Website address:
https://www.gesundheitsindustrie-bw.de/en/article/press-release/new-crispr-method-leads-better-understanding-cell-functions

New CRISPR method leads to a better understanding of cell functions

The 2020 Nobel Prize in Chemistry was awarded for the development of CRISPR/Cas9, a method also known as "gene scissors", which enables researchers to better understand how human cells function and stay healthy. Researchers at the University of Stuttgart have further developed CRISPR for this purpose. They present their CRISPRgenee method in Cell Reports Methods.

Cells carry out all essential functions in the human body such as producing energy, forming tissue, and defending against disease. Our genes play a central role in regulating cellular functions. Depending on which genes in a cell are currently switched on or off, different cellular processes are activated. "My research group is investigating how cells retain control over their genes and thereby establish and maintain a healthy cellular state", says Dr Phillip Rathert, Group Leader at the Institute of Biochemistry at the University of Stuttgart. "In particular, we are looking at proteins that are bound to chromatin,the packaging of our DNA in the cell nucleus: We examine how these proteins interact with each other to switch genes on or off at the right time."

To investigate this, Rathert and his team carry out genetic loss-of-function (LOF) analyses in the laboratory: "We specifically switch off individual genes or proteins in the cell in order to understand the effects of this loss of function on the cell. This allows us to draw conclusions about the role normally played by the missing gene and its encoded protein."

Novel analysis method: CRISPRgenee

State-of-the-art biotechnological tools are needed to carry out LOF analyses. One of these tools is CRISPR/Cas9, a method that allows scientists to modify genes in a highly precise and targeted manner, similar to using scissors to cut DNA at specific points. This raises fundamental ethical questions but also offers great benefits for research and medicine.

For example, LOF analyses help researchers to better understand how human cells function and remain healthy. "Our findings in fundamental research mainly benefit medical science for example, by helping us to better understand the causes of diseases such as cancer or to develop new approaches for personalized therapies", says Rathert.

Rathert and his team have developed a novel CRISPR method that makes LOF analyses much more efficient and reproducible: CRISPRgenee. "CRISPRgenee combines two mechanisms: silencing and cutting a target gene simultaneously within the same cell." This makes the method particularly effective for investigating genes that are difficult to switch off with conventional methods and studying complex cellular control processes", says Jannis Stadager, lead author of the study and doctoral researcher in Rathert's team. "With CRISPRgenee, not only can individual genes be switched off more efficiently and rapidly but two different genes can also be analyzed in combination at the same time. This enables a more precise and robust elucidation of cellular relationships".

Publication in Cell Reports Methods

In close interdisciplinary collaboration with Dr Franziska Traube from the Institute of Biochemistry, Dr Stefan Legewie from the Institute of Biomedical Genetics, and Dr Steven Johnsen from the Robert Bosch Center for Tumor Diseases, the researchers used CRISPRgenee in various biological systems from cell proliferation to epithelial-mesenchymal transition and neuronal differentiation in human iPS cells. They present their CRISPRgenee method and reporting on their results in *Cell Reports Methods*.

Publication:
CRISPR GENome and epigenome engineering improves loss-of-function genetic-screening approaches.
Stadager J, Bernardini C, Hartmann L, May H, Wiepcke J, Kuban M, Najafova Z, Johnsen SA, Legewie S, Traube FR, Jude J, Rathert P. CRISPR GENome and epigenome engineering improves loss-of-function genetic-screening approaches.
Cell Rep Methods. 2025 Jun 16;5(6):101078.
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Further information

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