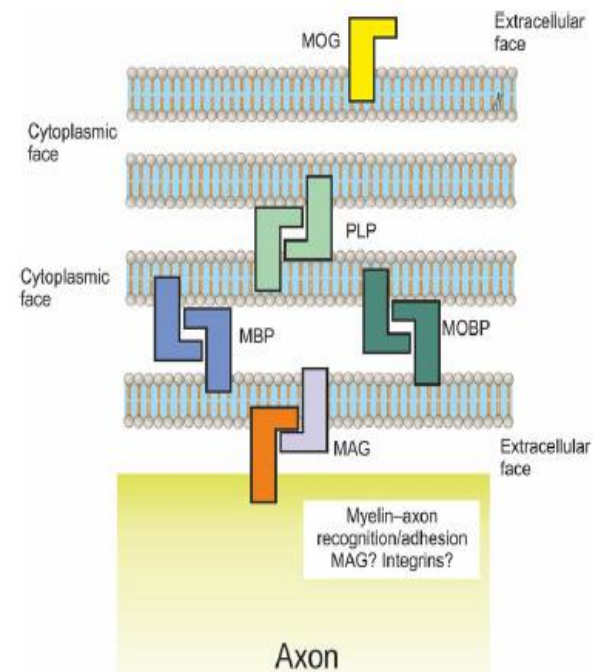
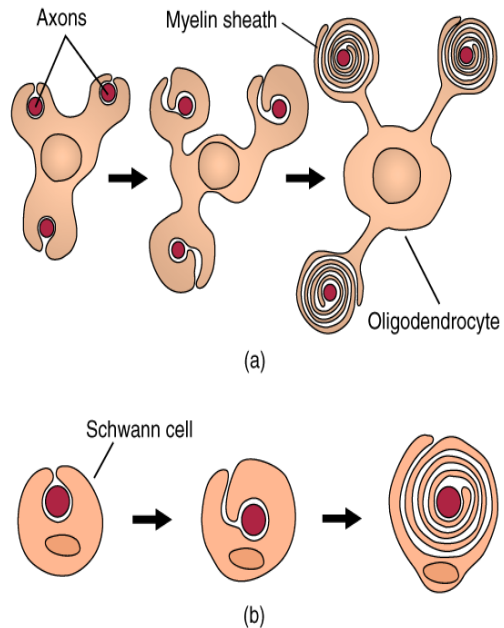
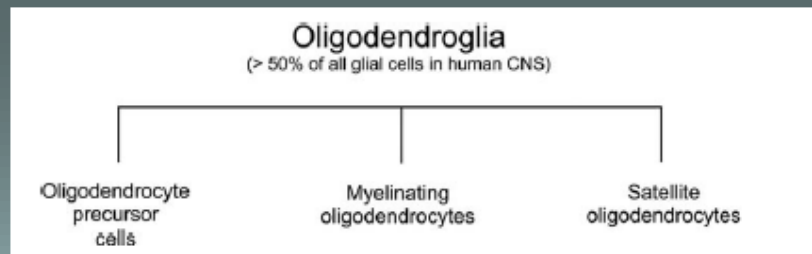


FIGURE 5.22 Biochemistry of CNS myelin. See text for details.

Proteina della mielina: MBP (Myelin basic protein)
MAG (Myelin associated glycoprotein)
PLP (Proteolipid protein)



Classificazione sulla base della densità del citoplasma: chiari, medi, scuri

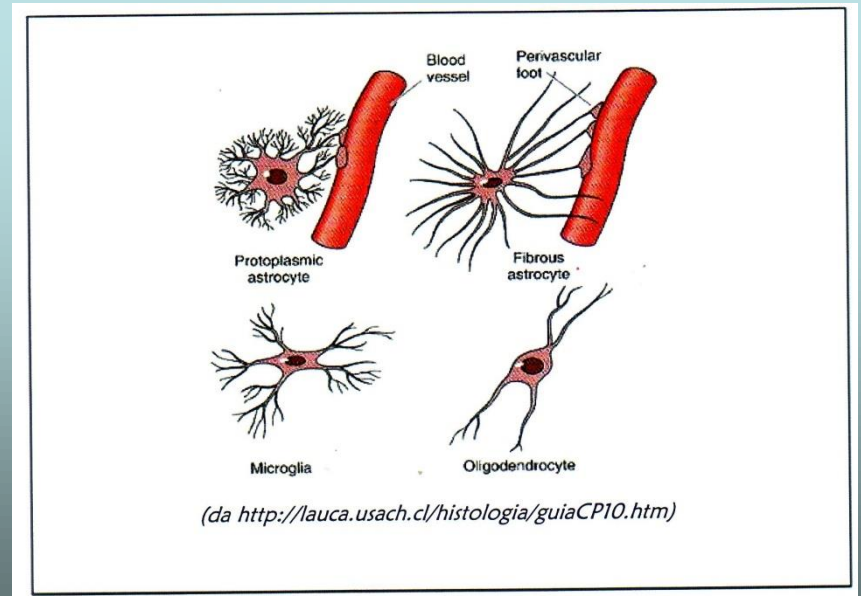
OL chiari sono attivamente proliferanti

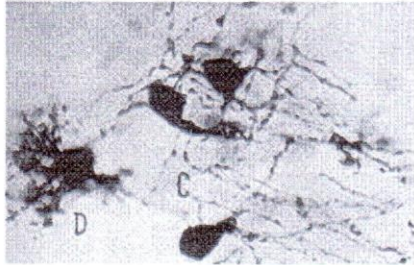
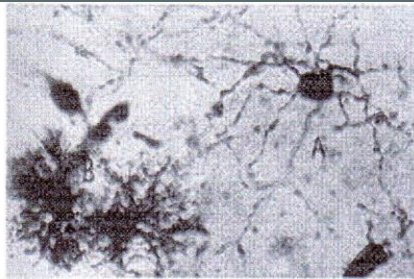
OL scuri sono più differenziati

- oligodendrociti mielinizzanti
- oligodendrociti satelliti

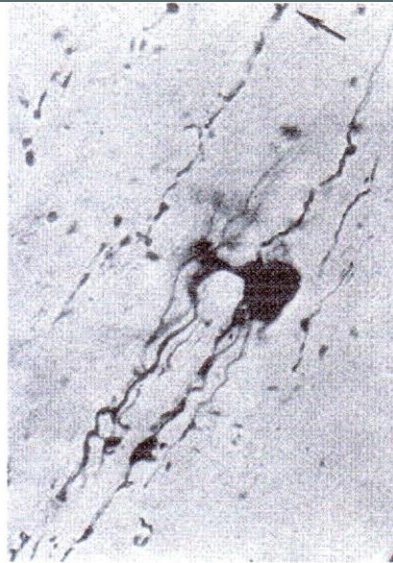


Rio-Ortega (1928)

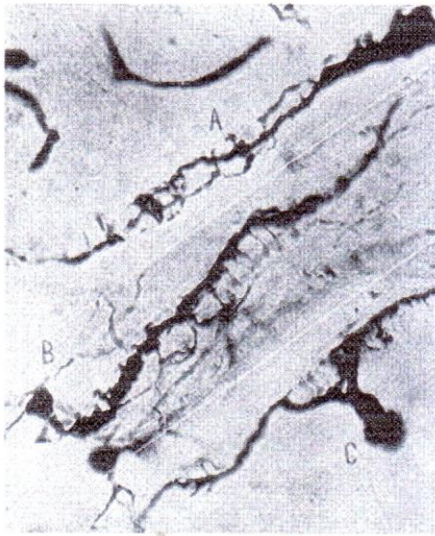




A



B



C



D

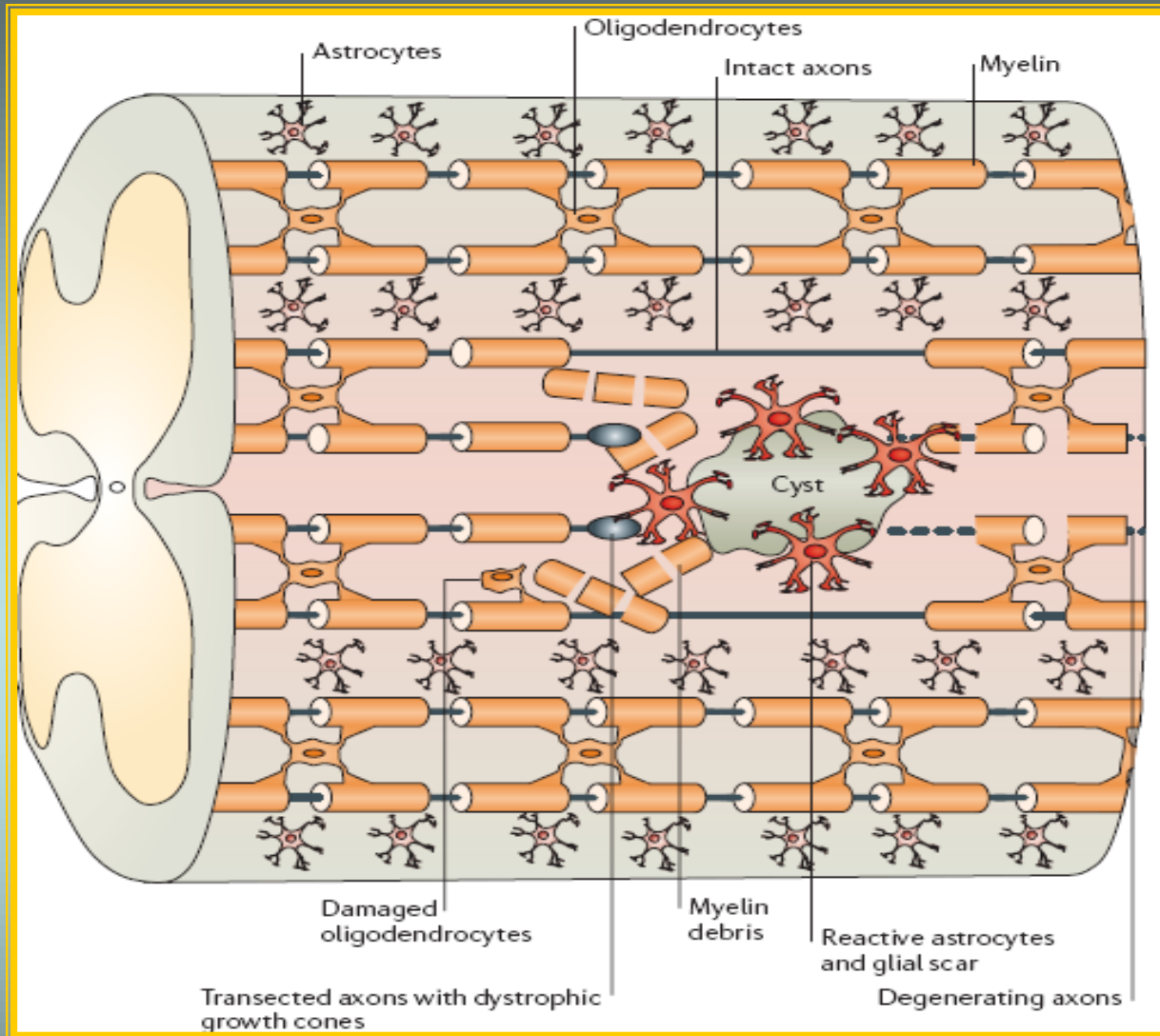
OL di tipo I e II: corpo cellulare piccolo, pochi processi che mielinizzano dai 10-30 assoni di piccolo calibro.

Tipo I : nella sostanza grigia del prosencefalo, cervelletto e midollo spinale

Tipo II: nella sostanza bianca

Tipo III: corpo cellulare grande e processi molto spessi che avvolgono pochi assoni di grande calibro (cervelletto)

Tipo IV: Non forma processi e forma un unico avvolgimento di mielina sugli assoni



In caso di danno l'oligodendrocita muore e deve essere sostituito in seguito a proliferazione e migrazione di un nuovo progenitore

