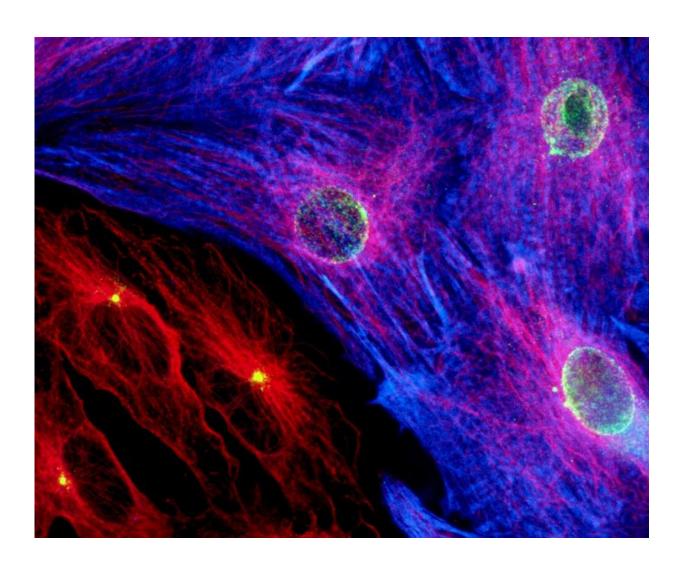


Why the human heart cannot regenerate

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Cardiac muscle cells. Credit: David C. Zebrowski, Felix B. Engel

The results of their research have recently been published in the high-



profile journal eLife.

The ability of most <u>cardiac muscle cells</u> to reproduce disappears in humans and all other mammals shortly after birth. What remains unclear, however, is how this happens and whether it is possible to restore this ability and therefore to regenerate the heart.

FAU researchers Dr. David Zebrowski and Prof. Dr. Felix B. Engel from the Department of Nephropathology at Universitätsklinikum Erlangen's Institute of Pathology and their colleagues have now found a possible explanation for this phenomenon. "In our study we discovered that the centrosome in cardiac muscle cells undergoes a process of disassembly which is completed shortly after birth," Prof. Engel explains. "This disassembly process proceeds by some proteins leaving the centrosome and relocating to the membrane of the cell nucleus in which the DNA is stored. This process causes the centrosome to break down into the two centrioles of which it is composed, and this causes the cell to lose its ability to reproduce."

The centrosome is an organelle found in almost every cell. In recent years, experiments have shown that if the centrosome is not intact, the cell can no longer reproduce. This raised the key question to what extent centrosome integrity could be manipulated - such as in cancer where cells reproduce at an uncontrolled rate.

The FAU researchers have now investigated whether the state of centrosome integrity is regulated naturally in the animal kingdom in order to control the reproduction of certain cells.

A dramatic difference

"We were incredibly surprised to discover that the centrosome in the cardiac muscle cells of zebrafish and amphibians remains intact into



adulthood," says Dr. David Zebrowski, who has been studying centrosomes for five years. "For the first time, we have discovered a significant difference between the cardiac muscle cells of mammals and those of zebrafish and amphibians that presents a possible explanation as to why the human heart cannot regenerate."

The discovery that there is a natural process that regulates centrosome integrity in the cardiac muscle cells of mammals opens up a range of possibilities for future research. Firstly, this observation provides a new starting point for attempts to stimulate the reproduction of cardiac muscle cells in humans to regenerate the heart. At the same time, centrosome integrity can be examined in order to find adult cardiac muscle cells that may have retained their ability to reproduce, which may enable new forms of medical treatment. Finally, a detailed understanding of the mechanism could also help researchers to develop methods of inhibiting the uncontrolled growth of cancer cells.

The study on heart regeneration was carried out as part of the project CYDER (Cell Cycle in Disease and Regeneration) that was set up by Prof. Dr. Felix B. Engel, an expert in the field of heart regeneration. CYDER has been funded by FAU's Emerging Fields Initiative since 2014. EFI aims to promote outstanding, preferably interdisciplinary research projects at an early stage and in a flexible and non-bureaucratic way. A strict selection process guarantees the high quality of the projects, approaches and the researchers funded within the scheme.

More information: eLife, dx.doi.org/10.7554/eLife.05563

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