MEDIA INFORMATION

Leibniz Institute for Farm Animal Biology

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LEIBNIZ INSTITUTE FOR FARM ANIMAL BIOLOGY

Mouse hearts as a key to better chances of healing in medicine

Research team from MV can for the first time fully display cell structures of the heart

An interdisciplinary research team consisting of scientists from the Leibniz Institute for Farm Animal Biology (FBN) in Dummerstorf and the University of Rostock has succeeded in completely deciphering the cell populations and in particular the subpopulations in the heart of adult mice as well as revealing the dynamics of the individual cell groups.

"This also led to the discovery of a group of vascular endothelial cells that have the characteristics of heart muscle cells. Since myocardial cells are generally unable to divide, resulting in permanent damage after an infarction, the discovery of a source for the formation of new myocardial cells would be of particular importance, especially for regenerative heart medicine", emphasized Dr. Anne-Marie Galow from the Institute of Genome Biology at FBN. In order to determine the cellular composition of a complete organ, thousands of cell nuclei from the heart of adult mice were sequenced for the first time, bioinformatically analyzed and thus assigned to specific cell populations.

The research success was achieved within the joint research project "Programmed pacemaker cells for in vitro drug testing (iRhythmics)" and was published in "Cells", an international open access journal for cell biology, molecular biology and biophysics, at the beginning of the year*. First authors are Dr. Anne-Marie Galow (FBN) as well as Paula Müller (Department of Cardiac Medicine, University Medicine Rostock) and Markus Wolfien (Chair of Systems Biology and Informatics, University of Rostock).

The project, which is funded by the EU and the State Government with approximately two million euros, has been running since October 2018 and includes University Medicine Greifswald under the leadership of University Medicine Rostock as well as the University of Rostock (Prof. Dr. Robert David) in addition to the Institute of Genome Biology at FBN in Dummerstorf. The aim of the State Excellence Research project is to produce beating heart muscle cells, so-called "programmed pacemaker cells", from immature heart muscle precursor cells. These offer the possibility of carrying out novel drug tests for cardiovascular diseases in the Petri dish and without animal experiments. In the joint project, FBN is responsible for the comprehensive gene expression analyses of the programmed pacemaker cells and the evaluation of the data.

New insights into the dynamics and networking of heart cells

The cellular composition of some other organs could already be determined previously. "However, the heart presented a particular challenge because the heart muscle cells could not be processed

with the standard systems due to their size, length and shape," explained Dr. Anne-Marie Galow. "For this reason, we chose an alternative approach that had previously only been described in neurology. Nerve cells can also become very large and are also branched. Using the still very new methodology of single nucleus sequencing, we have examined whole adult mammalian hearts and identified 24 different cell clusters. Analyses on the cellular level are indispensable for expanding our understanding of complex tissues such as mammalian hearts," said the Humanbiology researcher.

The elucidation of the cellular composition of the individual organs and the creation of cell marker profiles of the individual cell types is complex pioneering work in basic research. However, the data obtained provide scientists with valuable new insights into the dynamics and networking of heart cells and help to better understand certain molecular biological processes. In particular, the results on the vascular wall cells specified for the first time are promising for future application in regenerative heart medicine, for the restoration of cardiological cells, tissues and organs damaged by disease or accident. "In the long term, sequencing at the single cell level can be used to assign pathological changes in organs to specific cell populations, thus enabling more targeted therapeutic approaches in the future," said the scientist.

In a further step, corresponding analyses with pig hearts are now planned. These resemble the human heart much more closely. In addition, they have become increasingly important as a potential source of xenotransplants in cardiovascular research in recent decades..

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Photos FBN/Brunner:

With the help of gene expression analyses, Dr. Anne-Marie Galow and Dr. Ronald Brunner as well as their scientific colleagues were able for the first time to completely determine the cell structures of mouse hearts.
The Dummerstorf mouse line (Photo: FBN/nordlicht) served as model.

*Original Publications:

Integrative Cluster Analysis of Whole Hearts Reveals Proliferative Cardiomyocytes in Adult Mice Cells 2020, 9(5), 1144; https://doi.org/10.3390/cells9051144, Published: 6 May 2 2020
www.mdpi.com/2073-4409/9/5/1144

Single Nuclei Sequencing of Entire Mammalian Hearts: Strain-Dependent Cell Type Composition and Velocity
Cardiovascular Research, cvaa054; https://doi.org/10.1093/cvr/cvaa054, Published: 19 April 2020
https://academic.oup.com/cardiovascres/advance-article-abstract/doi/10.1093/cvr/cvaa054/5815573?redirectedFrom=fulltext

Single-Nucleus Sequencing of an Entire Mammalian Heart: Cell Type Composition and Velocity
Cells 2020, 9(2), 318; https://doi.org/10.3390/cells9020318, Published: 28 January 2020
www.mdpi.com/2073-4409/9/2/318

Leibniz Institute for Farm Animal Biology (FBN)
Wilhelm-Stahl-Allee 2, 18196 Dummerstorf
Director: Prof. Dr. Klaus Wimmers
T +49 38208-68 600
E wimmers@fbn-dummerstorf.de

Institut für Genombiologie
Head: Prof. Dr. Christa Kühn
T +49 38208-68 700
E kuehn@fbn-dummerstorf.de
Scientist: Dr. Anne-Marie Galow
T +49 38208-68 723
E galow@fbn-dummerstorf.de

Scientific Organisation:
Dr. Norbert K. Borowy
Wilhelm-Stahl-Allee 2, 18196 Dummerstorf
T +49 38208-68 605
E borowy@fbn-dummerstorf.de
www.fbn-dummerstorf.de