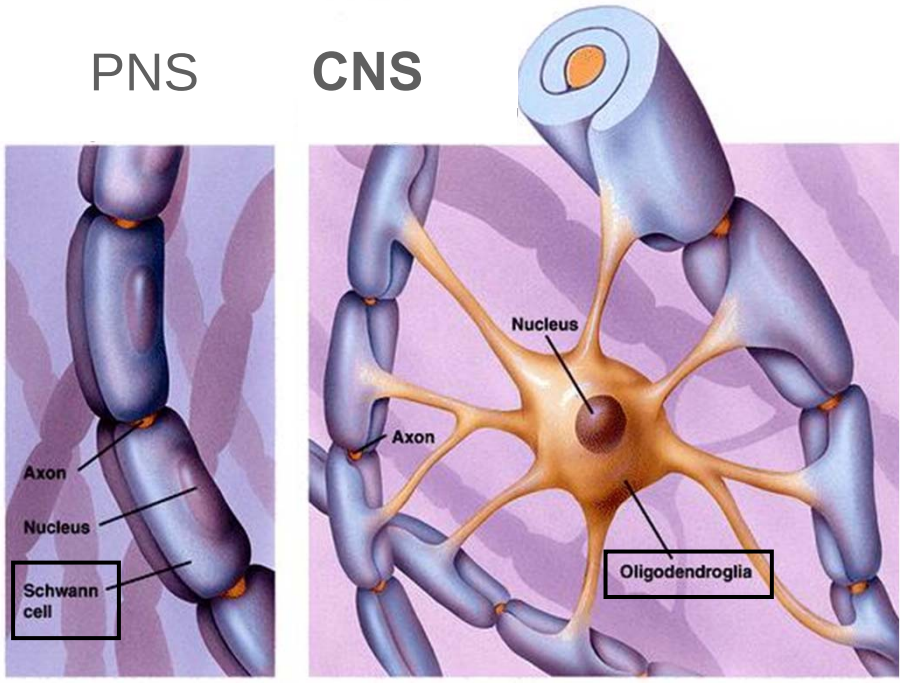
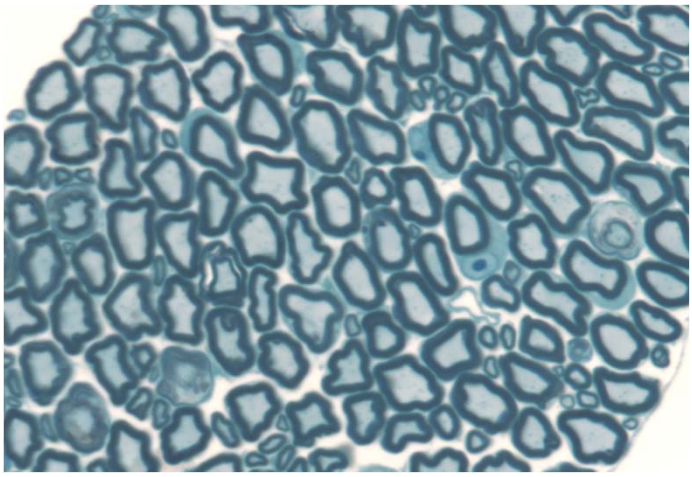
BSc Neuroscience: Module 1

Schwann cells

R. Reynolds 2011

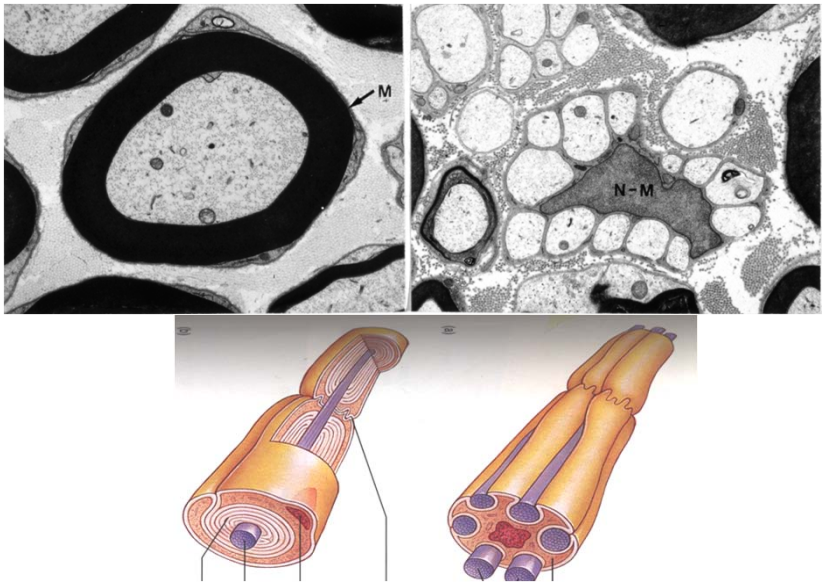


Schwann cells – myelin producing cells of the PNS

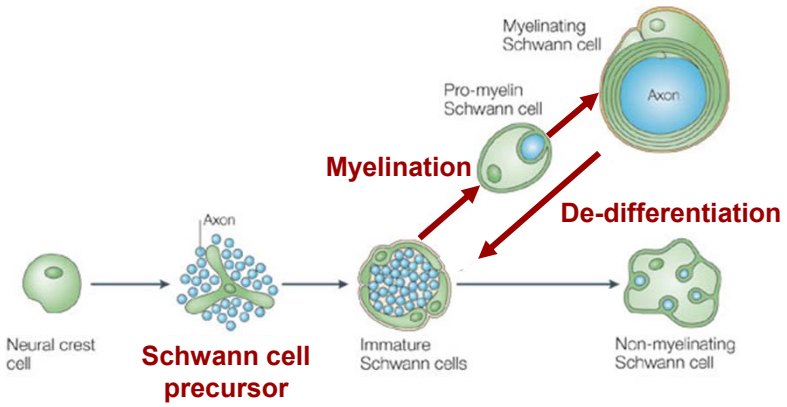


Myelinating schwann cells have a 1:1 relationship with an axon segment, whereas oligodendrocytes produce multiple myelin sheaths

Myelinating and non-myelinating Schwann cells in peripheral nerve

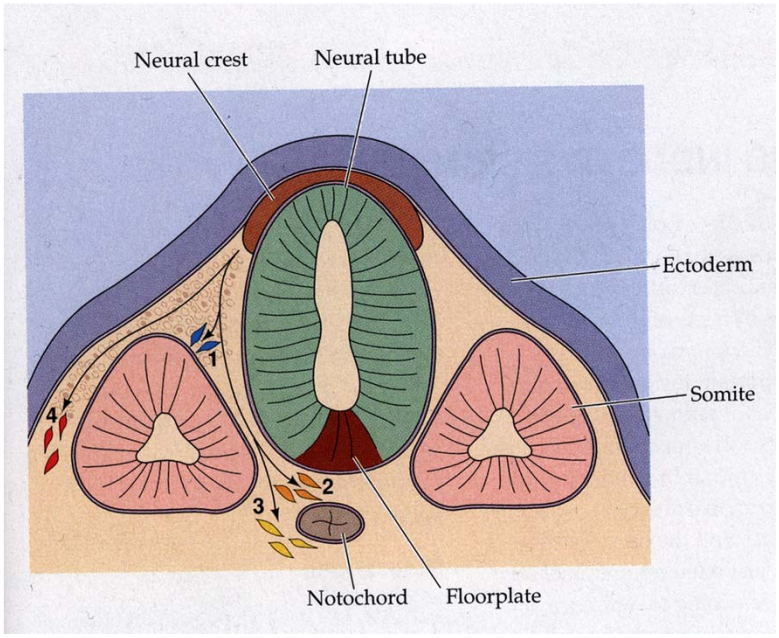


THE SCHWANN CELL LINEAGE IN RODENT SPINAL NERVES

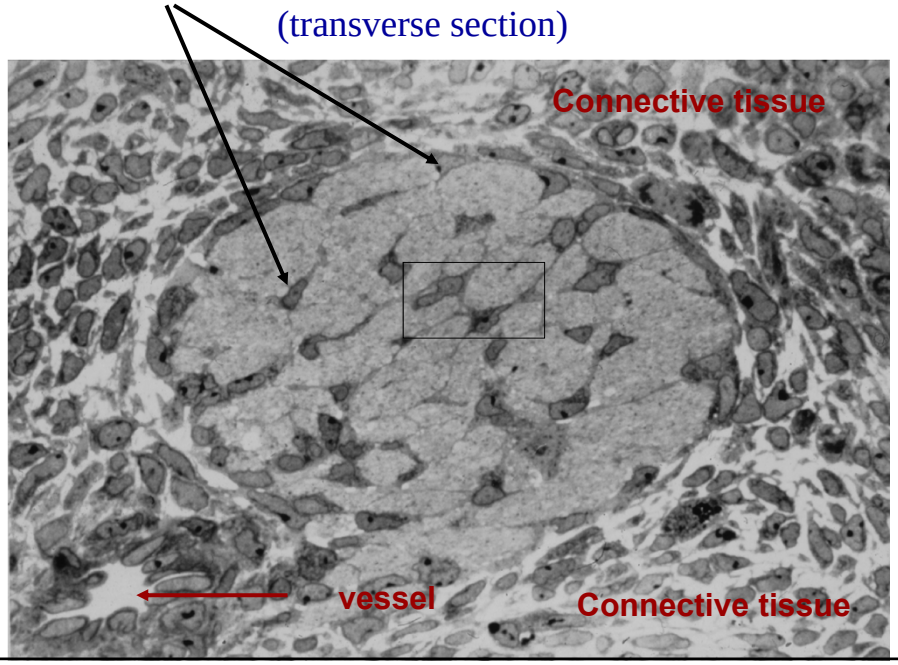


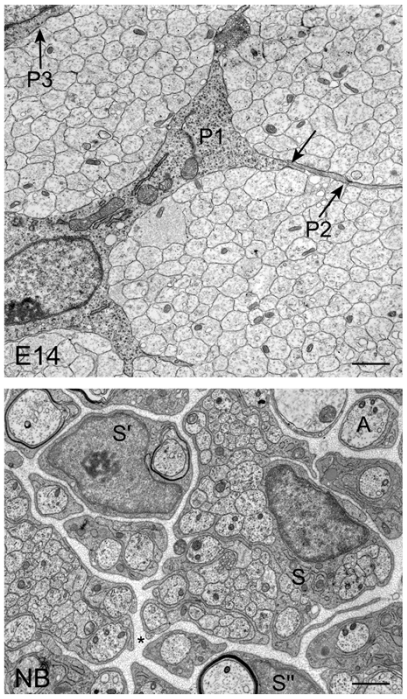
Jessen and Mirsky, Nature Reviews | Neuroscience

Schwann cells originate in the neural crest



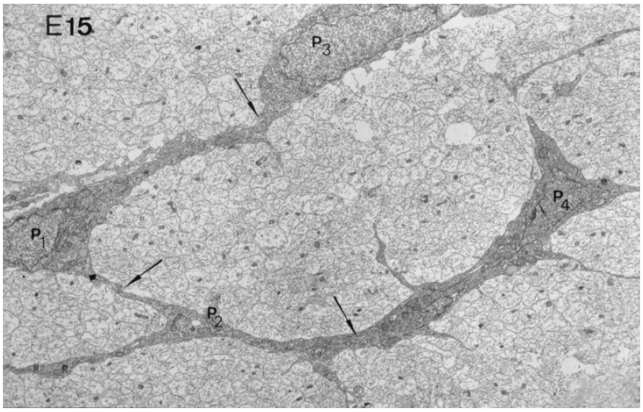
Schwann Cell Precursors in E 12/14 rat sciatic nerve (transverse section)





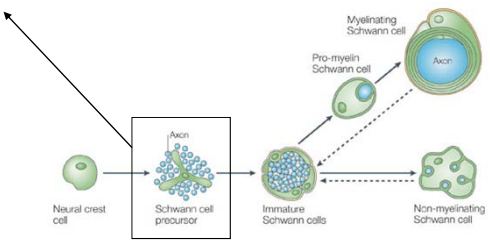
Precursors

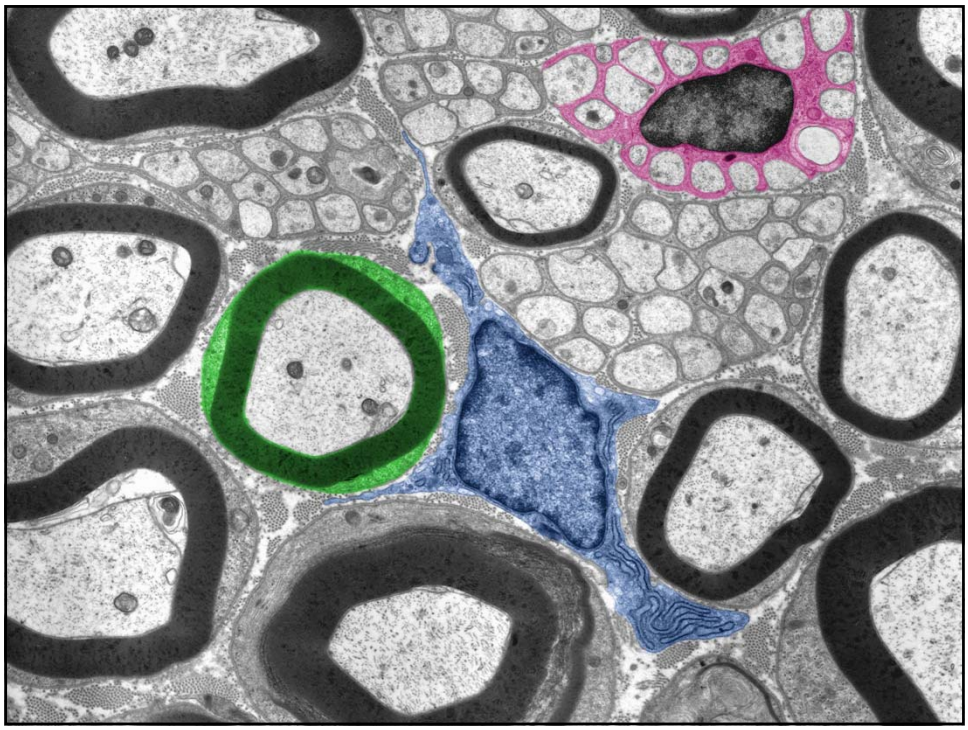
Schwann cells



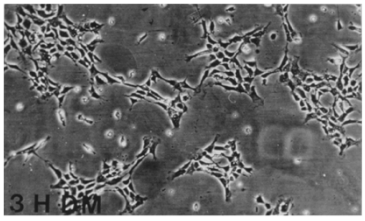
Embryo day 15 rat sciatic nerve

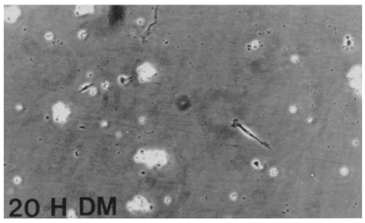
What is the function of SCPs ?



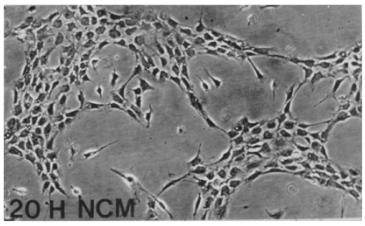


Schwann cell precursors
die under normal culture conditions

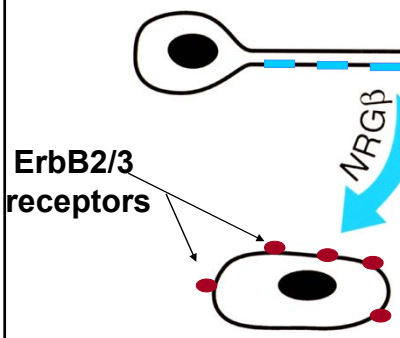




Schwann cell precursors are rescued by neurone-conditioned medium

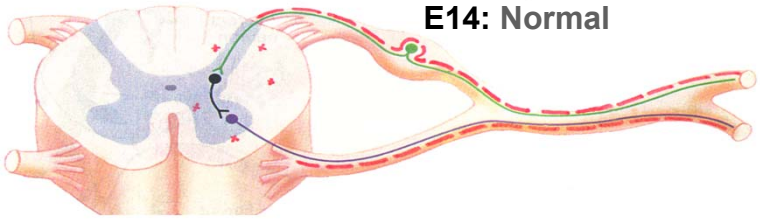


Neuregulin 1 β is an indispensable survival signal for Schwann cell precursors

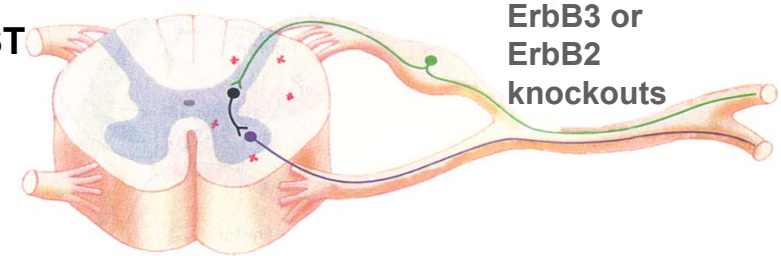


Neuregulin 1 is also:
- a mitogen
- lineage progression signal

CONTROL



TEST

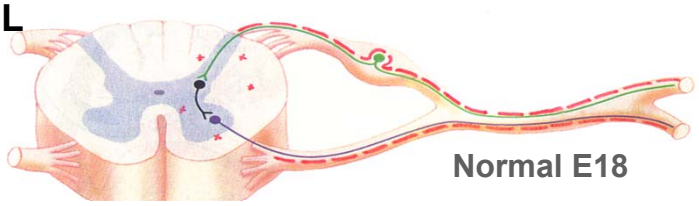


What this tells us about SCPs → Neuregulin is a key survival factor

What this tells us about neurons → Peripheral nerves form, even in the absence of glial cells

An unexpected observation: **80% of sensory & motor neurones eventually die, if glial cells are removed**

CONTROL



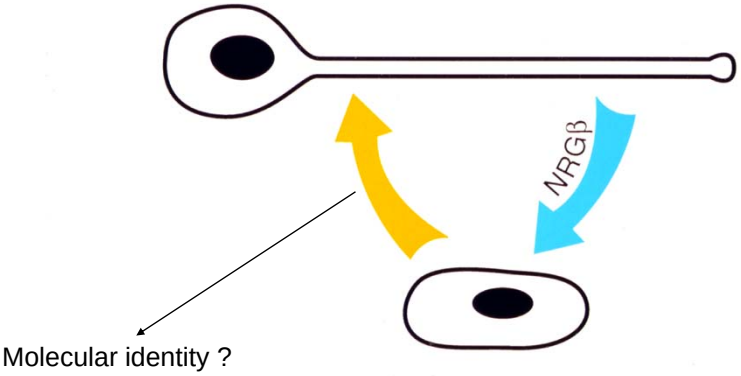
Normal E18

TEST

Knockout E 18:

Glial cells control neuronal survival

Neurones and Schwann cell precursors rescue each other during development

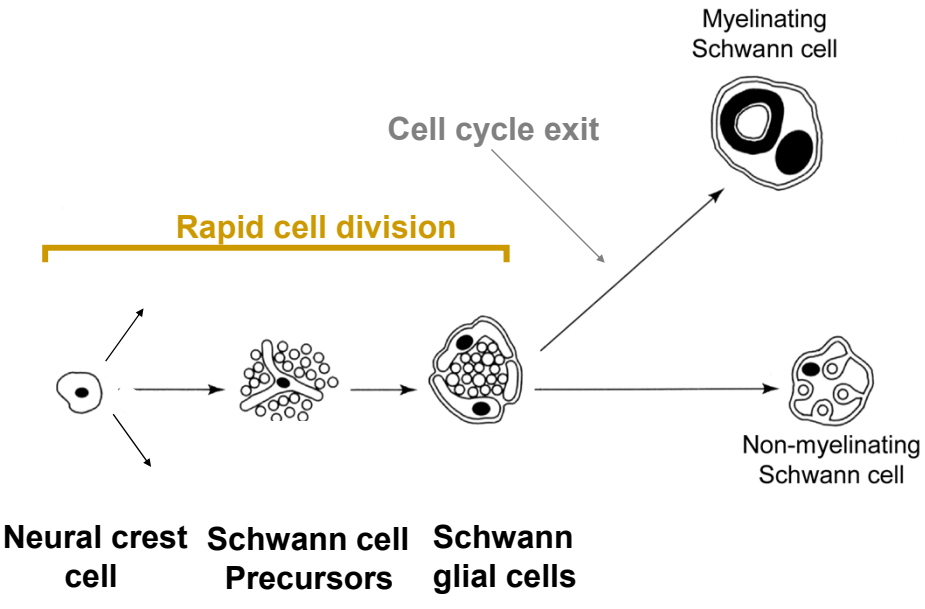


Molecular identity ?

Schwann cells are generated between E15 and E17

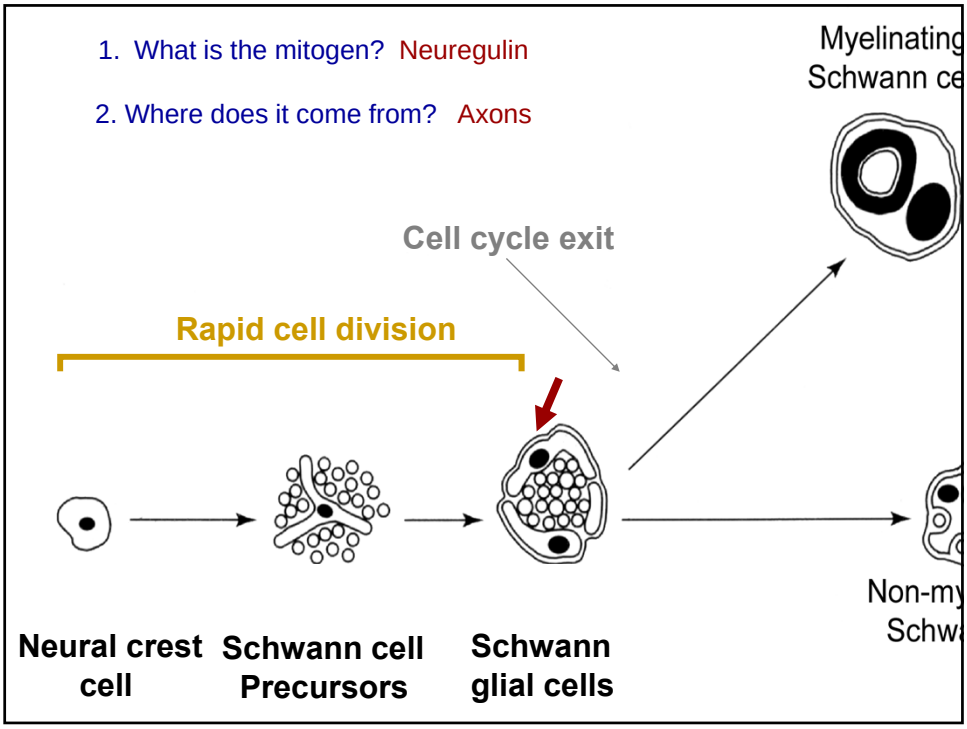
in nerves of the rat hind limb

PROLIFERATION

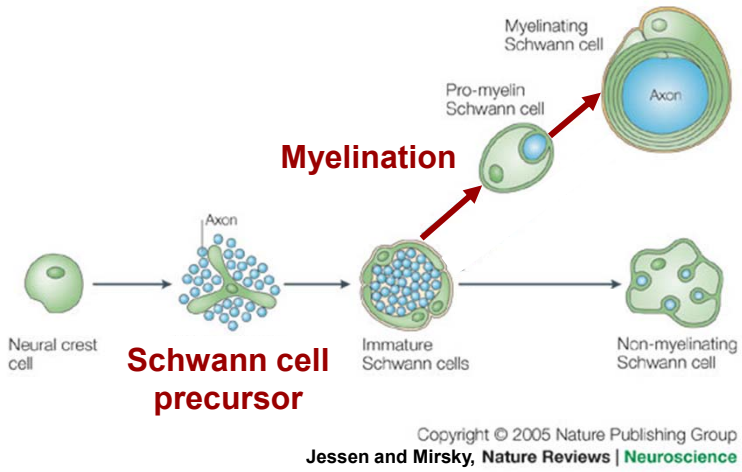


1. What is the mitogen? Neuregulin

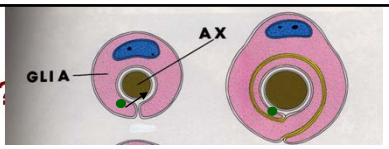
2. Where does it come from? Axons

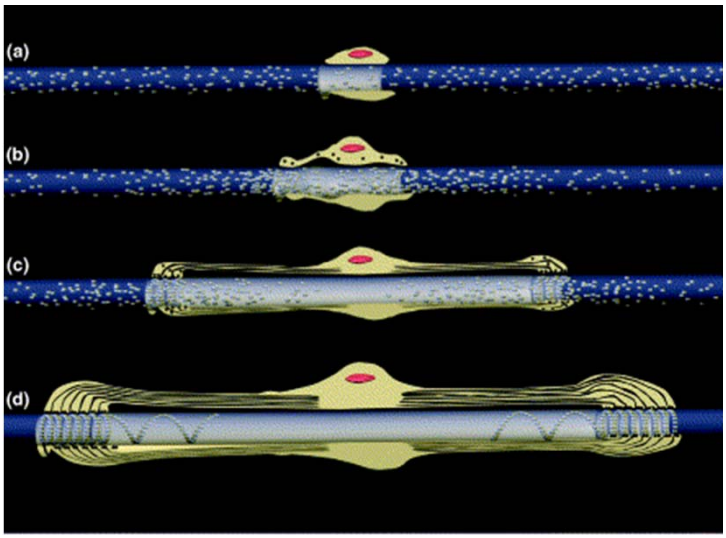


THE SCHWANN CELL LINEAGE IN RODENT SPINAL NERVES



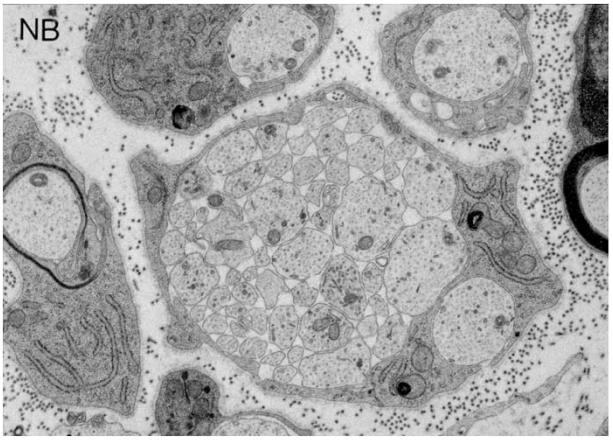
Myelin wrapping – how does it really happen?



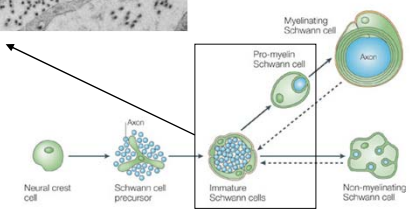


Current Opinion in Neurobiology

Myelination



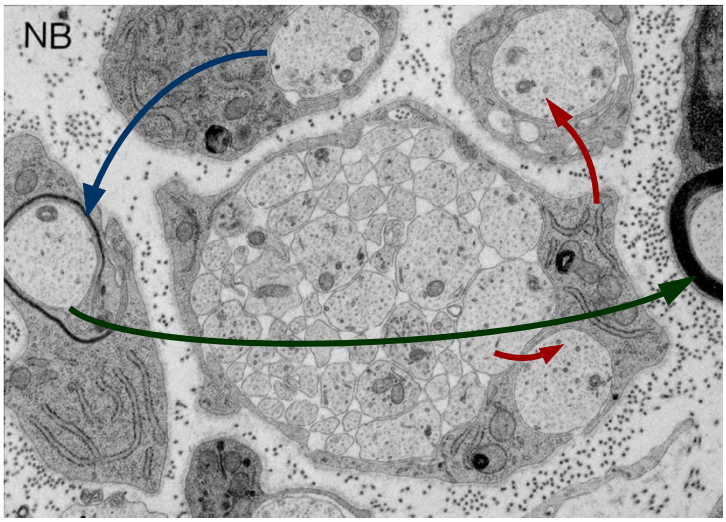
The sciatic nerve at birth



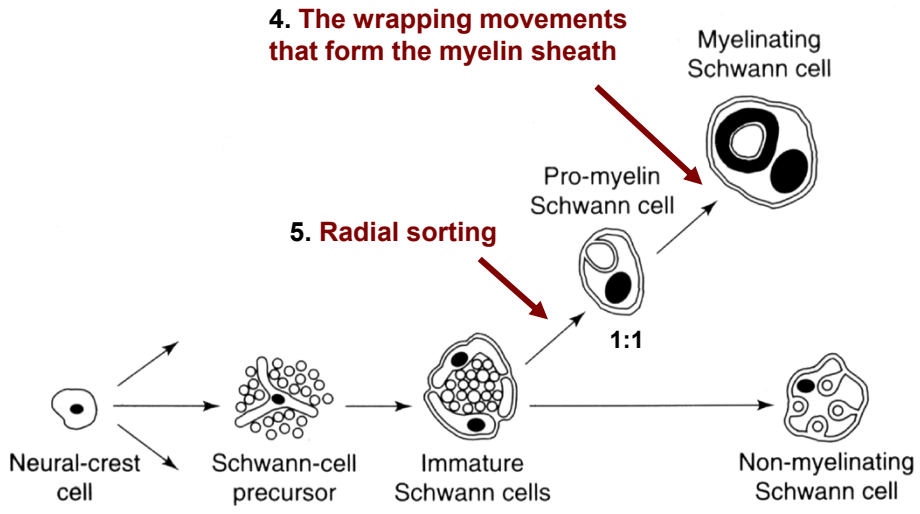
Radial sorting (formation of 1:1 relationship)

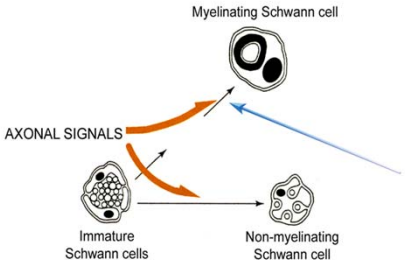
Activation of the myelin programme

Wrapping & myelin sheath formation



THE SCHWANN CELL LINEAGE IN RAT AND MOUSE





ACTIVATION OF THE MYELIN PROGRAMME:

1 **Withdrawal from the cell cycle**

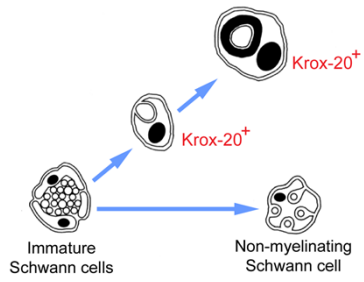
2 **Up-regulation of the myelin proteins (Pzero, MBP and many others)**

3 **Down-regulation of immature Sch proteins**

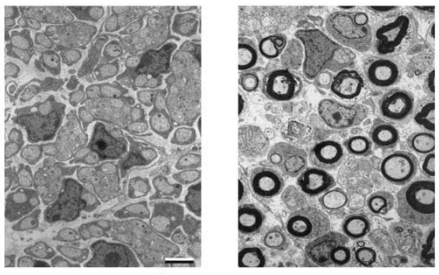
4 **Membrane synthesis and wrapping to form the myelin sheath**

The transcription factor Krox-20 :

Selectively expressed in myelinating cells



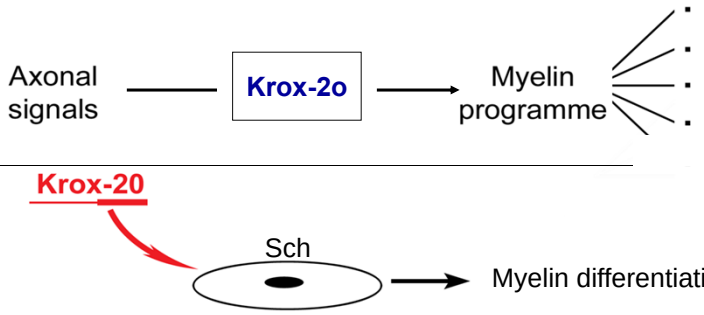
Essential for myelination



Krox-20$^{-/-}$ wildtype

From Topilko and Meijer 2001

Drives the myelination programme



Krox-20 expression is sufficient to activate the myelin programme in isolated Sch in vitro

Krox-20 is a global regulator of myelin differentiation

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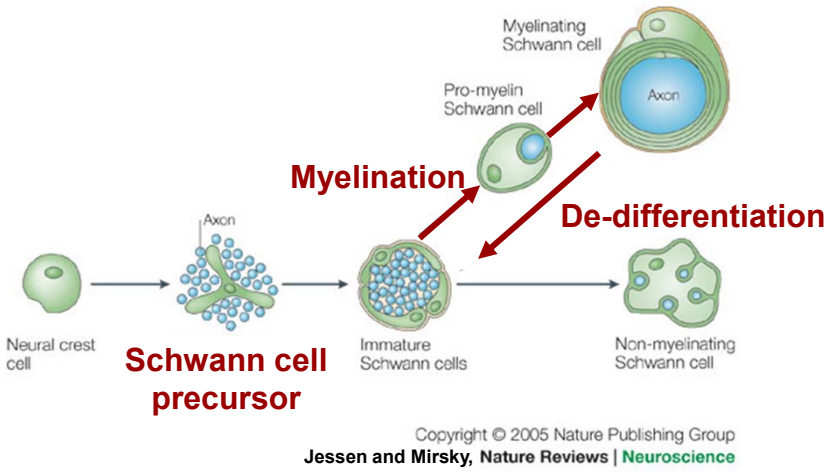

References

1. *KR Jessen & R Mirsky (2005) The origin and development of glial cells in peripheral nerves. Nat Rev Neuroscience 6:671-682*

2. *KR Jessen & R Mirsky (2008) Negative regulation of myelination. Glia 56:1552-65.*