Oligodendrocyte

Oligodendrocytes (OLs) are glial cells with great impact on brain development and neuronal function (Dugas et al., 2010; Lau et al., 2008; Zhao, et al., 2010).

From: Advances in Genetics, 2014

Related terms:

Multiple Sclerosis, Microglia, Glial Cells, Astrocyte, Myelinogenesis, Central Nervous System, Axon, Myelin, Protein

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Oligodendrocytes

R.P. Skoff, J.A. Benjamins, in Encyclopedia of the Neurological Sciences (Second Edition), 2014

Control of Oligodendrocyte Number: Regulation of Differentiation and Survival

Oligodendrocyte precursors differentiate into immature oligodendrocytes before they generate myelin (Figures 1 and 2). Both cell intrinsic and cell extrinsic signals regulate this critical transition. *In vitro*, clonally related oligodendrocyte precursors differentiate at approximately the same time, suggesting that the differentiation of these cells is in part regulated through an intrinsic clock that measures the number of cell divisions and/or elapsed time. Extrinsic signals also influence oligodendrocyte differentiation. Axonal signals promote the differentiation of oligodendrocyte precursors, and considerable circumstantial evidence suggests that axons provide a signal that initiates the process of myelination. Thyroid hormone also influences oligodendrocyte differentiation. Exposure to thyroid hormone elevates the number of mature oligodendrocytes and directly enhances the expression of myelin-specific genes.

Figure 2. (a) Cerebral cortex from an immature mouse at a time when premyelinating oligodendrocytes are abundant. The oligodendrocytes are immunostained to detect myelin basic protein, a major component of myelin. The cytoarchitecture of these premyelinating oligodendrocytes (arrows) dramatically differs from mature oligodendrocytes, shown in (b). Premyelinating oligodendrocytes are evenly spaced throughout the neuropil and they radiate numerous fine-branching processes in all directions creating the appearance of a spider web. Their perikarya are the densely stained spherical structures (arrows) in the center of the web. (b) Mature oligodendrocytes (OL) lose the webbing but still retain long processes (arrows) that form myelin (asterisk) around axons.

Although oligodendrocyte precursors are highly proliferative, mature differentiated oligodendrocytes do not proliferate extensively; therefore, the regulation of oligodendrocyte precursor number is crucial for generating sufficient oligodendrocytes in adults. The final number of oligodendrocytes that develop in a specific region of the CNS is closely correlated with the number of axons that require myelination. This matching of cell number is accomplished by regulation of cell proliferation and cell survival. As in neuronal lineages, during development oligodendrocyte precursors are produced in excess and programmed cell death removes extraneous cells. *In vitro*, newly formed oligodendrocytes depend on PDGF for survival, whereas more mature oligodendrocytes depend on insulin growth factor-1 and the neurotrophin-3 (NT-3) for survival. It seems likely that similar combinations of growth factors regulate oligodendrocyte survival during development in the intact CNS.

Oligodendrocyte precursors persist in the adult CNS, offering a potential source of cells for therapy and repair. Under normal conditions the proliferation of these adult cells is limited; however, in response to injury, or *in vitro*, adult oligodendrocyte precursors can proliferate extensively and generate large numbers of oligodendrocytes. Understanding how the proliferation and differentiation of these adult precursors are controlled will provide strategies for replacing oligodendrocytes lost during pathological conditions.

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MicroRNAs in Brain Development

Marion Coolen, Laure Bally-Cuif, in MicroRNA in Regenerative Medicine, 2015

Oligodendrocytes

Oligodendrocytes are the myelinating glia of the CNS. The first step in the generation of oligodendrocytes is the emergence of oligodendrocyte precursors (OPCs) from embryonic radial glia. OPCs constitute a pool of dividing progenitors dispersed in the parenchyma that will differentiate into mature oligodendrocytes. The generation of OPCs from radial glia is under some degree of spatial regulation [37]. A specialized ventral progenitor domain, in close contact with the Shh signaling source, has been shown to be a major embryonic source of OPCs, both in the spinal cord and brain. These progenitors express bHLH factors of the OLIG family. However, there are also dorsal sources of OPCs [37]. There is also a temporal restriction of oligodendrocyte production at work during development; during early phases of neurogenesis, only neurons are generated while later on oligodendrocytes start to appear as well [38].

Moreover, in the mouse telencephalon in particular, a gradual shift of OPC production from ventral to dorsal progenitor domains has been described [37]. The transition toward OPC production seems to coincide loosely with the transformation of neuroepithelial cells into RGCs and the induction of the expression of the transcription factor Sox9, suggesting a switch in progenitor competence (sometimes called the glial switch). However, it is still unclear whether neurons and OPCs are produced sequentially from the same progenitors at the single cell level. Likewise whether RGCs directly convert into OPCs or asymmetrically divide to give rise to one OPC and one RGC remains unclear. Clonal analyses of single progenitors are needed to resolve this issue. Of note, the signaling pathways and transcription factors that are required for OPCs to be specified (Shh, Notch, OLIG, SOX9) are used at later steps for the maintenance of the OPC dividing pool [39].

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Amyotrophic lateral sclerosis: mechanisms and therapeutic strategies

Ludo Van Den Bosch, in Disease-Modifying Targets in Neurodegenerative Disorders, 2017

Oligodendrocyte Dysfunction

Oligodendrocytes are another type of glial cells and these cells are responsible for the myelination of axons in the central nervous system (CNS). There is recent evidence that oligodendrocytes could also play an important role in ALS (for a review: [62]). Apart from their myelinating function, oligodendrocytes also provide trophic support to neuronal cells by releasing lactate. This release is mediated by the monocarboxylate transporter-1 (MCT1) [63]. While the number of oligodendrocytes remains the same [53,64], MCT1 levels significantly decrease in ALS patients and in the mutant SOD1 mouse model [63,64]. Oligodendrocytes start to degenerate before disease onset and are replaced by new oligodendrocytes. These new oligodendrocytes arise from precursor cells, also known as $NG2_+$ cells, [53,64]. However, these new oligodendrocytes have morphologic abnormalities and do not fully differentiate as indicated by the reduced expression of MCT1 and myelin basic protein (MBP) [53,64]. As a consequence, these oligodendrocytes are not fully mature and are not able to keep the motor neurons alive [63]. Strikingly, specific deletion of mutant SOD1 in the oligodendrocytes of mutant SOD1 mice significantly delays disease onset and survival [53]. All together, these results indicate that therapeutic strategies that preserve oligodendrocyte function and/or that induce the differentiation of $NG2_+$ oligodendrocyte precursor cells into fully differentiated oligodendrocytes could have therapeutic potential in ALS.

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Glia

Kathy L. Newell, E. Tessa Hedley-Whyte, in Encyclopedia of the Neurological Sciences, 2003

Oligodendrocytes

Oligodendrocytes maintain myelin in the central nervous system. Within white matter, interfascicular oligodendrocytes lie in longitudinal arrays, whereas gray matter oligodendrocytes frequently satellite neurons and possibly help regulate the neuronal microenvironment. Each oligodendrocyte membrane surrounds and forms the myelin sheath of several axons, including as many as 60 internodes. The round nuclei are similar in size and appearance to lymphocyte nuclei (Fig. 2). The oligodendrocyte's short and few processes are difficult to visualize at the light microscopic level and contain abundant microtubules but no intermediate filaments. Galactocerebroside, a surface antigen, and Rip, a cytosolic epitope, are markers for mature oligodendrocytes. Diseases affecting oligodendrocytes include those with genetic mutations, such as Pelizaeus–Merzbacher disease; immune-mediated diseases, such as multiple sclerosis; acute hemorrhagic leukoencephalitis; postinfectious encephalomyelitis; and viral infections, such as progressive multifocal leukoencephalopathy. Disorders of the oligodendrocyte cytoskeleton are seen in several brain degenerative diseases. Filamentous inclusions in oligodendrocyte cytoplasm have been identified in multiple system atrophy, progressive supranuclear palsy, and corticobasal degeneration, among others.

Figure 2. Interfascicular oligodendrocytes in white matter. A probable microglial nucleus is denoted by an arrow (luxol fast blue counterstained with hematoxylin and eosin; LHE).

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Oligodendrocyte Morphology

A.M. Butt, in Encyclopedia of Neuroscience, 2009

Oligodendrocytes are highly specialized neural cells whose function is to myelinate central nervous system axons. Myelin sheaths are extraordinarily large extensions of the oligodendrocyte cell membrane and are highly complex structures. The main constituents of myelin are lipids, which provide its insulating properties, and

proteins, which are largely specific to myelin and function to stabilize its structure. In addition to myelinating oligodendrocytes, oligodendrocyte progenitor cells persist in the adult brain and are capable of regenerating myelinating oligodendrocytes. The key issues are to determine the factors that regulate oligodendrocyte differentiation and myelination, which are relevant to basic neurobiology and demyelinating diseases, such as multiple sclerosis.

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Glial Responses to Injury

P.G. Popovich, ... D.M. McTigue, in Encyclopedia of Neuroscience, 2009

Oligodendrocytes and OPCs in the Normal CNS

Oligodendrocytes were first described by Robertson in 1899 as small cells with few processes. In 1921, Rio Hortega officially named these cells oligodendrocytes, which means 'few tree cells.' Like other glia, oligodendrocytes are found throughout the CNS gray and white matter, where individual oligodendrocytes can myelinate as many as 40–50 axons. This important function enables rapid saltatory conduction throughout the CNS. Although myelination is the typical, and sometimes only, function attributed to oligodendrocytes, these cells do more than just ensheath axons. Oligodendrocytes can influence neuron survival, axon transport, axon caliber, and ion channel clustering along axons. Many of these effects are independent of myelination. For instance, simple wrapping of axons by oligodendrocyte processes in the absence of compacted myelin triggers local neurofilament accumulation and axon caliber expansion. In addition, studies of transgenic mice in which oligodendrocytes lacked proteolipid protein or cyclic nucleotide phosphodiesterase revealed marked axon degeneration in the absence of demyelination.

Because oligodendrocytes are postmitotic, trauma or disease of the CNS can cause demyelination with subsequent loss of neurological function. However, in some circumstances, oligodendrocytes may be replaced by $NG2_+$ OPCs, which exist throughout the adult CNS. Currently, the complete functional repertoire of $NG2_+$ cells is unknown; however, it is clear that at least a subset function as OPCs and contribute to oligodendrocyte replacement in the injured or diseased CNS.

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Neuroglia, Overview

Angus M. Brown, Bruce R. Ransom, in Encyclopedia of the Human Brain, 2002

V.A Anatomy

Oligodendrocytes are the cells in the CNS that manufacture and maintain myelin, and as such they play an analogous role to the Schwann cells in the PNS. Hortega characterized oligodendrocytes in the 1920s using silver carbonate impregnation techniques. Not only did Hortega offer the first detailed morphological description of these cells, he also implied their role in myelination. Whereas oligodendrocytes are classified as a single cellular entity, they display a great degree of polymorphism. They are distributed throughout the entire CNS but are most prominent in white matter areas. They tend to be lineated in one of three ways: (1) aligned in rows along nerve fascicles, (2) juxtaposed against neuronal somata, and (3) abutting blood vessels. On the basis of these lineations, Hortega classified oligodendrocytes as interfascicular, perineuronal, and perivascular. In addition to categorizing oligodendrocytes on the basis of lineation, Hortega classified oligodendrocytes into four groups on the basis of morphology. Type 1 oligodendrocytes have spherical somata from which numerous processes project toward nerve fibers. Type 2 oligodendrocytes are located exclusively in white matter areas and have a cuboid cell body shape, with fewer and thicker processes associated with nerve fibers. Type 3 oligodendrocytes have only three or four processes emerging from the somata extending toward nerve fibers. Type 4 oligodendrocytes occur near the entrance of nerves into the CNS and adhere directly to nerve fibers. Improved staining technology using intracellularly injected dyes has increased morphological resolution and provides a more detailed picture of oligodendrocytes. In addition to improved intracellular staining techniques, specific markers for oligodendrocytes have been developed, of which antimyelin basic protein is one of the most commonly used.

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Cell Culture: Primary Neural Cells☆

L. Voloboueva, ... R.G. Giffard, in Reference Module in Neuroscience and Biobehavioral Psychology, 2017

Oligodendrocytes

Oligodendrocytes, the myelinating cells of the CNS, develop from precursor cells known as O-2A progenitors. Although oligodendrocytes traditionally have been defined as myelinating cells, a number of recent reports suggest that these cells

play additional roles. For example, oligodendrocytes in culture express a variety of trophic molecules.

Culturing oligodendrocytes is somewhat more difficult than culturing the other cell types discussed so far. In some cases, mixed glial cultures are the starting point. In other cases, white matter areas are isolated as starting material. More recently protocols have been developed to differentiate oligodendrocytes from precursor cells. When dissociated cells from cerebral hemispheres are cultured, they develop into a monolayer consisting mainly of astrocytes, with oligodendrocyte lineage cells on top of the monolayer. Similar to the case for microglia, cells enriched in oligodendrocyte lineage cells can be obtained from mixed glial cultures by shaking them off the monolayer and replating after centrifugation. Another method for obtaining purer cultures of oligodendrocytes or oligodendrocyte precursors is immunopanning. In this technique, dishes are coated with antibodies against a particular cell surface antigen, the cell suspension is added to the dish to allow selective binding of cells that express that antigen, and unbound cells are removed. Often several panning steps are done sequentially.

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Alcoholic Beverage and Insulin Resistance–Mediated Degenerative Diseases of Liver and Brain

Suzanne M. de la Monte, ... Miran Kim, in Molecular Nutrition and Diabetes, 2016

3.4 Ethanol Effects on Oligodendrocyte Function

Oligodendrocytes produce and maintain myelin in the CNS. Myelin insulates and supports CNS axons. Myelin is a specialized membrane that has a very high dry mass of lipids (70–85%) compared with proteins (15–30%). Oligodendrocytes develop from oligodendrocyte precursor cells, which differentiate into immature followed by mature myelin-producing oligodendrocytes. Mature oligodendrocytes express integral membrane proteins including myelin basic protein (MBP), myelin-associated glycoprotein (MAG), myelin oligodendrocyte glycoprotein, and proteolipid protein (PLP).[137] Myelin PLP (30 kDa) is the most abundant protein in CNS myelin, and its spliced variant is DM-20 (26 kDa).[138]

Oligodendrocytes are highly susceptible to the toxic effects of ethanol. Ethanol delays oligodendrocyte maturation, developmental expression of MBP and MAG, and de novo synthesis of myelin.[139,140] In addition, ethanol impairs insulin signaling by

reducing insulin/IGF receptor binding[141] and altering oligodendrocyte membrane phospholipid content and membrane fluidity.[142] Inhibition of de novo sphingolipid biosynthesis reduces WM myelination, which leads to cognitive impairment.[143]

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