



Discovery through Collaboration

Recent discoveries by MRF scientists – July 2004

NGF controls axonal receptivity of Myelination by Schwann Cells and Oligodendrocytes

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When it comes to the complex sets of interactions between axons and glia that leads to myelination, axons run the show. They provide the signals that dictate whether or not they become myelinated in both the central nervous system (CNS) and peripheral nervous system (PNS), but the identities of these signals and how they are regulated remain two of the central unanswered questions in myelin biology. Trent Watkins, an MRF researcher in Ben Barres's lab at Stanford University, has combined efforts with Jonah Chan of Eric Shooter's lab (also at Stanford), to take a big step forward in understanding the nature of these signals, uncovering a few surprises along the way. They found that the neurotrophin nerve growth factor (NGF), long known to play a role in the early survival decisions of certain populations of developing sensory neurons, later regulates the expression of the axonal signals that control myelination of those neurons. Axons that are exposed to NGF display a different receptivity to myelination than axons that are deprived of the growth factor, pinpointing NGF as the first known regulator of axonal signals for myelination. The specificity of NGF for a particular population of axons raises the interesting possibility that each population of neurons is regulated by a different set of growth factors.

The real surprise came when the researchers compared how NGF-treated and NGF-deprived axons interacted with the two different types of myelinating glia, the Schwann cells of the PNS and the oligodendrocytes of the CNS. Although researchers have long suspected that axons use the same sets of signals to direct myelination, regardless of the myelinating cell, NGF-treated axons present a set of signals that encourage Schwann cell myelination, whereas only NGF-deprived axons provided signals that could promote both oligodendrocyte maturation and myelination. It seems then that, instead of using a universal signal to tell glia, "myelinate me," axons may have the ability to regulate myelination in distinct ways for each glial cell, a finding that has interesting implications for the types of cells that may be appropriate for transplantation-based remyelination strategies.

The discovery also has led the way to the first rapid CNS myelinating coculture system using defined populations of neurons and glia, providing a platform for the long-sought goal of identifying the precise axonal signals that control myelination. Researchers hope that this new approach will lead to insights relevant to promoting remyelination in both MS and peripheral neuropathies.