Nerves under control

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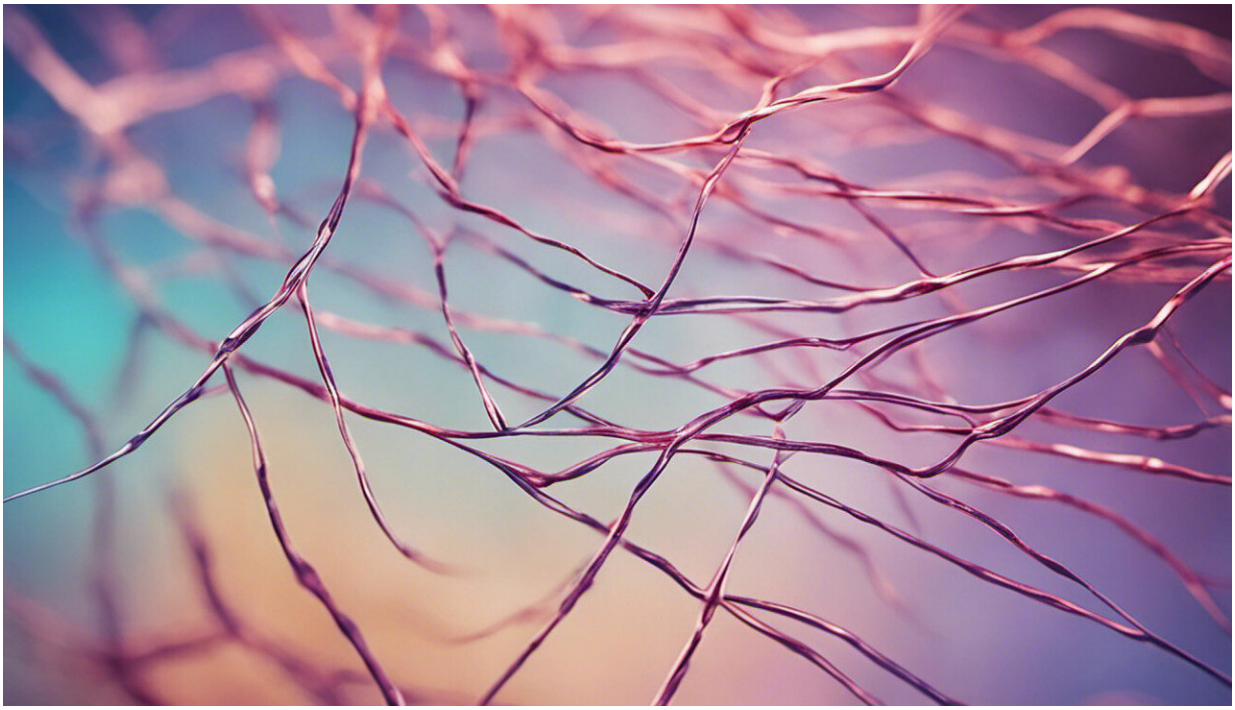

Credit: AI-generated image (disclaimer)

The proper transmission of nerve signals along body nerves requires an insulation layer, named myelin sheath. To be efficient this sheath is designed to have a certain thickness and Swiss researchers from the ETH Zurich have now discovered that proteins Dlg1 and PTEN interact to control the myelin sheath thickness. Recently published in Science their discovery improves our understanding of Charcot-Marie-Tooth neurodegenerative diseases and open a new avenue in the potential

treatment of these incurable and debilitating diseases.

A crucial factor in the transmission of nerve signals is the myelin layer - also known as the myelin sheath - which surrounds the axons. Axons are nerve cell projections through which the signals are relayed; the myelin sheath is formed by the Schwann cells in the peripheral nervous system, i.e. in the nervous system outside the brain and spinal chord. If it is too thick or too thin, the signal transmission slows down; if the myelin sheath becomes too badly damaged, it can cause diseases like Charcot-Marie-Tooth diseases. Patients suffer from an increasing weakness of the hands and feet, which gradually spreads to the arms and legs, sometimes even making them wheelchair-bound for the rest of their lives.

But which molecules regulate the thickness of the myelin sheath? Scientists at ETH Zurich from the research groups around biologists Ueli Suter and Nicolas Tricaud set about finding out. They have now published their findings in an online article in the journal *Science*.

The scientists didn't have to start their search entirely from scratch, however, having already developed a mouse model for a sub-type of Charcot-Marie-Tooth disease; the model is based upon a mutation in the gene for the protein MTMR2 and leads to hypermyelination by the Schwann cells. What's more, the researchers already knew from other studies that MTMR2 interacts with Dlg1.

In experiments conducted on cell cultures and the sciatic nerve in mice, the researchers were now able to demonstrate that Dlg1 inhibits myelin growth. For this to work, however, it needs to enlist the help of another signal protein: PTEN. Together, they ensure that the growth of the myelin sheath does not go to excess in the mouse's development. If the brake is "released" by suppressing Dlg1 or PTEN, it results in myelin excess that not only leads to an extra-thick myelin sheath, but also to its

degeneration. This process is characteristic of various diseases of the peripheral nervous system and , as it was revealed in the mouse model of Charcot-Marie-Tooth disease the Dlg-PTEN brake no longer works in these diseases. Nicolas Tricaud is convinced that the project helps to understand the basic molecular mechanisms of myelination, as well as offering new opportunities to define how the misdirection of these processes can cause neurodegenerative diseases and how this might be remedied.

More information: Cotter L, Ozçelik M, Jacob C, Pereira JA, Locher V, Baumann R, Relvas JB, Suter U, Tricaud N.: Dlg1-PTEN Interaction Regulates Myelin Thickness to Prevent Damaging Peripheral Nerve Overmyelination. Science. 2010 May 6. [Epub ahead of print] DOI:10.1126/science.1187735

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