Discovery of HDAC8's role in Schwann cell repair offers new insights into nerve regeneration

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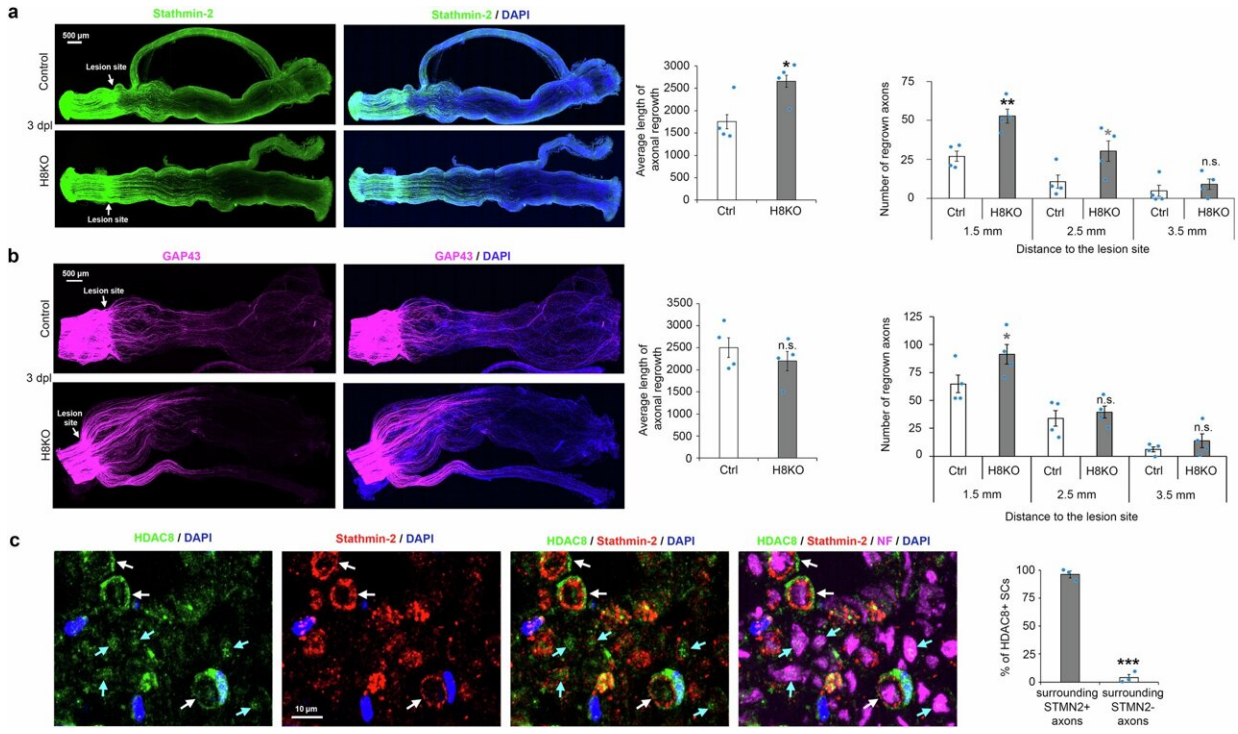


HDAC8 ablation in SCs promotes sensory axon regeneration. Credit: *Nature Communications* (2025). DOI: 10.1038/s41467-025-55835-9

Following an injury, such as a traumatic crush injury, the peripheral nervous system is itself often able to effectively regenerate. This regeneration capacity is mainly attributable to the Schwann cells of the

peripheral nervous system. These cells are quick-change artists that can transform themselves into repair cells when needed.

Unfortunately, the regeneration of nerve cells can be inefficient in some cases. A team of researchers at Johannes Gutenberg University Mainz (JGU) has recently discovered a mechanism that slows down the peripheral nervous system recovery process.

"Responsible for this is a protein called histone deacetylase 8, or HDAC8 in short," explained neurobiologist Professor Claire Jacob of JGU. "This protein is expressed in Schwann cells. If we remove HDAC8, regeneration occurs more rapidly."

Interestingly, HDAC8 is specifically produced in Schwann cells surrounding sensory neurons that transmit information on sensations, such as touch, temperature, and pain. The findings are published in the journal *Nature Communications*.

After injuries, Schwann cells become the 'repair task force' that restores axons

The peripheral nervous system largely owes its ability to regenerate to the high level of plasticity of Schwann cells. Schwann cells, which are also known as neurolemmocytes, provide the myelin sheath that protects the axons of nerve cells. Schwann cells become active immediately after an injury and transform into repair cells that release proteins called neurotrophins.

As a result, damaged axons—the long slender projections of nerve cells—can regrow and be guided back to their former targets. Once they reach their targets, Schwann cells remyelinate the regenerated axons, leading to successful functional recovery. This process tends to be

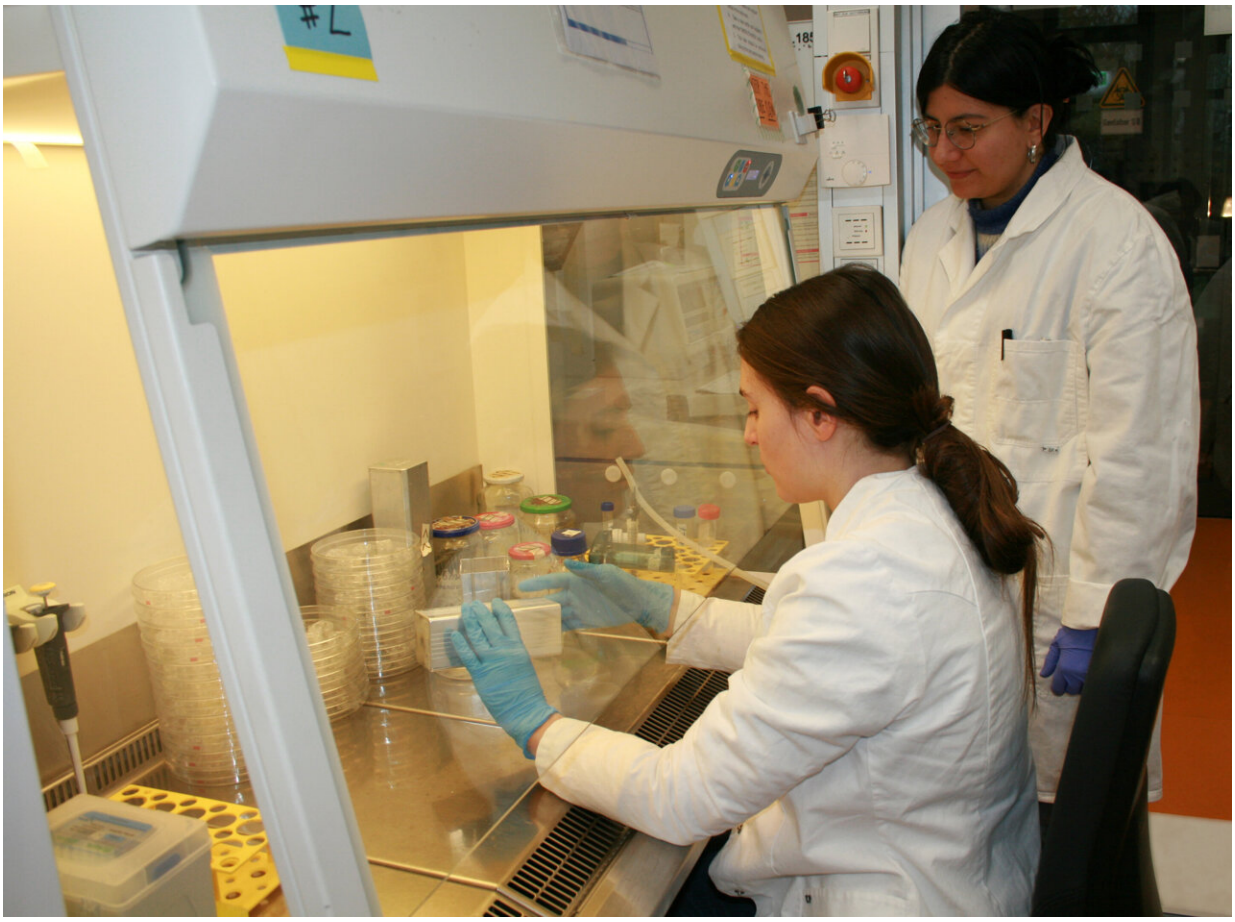
particularly efficient in young individuals.

Under certain circumstances, however, where there is a large gap between damaged axons and their intended targets or in older people, reinnervation can partially or completely fail.

"It is thus important for us to understand the mechanisms that underlie the plasticity of Schwann cells and determine their function," added Professor Jacob, head of the Cellular Neurobiology research group at JGU.

Her team has now discovered that HDAC8 counteracts the conversion of Schwann cells into their repair phenotype. This transformation process is to some extent triggered by the interruption of oxygen supply that occurs automatically in the case of damage to the peripheral nervous system.

"If we get rid of the inhibitor, namely HDAC8, sensory axons regrow faster and sensory function is restored earlier. In fact, the whole process becomes much more efficient," emphasized Jacob.



Nadège Hertzog (left), first author of the article on HDAC8 published in *Nature Communications*, and co-author Sofia Raigón López (right) working together in the cell culture lab at the JGU Faculty of Biology. Credit: Doris Franke

Role of HDAC8 in connection with Schwann cells previously unknown

The researchers were surprised to find that HDAC8 actually regulates the process specifically in Schwann cells that interact with sensory axons and thereby controls the regeneration of sensory axons and the recovery of sensory functions.

"This was new to us. We knew that upon injury to the peripheral nervous system, Schwann cells change their identity and turn into their repair phenotype. But it turns out this occurs differently in sensory and motor Schwann cells."

According to Professor Jacob, these new findings raise many conceptual questions. For instance, why do Schwann cells have such a mechanism? One possible explanation could be related to the lack of oxygen, so-called hypoxia, after an injury. In this case, hypoxia promotes the formation of new blood vessels—and HDAC8 could be a regulator of blood vessel formation. The next step could be a drug that removes the HDAC8 protein, prevents its production, or inhibits its function in this process.

Research focus: Regeneration of the nervous system

Injury to and regeneration of the nervous system has been at the core of Jacob's research for 20 years. It is also the subject of a new research project that began in early 2025. The team working on this project, titled Interactive Biomaterials for Neural Regeneration (InteReg), is composed of researchers from the fields of neurobiology, neuroimmunology, chemistry, and polymer research. Their aim is to produce precisely engineered synthetic biomaterials that can be used in the treatment of neurological diseases and disorders.

Professor Jacob is the spokesperson of InteReg and is also a member of the research network CoM2Life—Communicating Biomaterials: Convergence Center for Life-Like Soft Materials and Biological Systems.

More information: Nadège Hertzog et al, Hypoxia-induced conversion of sensory Schwann cells into repair cells is regulated by HDAC8, *Nature Communications* (2025). DOI:

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