Oligodendrocyte calcium signaling promotes actin-dependent myelin sheath extension.

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Presenter: Tzu-Chia Lin
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Location: Room 601, Med College Building

Background:

The major role of oligodendrocytes in the central nervous system (CNS) is to form the myelin, a lipid-rich, spirally-wrapped structure that is important for action potential propagation of neuronal axon, memory acquisition, and learning. After terminal differentiation of oligodendrocyte precursor cells (OPCs) into myelinating oligodendrocytes, the morphology, namely length and thickness, of forming myelin sheath is tightly regulated under unknown mechanisms. A potential candidate for regulating oligodendrocyte cell biology during myelination and remodeling is calcium signaling (Ca^{2+}), which is indispensable in cell biological processes relevant to myelination, such as cytoskeletal dynamics, exocytosis, and gene expression. However, the detailed mechanisms regulating myelin sheath morphology are under investigation.

Objective/Hypothesis:

To determine the role of oligodendrocyte calcium signaling during myelination of the mouse CNS by using newly-developed genetic tools.

Results:

The authors used a transgenic mouse model- ‘‘CalEx^{flox}’’ (short for Calcium Extrusion)- to attenuate calcium signaling specifically in pre-myelinating cells of the central and peripheral nervous system (OL-CalEx). They demonstrated that oligodendrocyte survival or differentiation and myelin thickness were unaffected in OL-CalEx mice. Instead, increased myelin outfolding and shorter myelin sheaths were observed during development in OL-CalEx mice. Using specific labeling approaches, the authors also confirmed that actin filament levels in nascent myelin sheaths during development were positively regulated by oligodendrocyte calcium signaling. By in vivo injection of an oligodendrocyte-specific DeAct adeno-associated virus construct, which selectively induced actin disassembly using the myelin basic protein promoter (pMBP), the author’s data suggested that cortical actin—actin was closely associated with the plasma membrane, and had the potential to prevent outfoldings. Finally, stabilizing actin via a genetically construct rescued myelin morphology defects in OL-CalEx mice.

Conclusion:

In summary, these results indicate that oligodendrocyte calcium signaling is required for actin-dependent regulation of myelin membrane morphology.