NEUROIMMUNOLOGY AND NEUROINFLAMMATION

■ OLIGODENDROCYTES AND MYELIN

Myelin is the multilayered insulating substance that surrounds axons and speeds impulse conduction by permitting action potentials to jump between naked regions of axons (nodes of Ranvier) and across myelinated segments. Oligodendrocytes contact axons at paranodes, where sodium and potassium channels essential for saltatory conduction are clustered. Molecular interactions between the myelin membrane and axon are required to maintain the stability, function, and normal life span of both structures. The process of myelination is directed both by axon-derived cues as well as the physical properties of the axon-membrane curvature. Importantly, ongoing neuronal activity influences both the differentiation of oligodendrocytes as well as the extent of myelination, a process referred to as *adaptive myelination*. A single oligodendrocyte usually ensheaths multiple axons in the central nervous system (CNS), whereas in the peripheral nervous system (PNS), each Schwann cell typically myelinates a single axon. Myelin is a lipid-rich material formed by a spiraling process of the membrane of the myelinating cell around the axon, creating multiple membrane bilayers that are tightly apposed (compact myelin) by charged protein interactions. A number of clinically important neurologic disorders are caused by inherited mutations in myelin proteins **(Chap. 446)**, and constituents of myelin also have a propensity to be targeted as autoantigens in autoimmune demyelinating disorders **(Chap. 447)**.

Premyelinating oligodendrocyte precursor cells (OPCs) are highly motile cells that migrate extensively during development and in the adult brain following injuries to the myelin sheath. OPCs migrate along the inner (or abluminal) surface of endothelial cells, a process regulated by *Wnt* pathway signaling and upregulation of the chemokine receptor Cxcr4 that drives their attachment and retention to the vasculature. In the normal adult brain, large numbers of OPCs are widely distributed. Following demyelination, remyelination is largely dependent on OPCs that differentiate into myelin-producing oligodendrocytes and produce characteristic thinly remyelinated