GLIA

# Changing places

File name: NRN0306_JQ1_HL
Word count: 431
Accompanying picture: Yes
File name of picture:

**URLs**

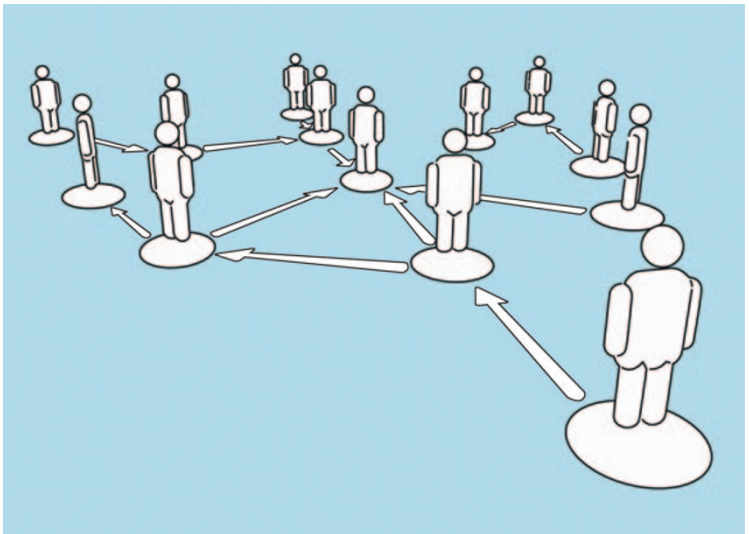
Although myelin serves similar functions in the PNS and CNS, its main protein constituent differs: the type I integral membrane protein $P_0$ (protein zero) is present in PNS myelin, whereas the tetraspan membrane protein PLP (proteolipid protein) resides in the CNS. It is thought that $P_0$ was initially the primary structural protein of both PNS and CNS myelin — which first appeared ~440 million years ago in cartilaginous fishes — but was replaced by PLP in the CNS after the divergence of the bony fishes ~400 million years ago. What could be the benefits of the $P_0$ to PLP conversion during evolution?

To address this issue, Yin and colleagues reversed the evolutionary step by generating transgenic mice that expressed $P_0$, rather than PLP, in the CNS. In these $P_0$-CNS animals, the level of $P_0$ expression in the CNS is similar to that of PLP in normal mice, and replacing PLP with this ancestral protein in the CNS does not affect the expression of other myelin proteins. In addition, $P_0$, like PLP, is able to stabilize compact CNS myelin, and its distribution is indistinguishable from that of PLP in wild-type mice. Electron microscopy studies show that $P_0$-CNS myelin is structurally similar to its PNS counterpart, and has greater periodicity (membrane spacing) than that of wild-type CNS myelin.

Next, the researchers studied the effect of replacing PLP with $P_0$ by measuring the animals' motor function. In $P_0$-CNS mice, motor performance was normal at 6 months of age, but declined significantly (by 90%) by 1 year — by which time 50% of the animals had died. These observations are consistent with the precocious accumulation of the amyloid precursor protein — a reliable indicator of axonal pathology in primary myelin disease affecting PLP-deficient mice — in the brains of $P_0$-CNS mice at a young age. So, PLP, but not $P_0$, might provide trophic support for axons in the CNS, thereby delaying the onset of neurodegeneration.

This elegant study indicates that the shift from $P_0$ to PLP during CNS myelin evolution was associated with an important neuroprotective function of myelin-forming glia. This finding may further our understanding of human myelin diseases, in which a spectrum of neurological disabilities is associated with null mutations, deletions and point mutations in the *PLP* gene.

*Jane Qiu*



**ORIGINAL RESEARCH PAPER** Yin, X. *et al.* Evolution of a neuroprotective function of central nervous system myelin. *J. Cell Biol.* 30 January 2006 (doi:10.1083/jcb.200509174)
**FURTHER READING** Yoshida, M. & Colman, D. Parallel evolution and coexpression of the proteolipid proteins and protein zero in vertebrate myelin. *Neuron* **16**, 1115–1126 (1986)
**WEB SITE**
**Trapp's laboratory:** http://www.lerner.ccf.org/neurosci/trapp/