Self-healing hearts - How Zebrafish regenerate heart muscle cells

Zebrafish can completely replace damaged heart muscle cells: The affected organ becomes fully functional again. How do they manage this? Researchers at Ulm University have discovered that a specific cell-to-cell communication signal helps them to cope better with replication stress. This stress occurs during cell division and inhibits tissue regeneration in humans and mammals as they age. In Zebrafish, on the other hand, a signalling protein ensures that the cells of the damaged organ continue to divide and thus multiply. The results were published in the journal Nature Communications.

In humans, a heart attack often leads to permanent damage because the affected tissue does not regenerate sufficiently. Zebrafish, on the other hand, can compensate for injuries to the heart that involve up to a third of the organ. "A sufficiently successful division activity of the heart muscle cells is crucial for the successful regeneration of injured tissue," explains Professor Gilbert Weidinger from the Institute of Biochemistry and Molecular Biology (iBMB) at Ulm University. The scientist coordinated a study that revealed why Zebrafish are so much better at repairing tissue damage to the heart than humans. The research team discovered that a special cell-to-cell communication signal is crucial. This so-called BMP signalling protein helps Zebrafish to deal with replication stress.

Replication stress hinders cell division in humans, but not in zebrafish

When DNA is replicated during cell division, the cell can come under replication stress: DNA lesions, strand breaks or even a lack of nucleotides - the building blocks of DNA - lead to a slowdown or even a halt in replication. The cells can no longer divide and multiply sufficiently and the tissue no longer regenerates. "Our research results have shown that zebrafish cells are also exposed to this stress during the repair of tissue damage, but are much better able to cope with it," explains Weidinger. The BMP signalling protein helps them to do this. The abbreviation BMP stands for "Bone Morphogenetic Protein". BMPs are part of a signalling system that plays a key role in embryonic development and organ development. These signalling molecules, which act locally on surrounding cells, help zebrafish cells to exploit their full regenerative potential. "Even with injuries that affect up to a third of the heart muscle cells, Zebrafish are able to restore the original number of cardiomyocytes within 30 days," says Denise Posadas Pena. The PhD student at the iBMB co-authored the study published in Nature Communications.

The research team also succeeded experimentally in significantly improving the regenerative capacity of human cells. The female and male scientists tested this on haematopoietic stem and progenitor cells (HSPCs) and skin cells. When these cells are subjected to replication stress in culture, BMP signalling can protect them from this. "The research results may help to develop new therapeutic approaches for better tissue regeneration. So that injured tissue can heal itself better," believes Gilbert Weidinger.

Regenerating Zebrafish hearts as an anti-ageing model

"Our results show that regenerating Zebrafish hearts can serve as a model for anti-ageing processes. It helps us to identify factors that could alleviate or even reverse ageing processes," says stem cell expert Professor Hartmut Geiger. The head of the Ulm Institute of Molecular Medicine was also involved in the study. Female and male scientists from Ulm, Bonn, Heidelberg, Bologna, Oxford and Zurich were involved in the research project. The study was funded as part of the Ulm Collaborative Research Centre SFB 1506 "Aging at Interfaces".

Publication:
Mohankrishna Dalvoy Vasudevarao, Denise Posadas Pena, Michaela Ihle, Chiara Bongiovanni, Pallab Maity, Dominik Geissler, Hossein Falah Mohammadi, Melanie Rall-Scharpf, Julian Niemann, Mathilda T.M. Mommersteeg, Simone Redaelli, Kathrin Happ, Chi-Chung Wu, Arica Beisaw, Karin Scharffetter-Kochanek, Gabriele D'Uva, Mona Malek Mohammadi, Lisa Wiesmüller, Hartmut Geiger and Gilbert Weidinger (2025). BMP signaling promotes zebrafish heart regeneration via alleviation of replication stress. Nat. Commun. 16, 1708. doi.org/10.1038/s41467-025-56993-6.

Press release

25-Feb-2025
Source: Ulm University

Further information

Prof. Dr. Gilbert Weidinger,
Institute of Biochemistry and Molecular Biology (iBMB)
Ulm University
Email: gilbert.weidinger(at)uni-ulm.de

- Ulm University