

# The Effect of PMP2 on Myelination During Development

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Presented by Ei Aung

Mentored by Dr. Sophie Belin, Dr. Yannick Poitelon, Sophia Elston, Jiayue Hong, Ethan Macfarland

# About Me

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## Education

Columbia High School

## NextGen Immersion Program

Myelin Lab

## Interests

Running

Thrifting

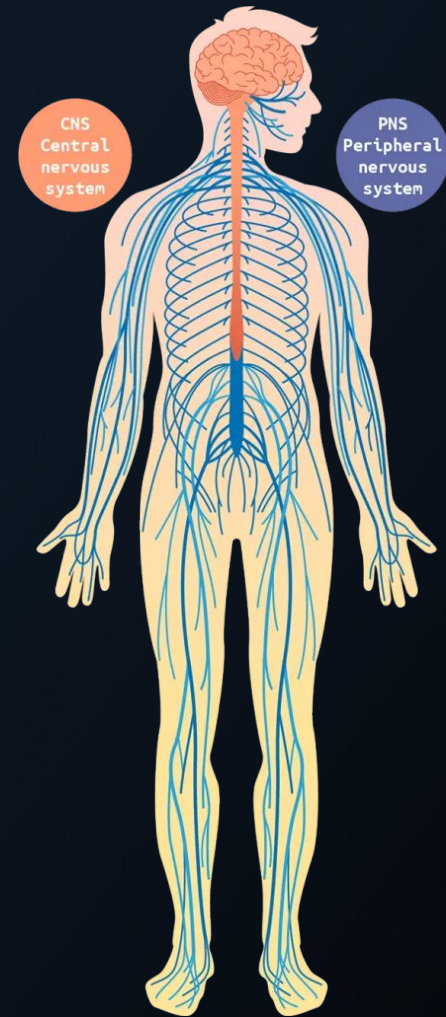
Painting & Journaling



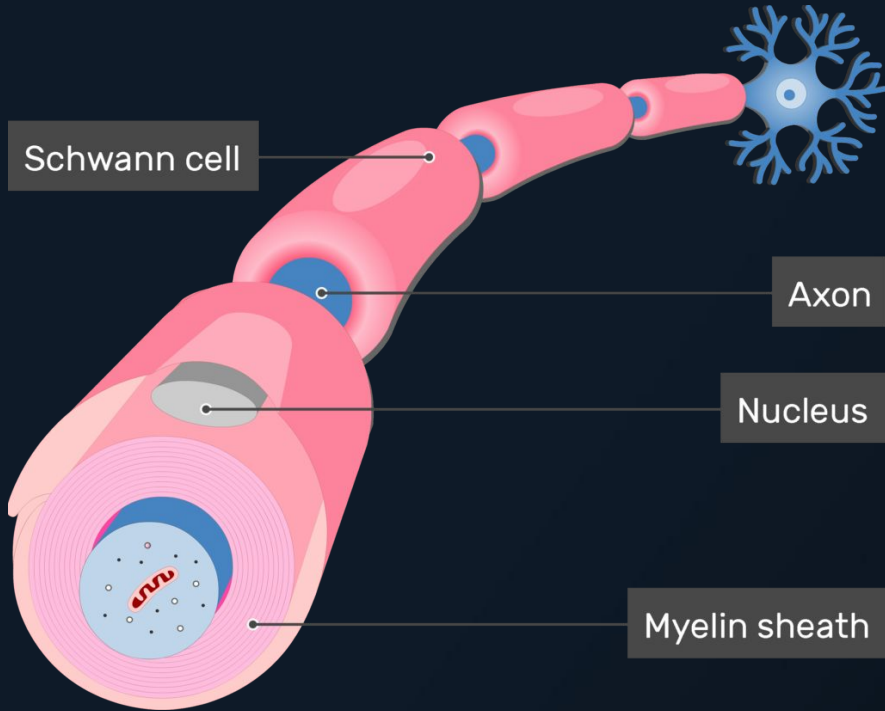
# Introduction to the Peripheral Nervous System

- ❖ The PNS is a network of nerves that run through the head, neck and body
- ❖ Allows the brain and spinal cord to send and receive information throughout the body.
- ❖ Action Potential

Professional, C. C. M. (n.d.). Peripheral Nervous System (PNS). Cleveland Clinic.  
<https://my.clevelandclinic.org/health/body/23123-peripheral-nervous-system-pns>



# Myelination



# Peripheral Neuropathies

- ❖ Peripheral neuropathies occur when nerves are damaged
- ❖ It can be caused by demyelination
- ❖ Charcot-Marie-Tooth Disease
- ❖ Motor, sensory and autonomic nerves can all be damaged

Peripheral neuropathy - Symptoms and causes - Mayo Clinic. (2023, September 2). Mayo Clinic. <https://www.mayoclinic.org/diseases-conditions/peripheral-neuropathy/symptoms-causes/syc-20352061>



# Peripheral Myelin Protein 2 (PMP2)

- ❖ Fatty Acid Binding Protein 8 (FABP8)
- ❖ PMP2 is a major myelin protein
- ❖ PMP2 is only expressed in a subset of myelinating Schwann cells
- ❖ PMP2 gene mutations can cause CMT Type 1
- ❖ A loss of PMP2 does not impede myelin thickness

Zenker, J., Stettner, M., Ruskamo, S., Domènech-Estévez, E., Baloui, H., Médard, J. J., Verheijen, M. H., Brouwers, J. F., Kursula, P., Kieseier, B. C., & Chrast, R. (2014). A role of peripheral myelin protein 2 in lipid homeostasis of myelinating Schwann cells. *Glia*, 62(9), 1502–1512. <https://doi.org/10.1002/glia.22696>

Hong, J., Garfalo, R., Kabre, S., Humml, C., Velanac, V., Roué, C., Beck, B., Jeanette, H., Haslam, S., Bach, M., Arora, S., Acheta, J., Nave, K. A., Schwab, M. H., Jourdain, D., Poitelon, Y., & Belin, S. (2024). PMP2 regulates myelin thickening and ATP production during remyelination. *Glia*, 72(5), 885–898. <https://doi.org/10.1002/glia.24508>

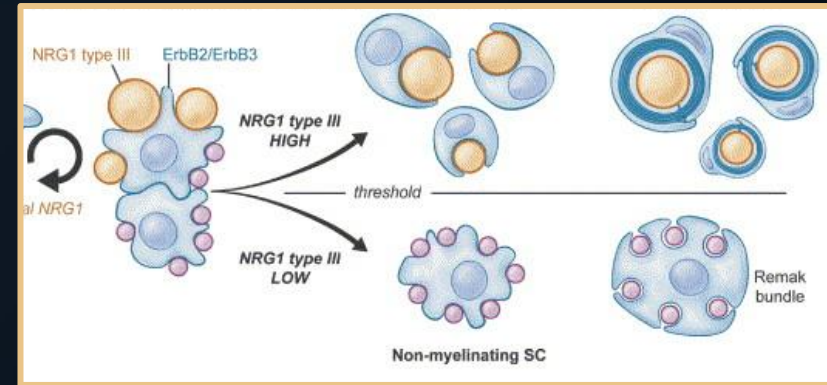
Ruskamo, S., Nieminen, T., Kristiansen, C. K., Vatne, G. H., Baumann, A., Hallin, E. I., Raasakka, A., Joensuu, P., Bergmann, U., Vattulainen, I., & Kursula, P. (2018). Publisher Correction: Molecular mechanisms of Charcot-Marie-Tooth neuropathy linked to mutations in human myelin protein P2. *Scientific reports*, 8(1), 517. <https://doi.org/10.1038/s41598-017-18751-7>

# Neuregulin-1 Type III (NRG1 Type III)

- ❖ Determines schwann cell fate and the capacity of schwann cells to produce myelin and its thickness
  - Myelinating schwann cells are high in NRG1t3

Belin, S., Ornaghi, F., Shackelford, G., Wang, J., Scapin, C., Lopez-Anido, C., Silvestri, N., Robertson, N., Williamson, C., Ishii, A., Taveggia, C., Svaren, J., Bansal, R., Schwab, M. H., Nave, K., Fratta, P., D'Antonio, M., Poitelon, Y., Feltri, M. L., & Wrabetz, L. (2019). Neuregulin 1 type III improves peripheral nerve myelination in a mouse model of congenital hypomyelinating neuropathy. *Human molecular genetics*, 28(8), 1260–1273. <https://doi.org/10.1093/hmg/ddy420>

- ❖ Increasing NRG1 Type III expression can improve myelination in peripheral neuropathy mouse models.
- ❖ PMP2 is a key molecular event downstream of NRG1tIII overexpression mediated remyelination



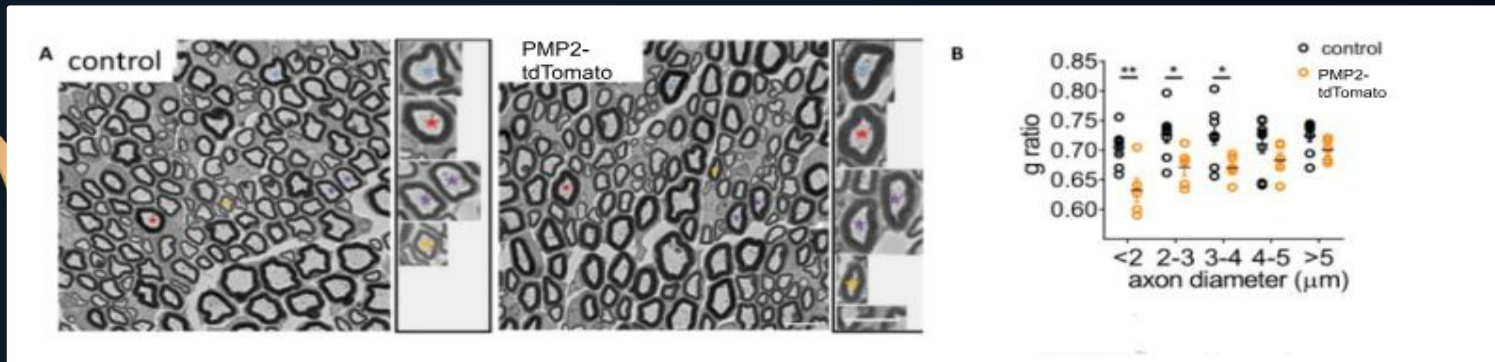
Nave, K. A., & Salzer, J. L. (2006). Axonal regulation of myelination by neuregulin 1. *Current opinion in neurobiology*, 16(5), 492–500. <https://doi.org/10.1016/j.conb.2006.08.008>

Hong, J., Garfalo, R., Kabre, S., Humml, C., Velanac, V., Roué, C., Beck, B., Jeanette, H., Haslam, S., Bach, M., Arora, S., Acheta, J., Nave, K. A., Schwab, M. H., Jourdain, D., Poitelon, Y., & Belin, S. (2024). PMP2 regulates myelin thickening and ATP production during remyelination. *Glia*, 72(5), 885–898.

<https://doi.org/10.1002/glia.24508>

# Preliminary Data

- ❖ Previously a mouse model overexpressing a tagged form for PMP2 called PMP2-tdTomato
- ❖ PMP2-tdTomato effects PMP2 molecular weight drastically from 15kDa to 75 kDa
- ❖ Myelin thickness was increased sciatic nerves at 1 month
- ❖ The tag may impact PMP2's function and expected effect on myelin thickness



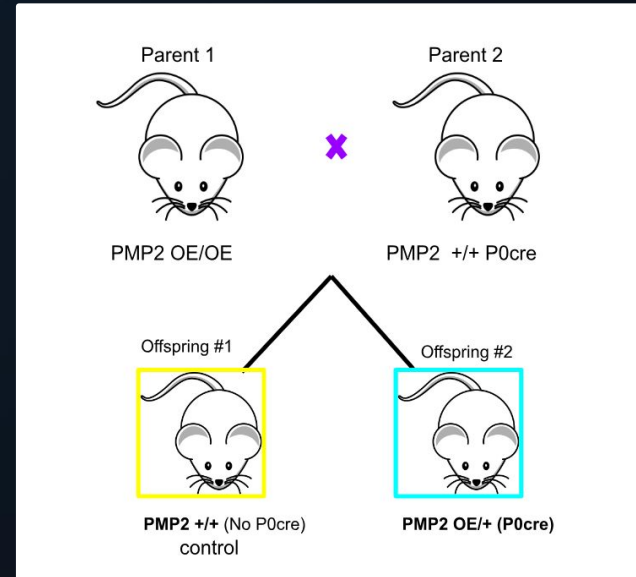
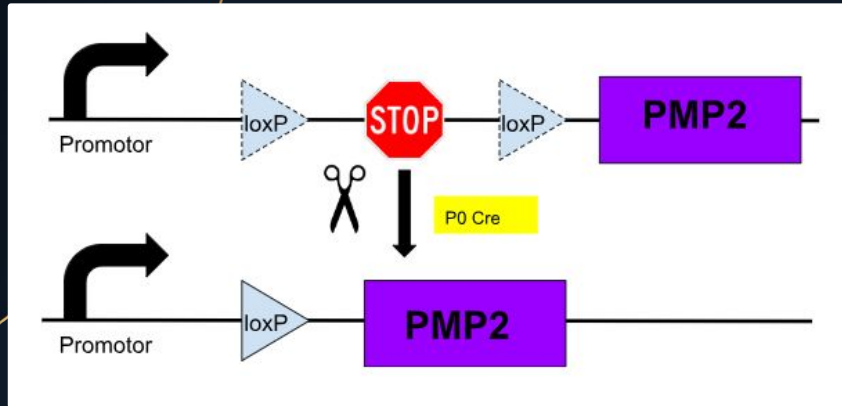
# Project

- ❖ New Mouse Model: PMP2Oe-NT
- ❖ Objective

# Hypothesis

Overexpressing PMP2, without the tdTomato tag, increases myelin thickness

# Methods

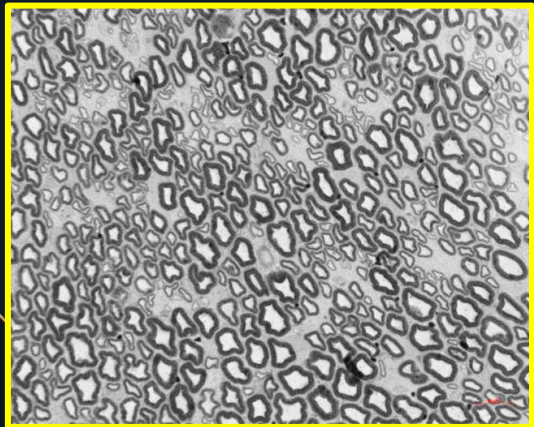


## ❖ Cre-Lox Breeding

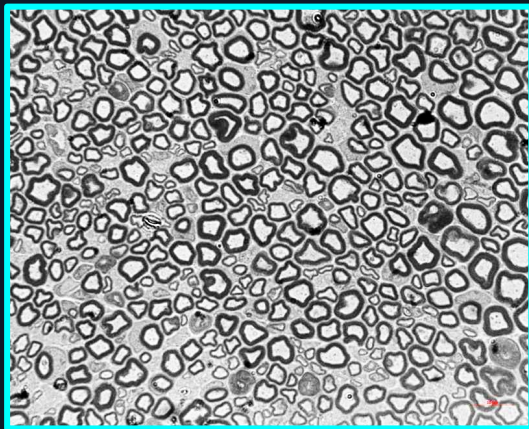
- A genetic tool to control gene expression and manipulate DNA
- Cre Recombinase and LoxP sites
- Deletion

# Methods

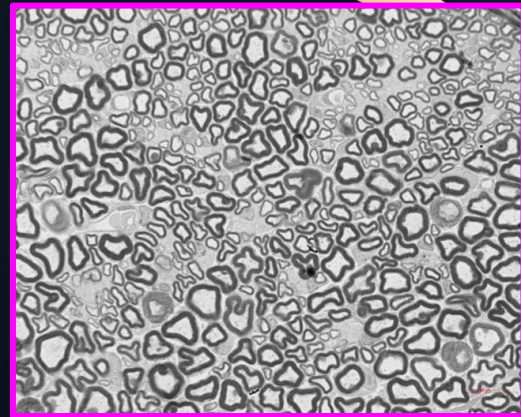
Sciatic Nerves of Mouse models



**PMP2<sup>+/+</sup>** (control)



**PMP2<sup>OE/+</sup>** ;Po-Cre



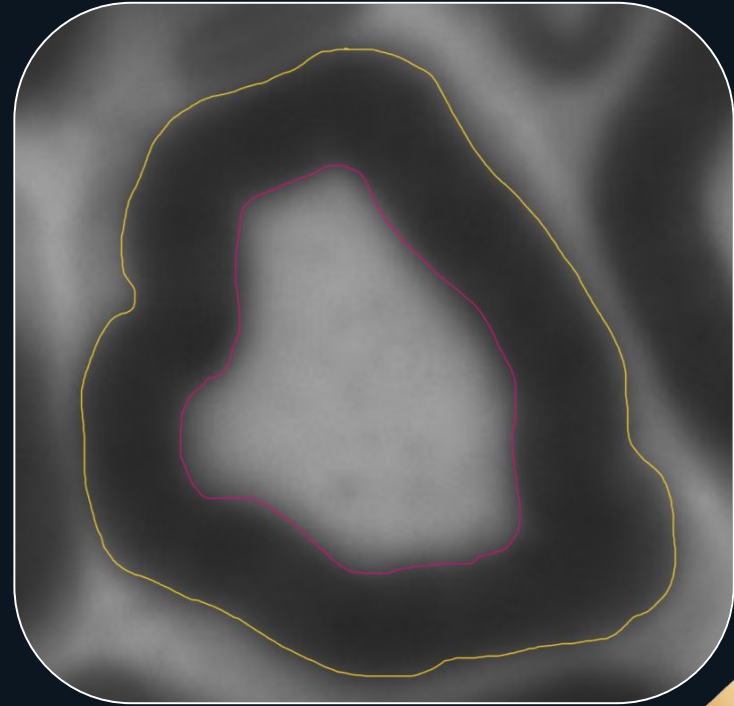
**PMP2<sup>OE/OE</sup>** ;Po-Cre

- ❖ Myelin Thickness
- ❖ ImageJ

# G-Ratio Calculation

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- ❖ Axon/Fiber
- ❖ Inner/Outer
- ❖ Lower G-ratios indicate greater myelin thickness



Mouse sciatic nerves

# Results

- ❖ Research is still ongoing
- ❖ Future conclusions and approaches
  - If hypermyelination is:
    - Lower
    - The same
    - Higher

# Thank you to everyone at Myelin Lab!



- ❖ Myelin Lab
- ❖ Ellinor Grinde
- ❖ Heidi Gleason



The background is a dark blue gradient with several thick, gold-colored curved lines that sweep across the frame from the corners towards the center. The text is centered in the middle of the image.

Thank *you* for  
listening!