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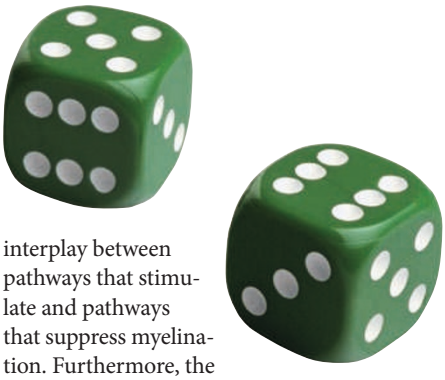

DEVELOPMENT

Schwann cells roll the dice

Myelination by Schwann cells greatly increases the conduction velocity of action potentials in peripheral neurons. MicroRNAs (miRNAs) are known to regulate diverse processes in neurons, but their role in myelination had not been investigated. Now, Pereira *et al.* show that mice with a conditional knockout of *Dicer*, which encodes a key player in the downregulation of mRNA levels by miRNAs, have impaired Schwann cell maturation and axon myelination.

During development, pro-myelinating Schwann cells surround groups of axons before selecting one axon for myelination — a process known as radial sorting. The switch by Schwann cells from a pro-myelinating to a myelinating state is accompanied by a dramatic change in gene expression.

Mice that lacked *Dicer* in Schwann cells displayed discoordination, tremor and ataxia at postnatal day 24, and these symptoms worsened with age. These animals also had thinner and more transparent sciatic nerves than wild-type controls, indicating a defect in myelination. Investigation of sections of the sciatic nerve revealed that Schwann cells of *Dicer*-mutant mice were generally successful in radial sorting, but failed to myelinate axons.

Next, the authors measured the levels of mRNA with gene chip arrays and determined protein levels to identify factors that were deregulated in *Dicer* mutants. The expression levels of factors that induce myelination, such as the transcription factor early growth response protein 2 (EGR2; also known as KROX20), were downregulated in *Dicer* mutants, whereas levels of myelination inhibitors (such as SOX2), which are normally downregulated during Schwann cell differentiation, remained unchanged. These findings suggest that loss of *Dicer* causes deregulation of the interplay between pathways that stimulate and pathways that suppress myelination. Furthermore, the authors found that ERBB2 levels were reduced in Schwann cells of *Dicer* mutants. ERBB2 is part of a receptor complex that is required for neuregulin-dependent axon–Schwann cell signalling. Downregulation of ERBB2 in *Dicer* mutants might therefore also contribute to the myelination defects.

In summary, Dicer has several functions in Schwann cell maturation. The identification of the miRNAs involved at different stages of this process might inform our understanding of demyelinating disorders.

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ORIGINAL RESEARCH PAPER Pereira, J. A. *et al.* Dicer in Schwann cells is required for myelination and axonal integrity. *J. Neurosci.* **30**, 6763–6775 (2010)