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·**Editorial**·

Myelin in development and disease

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Myelin is an evolutionarily novel and important structure for the proper functioning of the vertebrate nervous system. In the central nervous system (CNS), the myelin sheath is elaborated by oligodendrocytes, and is composed of multiple layers of specialized cell membrane wrapping around axons with periodic interruptions at the nodes of Ranvier. The major function of the myelin sheath is to provide ionic insulation to ensure rapid and saltatory conduction of electrical pulses along axons. In addition, myelin provides neurotrophic support for axons, as they become increasingly dependent on myelin-derived signals for survival. Despite the importance of myelin in the functioning of the CNS, oligodendrocytes are particularly susceptible to genetic and environmental perturbations, and demyelination can be triggered by many pathological conditions including traumatic injury, autoimmune disease (multiple sclerosis, MS), heavy metal toxicity, and hypoxia. Loss of myelin sheaths in the CNS not only results in the compromised conduction of electrical signals, but also causes progressive degeneration of axons and ultimately neuronal loss. Spontaneous myelin repair from immature oligodendrocyte progenitor cells (OPCs) is not effective in demyelinating lesions, due either to the absence of stimulatory developmental signals that are no longer produced in the adult environment, or to the presence of inhibitory factors peculiar to this environment. Understanding the early molecular events that regulate myelin formation during normal development can provide important insights into the creation of therapeutic strategies to promote axonal remyelination in demyelinating patients.

Myelin development starts with the generation of OPCs from restricted loci of neuroepithelial cells in the developing neural tube. Before their differentiation into mature myelinating cells, OPCs undergo extensive migration and proliferation followed by a series of morphological and molecular changes. The past decade has witnessed great advances in understanding the molecular and genetic control of oligodendrogenesis and myelin development. In this special issue, He and Lu[1] first provide a comprehensive overview of the molecular regulation of oligodendrocyte specification and differentiation by both genetic and epigenetic mechanisms. Huang *et al.*[2] further discuss the timing control of oligodendrocyte differentiation during development and the possible underlying mechanisms. The next two papers[3,4] describe a special type of oligodendrocyte progenitor, the NG2-positive polydendrocyte, and provide strong evidence for its active participation in myelin repair following demyelinating lesions.

Oligodendrocyte differentiation is accompanied by the formation of compact myelin sheaths around axons. Axonal myelination is a complicated, coordinated biological process. In this issue, Dr. Macklin provides a thorough review of both positive and negative regulators of CNS myelination, and presents additional original data on the negative regulation of axonal myelination[5]. Mei *et al.*[6] discuss the interesting and important topic of how the numbers and lengths of myelin internodes formed by oligodendrocytes are controlled at the molecular level.

Once myelin is formed, there are extensive and intimate interactions between axons and oligodendrocyte processes. Bankston *et al.*[7] describe how neurons are supported by oligodendrocytes *via* diverse molecular and cellular mechanisms including metabolic and neurotrophic support, and suggest that oligodendrocyte pathology may

be an important mechanism contributing to the initiation and/or progression of neurodegeneration. It is well known that myelin loss in the autoimmune disease MS can cause secondary axonal degeneration and neuronal loss. Zhang *et al.*[8] provide an in-depth review of the pathophysiology of MS, current treatments, and potential strategies for the development of drug candidates that directly target remyelination and neuroprotection. Also, Cao and He discuss the response and polarization of microglia and macrophages in MS, and their effects on its pathogenesis and repair[9]. Furthermore, Liu *et al.*[10] consider another form of demyelinating disease, periventricular leukomalacia, which is characterized by selective white-matter myelin damage in premature infants and is the leading cause of cerebral palsy in these infants. In adult animals, demyelination can be selectively induced in the corpus callosum by cuprizone, and this demyelination can cause deficits in exploratory behavior. Interestingly, the vulnerability of myelin to this chemical appears to be age-dependent[11].

In summary, the articles presented in this special issue cover a wide spectrum of oligodendrocyte biology and pathology. We hope that this special issue will further stimulate interest in the further identification and characterization of regulatory molecules involved in normal myelination, and more importantly, in developing novel molecular and cellular approaches to facilitating myelin repair in demyelinating diseases and in spinal cord/brain injury.

REFERENCES

[1] He L, Lu QR. Coordinated control of oligodendrocyte development by extrinsic and intrinsic signaling cues. Neurosci Bull 2013, 29(2): 129–143.

[2] Huang H, Zhao XF, Zheng K, Qiu M. Regulation of the timing of oligodendrocyte differentiation: mechanisms and perspectives. Neurosci Bull 2013, 29(2): 155–164.

[3] Zuo H, Nishiyama A. Polydendrocytes in development and myelin repair. Neurosci Bull 2013, 29(2): 165–176.

[4] Bai L, Hecker J, Kerstetter A, Miller RH. Myelin repair and functional recovery mediated by neural cell transplantation in a mouse model of multiple sclerosis. Neurosci Bull 2013, 29(2): 239–250.

[5] Ahrendsen J, Macklin W. Signaling mechanisms regulating myelination in the central nervous system. Neurosci Bull 2013, 29(2): 199–215.

[6] Mei F, Chong SYC, Chan JR. Myelin-based inhibitors of oligodendrocyte myelination: clues from axonal growth and regeneration. Neurosci Bull 2013, 29(2): 177–188.

[7] Bankston AN, Mandler MD, Feng Y. Oligodendroglia and neurotrophic factors in neurodegeneration. Neurosci Bull 2013, 29(2): 216–228.

[8] Zhang Y, Guo TB, Lu H. Promoting remyelination for the treatment of multiple sclerosis: opportunities and challenges. Neurosci Bull 2013, 29(2): 144–154.

[9] Cao L, He C. Polarization of macrophages and microglia in inflammatory demyelination. Neurosci Bull 2013, 29(2): 189–198.

[10] Liu XB, Shen Y, Plane JM, Deng W. Vulnerability of premyelinating oligodendrocytes to white-matter damage in neonatal brain injury. Neurosci Bull 2013, 29(2): 229–238.

[11] Wang H, Li C, Wang H, Mei F, Liu Z, Shen HY, *et al.* Cuprizone-induced demyelination in mice: age-related vulnerability and exploratory behavior deficit. Neurosci Bull 2013, 29(2): 251–259.