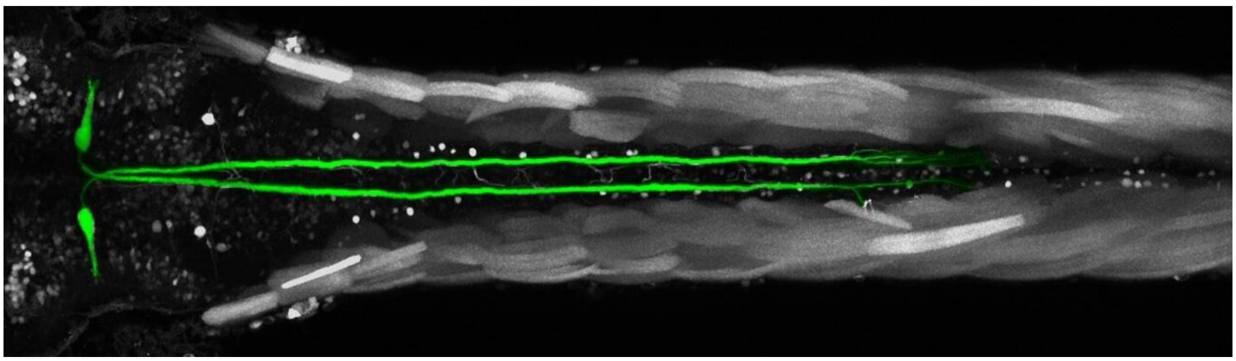
Scientists discover extraordinary regeneration of neurons

July 10 2020



Color-processed microscopic image of a pair of Mauther cells (green) in a zebrafish. On the left is the head of the fish, on the right the tail. The two green areas on the left are the cell bodies of the Mauther cells, the structures running to the right are the axons. The image was taken two days after the two axons were severely injured in their middle section, leaving their function significantly damaged. The several smaller branches at the end of the axons demonstrate how axonal regeneration usually occurs. Credit: Alexander Hecker

Biologists from the University of Bayreuth have discovered a uniquely rapid form of regeneration in injured neurons and their function in the central nervous system of zebrafish. They studies the Mauthner cells, which are solely responsible for the escape behavior of the fish, and previously regarded as incapable of regeneration. However, their ability to regenerate crucially depends on the location of the injury. In central nervous systems of other animal species, such a comprehensive regeneration of neurons has not yet been proven beyond doubt. The scientists report their findings in the journal *Communications Biology*.

Mauthner cells are the largest cells found in animal brains. They are part of the central nervous system of most fish and amphibian species and trigger life-saving escape responses when predators approach. The transmission of signals in Mauthner cells to their motoneurons is only guaranteed if a certain part of these cells, the axon, is intact. The axon is an elongated structure that borders the cell body with its cell nucleus at one of its two ends. If the injury of the axon occurs close to the cell body, the Mauthner cell dies. If the axon is damaged at its opposite end, lost functions are either not restored at all or only slowly and to a limited extent. However, the Mauthner cell reacts to an injury in the middle of the axon with rapid and complete regeneration. Indeed, within a week after the injury, the axon and its function are fully restored, and the fish is able to escape approaching predators again.

"Such a rapid regeneration of a neuron was never observed anywhere in the central nervous system of other animal species until now. Here, regeneration processes usually extend over several weeks or months," says Dr. Alexander Hecker, first author of the new study and member of the Department of Animal Physiology. This finding clearly disproves the widely accepted view in the scientific community that Mauthner cells are unable to regenerate.

However, the observation that the escape response of zebrafish were fully intact so soon after regeneration did not necessarily prove the functional regenerative capacity of the Mauthner cell. It might be possible that other neurons in zebrafish are able to induce this life-saving escape behavior and thus take over the lost function of Mauthner cells. However, precisely this possibility was ruled out by findings published by the Bayreuth biologists led by Prof. Dr. Stefan Schuster in *PNAS* in January 2020. They were able to show for the first time that it is only the

Mauthner cells that control the escape behavior of zebrafish. If the axon is irreversibly destroyed, there are no other cells in the fish that are able to compensate for the loss.

"Mauthner cells now offer us the possibility to investigate the very different responses to injuries of individual cells within the same nervous system: an absence of or insufficient regeneration processes on the one hand, and robust and complete regeneration on the other. Surprisingly, the injuries to the axon, which led to such contradictory responses, were not very far apart. Elucidating the causes is an exciting field of research, which also includes the identification of the genes that are active in the regeneration of neurons. And if we find out the reasons why regeneration processes in Mauthner cells fail to occur, we might also be able to better understand the mechanisms that prevent the regeneration of neurons in humans," said Hecker.

More information: Alexander Hecker et al. High-resolution mapping of injury-site dependent functional recovery in a single axon in zebrafish, *Communications Biology* (2020). DOI: 10.1038/s42003-020-1034-x

Provided by University of Bayreuth