

Pressemitteilung

Leibniz-Institut für Alternsforschung - Fritz-Lipmann-Institut e.V. (FLI)

Dr. Kerstin Wagner

26.07.2023

<http://idw-online.de/de/news818359>

Forschungsergebnisse, Wissenschaftliche Publikationen
Biologie, Chemie, Ernährung / Gesundheit / Pflege, Medizin
überregional



On the right track - Novel treatment approach for soft tissue tumors

Researchers from the Leibniz Institute on Aging in Jena and the Brandenburg University of Technology Cottbus-Senftenberg have discovered a novel treatment approach for soft tissue tumors, which are frequently occurring in children and are often malignant. Through the targeted transformation of the tumor cells into muscle cells, they succeeded in stopping the growth of the cells and thereby the growth of the tumor. This opens completely new therapeutic options in cancer treatment.

Jena/Senftenberg. Rhabdomyosarcoma, a malignant tumor, is one of the most common soft tissue tumors occurring during childhood. The tumors are associated with skeletal muscle and can emerge anywhere in the body. Consequently, the clinical presentation is very diverse and complete removal of the tumors is often difficult and sometimes nearly impossible due to their location. This is why intensive research is being conducted into alternative treatment approaches.

A team led by Prof. Julia von Maltzahn, a former research group leader at the Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) and now professor of Stem Cell Biology of Aging at the Brandenburg University of Technology Cottbus-Senftenberg (BTU), has discovered a new treatment approach for rhabdomyosarcoma that could be used as a complementary treatment supporting traditional chemotherapy and radiation therapy. By targeting tumor cells and transforming them into muscle cells, her team was able to stop the growth of the cells and, thereby, tumor growth. The research results have now been published in the renowned journal *Molecular Therapy*.

Increased TRPS1 levels in soft tissue tumors

Rhabdomyosarcomas can occur as two subtypes, the alveolar and the embryonal subtype. In the embryonal subtype, the molecular causes of tumor progression are largely unknown so far or very diverse, making it difficult to develop therapeutic approaches. Current knowledge suggests that tumors arise from muscle progenitor cells.

“Through our studies on human embryonal rhabdomyosarcoma tumor cells, we found that the levels of the transcriptional repressor TRPS1, a protein that can bind to DNA and thus repress gene expression, are consistently elevated,” Prof. von Maltzahn explained. In skeletal muscle tissue these increased TRPS1 levels then lead to impaired differentiation of stem cells and in embryonic rhabdomyosarcoma cells to increased cell growth, which consequently promotes the tumor growth.

Influence of TRPS1 on stem cell differentiation

“During normal development of skeletal muscle, TRPS1 levels must be downregulated in cells at the onset of differentiation, since only then a proper development and growth of muscle can be achieved,” Dr. Sören S. Hüttner adds, who conducted the studies during his PhD thesis at the FLI. However, the question remains what is the exact role of TRPS1 in myogenic differentiation?

The researchers found that aberrantly high levels of TRPS1 in normal muscle cells severely impaired muscle formation (myogenesis), similar to what can be observed in tumors. “Thus, elevated TRPS1 levels appear to be one of the main inhibitors of terminal myogenic differentiation, interfering with skeletal muscle formation and development,” Prof. von Maltzahn reported. “This made us come up with the idea that decreasing TRPS1 levels in tumor cells might reduce tumor growth.”

Reprogramming – Tumor cells become muscles cells again

Through collaboration with Dr. Björn von Eyss from the FLI and Prof. Ursula Anderer from the BTU and by the use of various techniques (e.g. shRNAs, Crispr/Cas9), the researchers actually succeeded in demonstrating – in cell culture and in a mouse model – that the targeted reduction of TRPS1 levels in tumor cells can drive differentiation: the tumor cells become muscle cells. At locations where a tumor was located beforehand, muscle cells start to develop, a cell type which cannot divide anymore.

New treatment approach for soft tissue tumors

“Based on these promising results, we believe that we found an effective, new therapeutic approach for the treatment of embryonal rhabdomyosarcomas, which could be used in the future – in addition to traditional chemotherapy and radiotherapy – to stop the growth and spreading of the tumors,” Dr. Hüttner explains, emphasizing the relevance of the results.

The research findings are expected to have far-reaching implications for cancer research, particularly for the study of soft tissue tumors in children and the development of new strategies for the treatment of rhabdomyosarcoma. All indications are suggesting that TRPS1 is a promising therapeutic target with high potential to transform tumor cells into muscle cells, a cell type which cannot undergo cell divisions anymore, thus helping to stop tumor growth.

Publication

A dysfunctional miR-1-TRPS1-MYOG axis drives ERMS by suppressing terminal myogenic differentiation. Hüttner SS, Henze H, Elster D, Koch P, Anderer U, von Eyss B, von Maltzahn J. Mol Ther. 2023, S1525-0016(23)00383-0. doi: 10.1016/j.ymthe.2023.07.003.

The project “Driving rhabdomyosarcoma into differentiation” was funded as part of SPARK-FLI from 2020–2021. The internal technology transfer program SPARK-FLI helps to translate fundamental scientific findings from biomedical research into diagnostics or medical applications and ensures that government-funded research contributes to improving the health of our society. This targeted funding not only increases the chances of success of the respective research project, but also reduces the costs as well as the time required to achieve the goal.

Contact

FLI:
Dr. Kerstin Wagner
Press and Public Relations
Phone: 03641-656378, email: presse@leibniz-fli.de

BTU:
Ilka Seer
Press Officer, Head of Corporate Identity Department

Phone: 0355-693612, email: ilka.seer@b-tu.de

Background information

The Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) – upon its inauguration in 2004 – was the first German research organization dedicated to research on the process of aging. More than 350 employees from around 40 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. For more information, please visit www.leibniz-fli.de

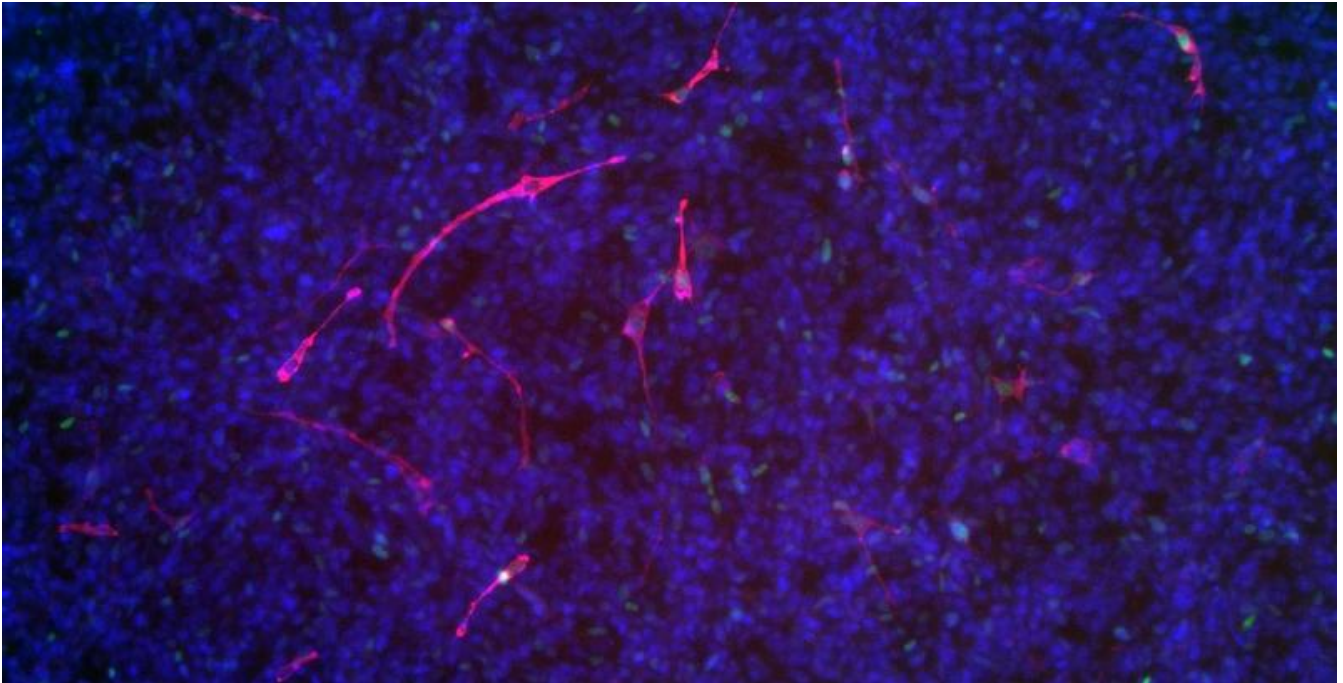
The Leibniz Association connects 97 independent research institutions that range in focus from natural, engineering and environmental sciences to economics, spatial and social sciences and the humanities. Leibniz Institutes address issues of social, economic and ecological relevance. They conduct basic and applied research, including in the interdisciplinary Leibniz Research Alliances, maintain scientific infrastructure, and provide research-based services. The Leibniz Association identifies focus areas for knowledge transfer, particularly with the Leibniz research museums. It advises and informs policymakers, science, industry and the general public. Leibniz institutions collaborate intensively with universities – including in the form of Leibniz ScienceCampi – as well as with industry and other partners at home and abroad. They are subject to a transparent, independent evaluation procedure. Because of their importance for the country as a whole, the Leibniz Association Institutes are funded jointly by Germany's central and regional governments. The Leibniz Institutes employ around 20,500 people, including 11,500 researchers. The financial volume amounts to 2 billion euros. For more information: www.leibniz-gemeinschaft.de/en/.

The Brandenburg University of Technology Cottbus-Senftenberg (BTU) is a young university that meets current scientific challenges. The second largest university and the only technical university in the state of Brandenburg offers a portfolio of more than 60 study programmes that is unique in Germany, including dual and international study programmes. Of the approximately 6,800 students, about 40 percent come from more than 120 different countries. In its research, the BTU focuses on four profile lines: energy transition and decarbonization, global change and transformation processes, health and life sciences, and artificial intelligence and sensor technology. On this basis, the university uses its scientific expertise to develop practice-relevant solutions for shaping the major issues of the future worldwide. Interdisciplinary clusters and close cooperation with its partners in science and industry enable the university to raise its profile and establish international connections. Under the leadership of the BTU, an innovation landscape with international appeal is to be created in the Lausitz Science Park at the Cottbus location in the next few years, which will sustainably bundle top-level research and transfer. www.b-tu.de/en/

Originalpublikation:

A dysfunctional miR-1-TRPS1-MYOG axis drives ERMS by suppressing terminal myogenic differentiation. Hüttner SS, Henze H, Elster D, Koch P, Anderer U, von Eyss B, von Maltzahn J. Mol Ther. 2023, S1525-0016(23)00383-0. doi: 10.1016/j.jymthe.2023.07.003.
[https://www.cell.com/molecular-therapy-family/molecular-therapy/fulltext/S1525-0016\(23\)00383-0](https://www.cell.com/molecular-therapy-family/molecular-therapy/fulltext/S1525-0016(23)00383-0)

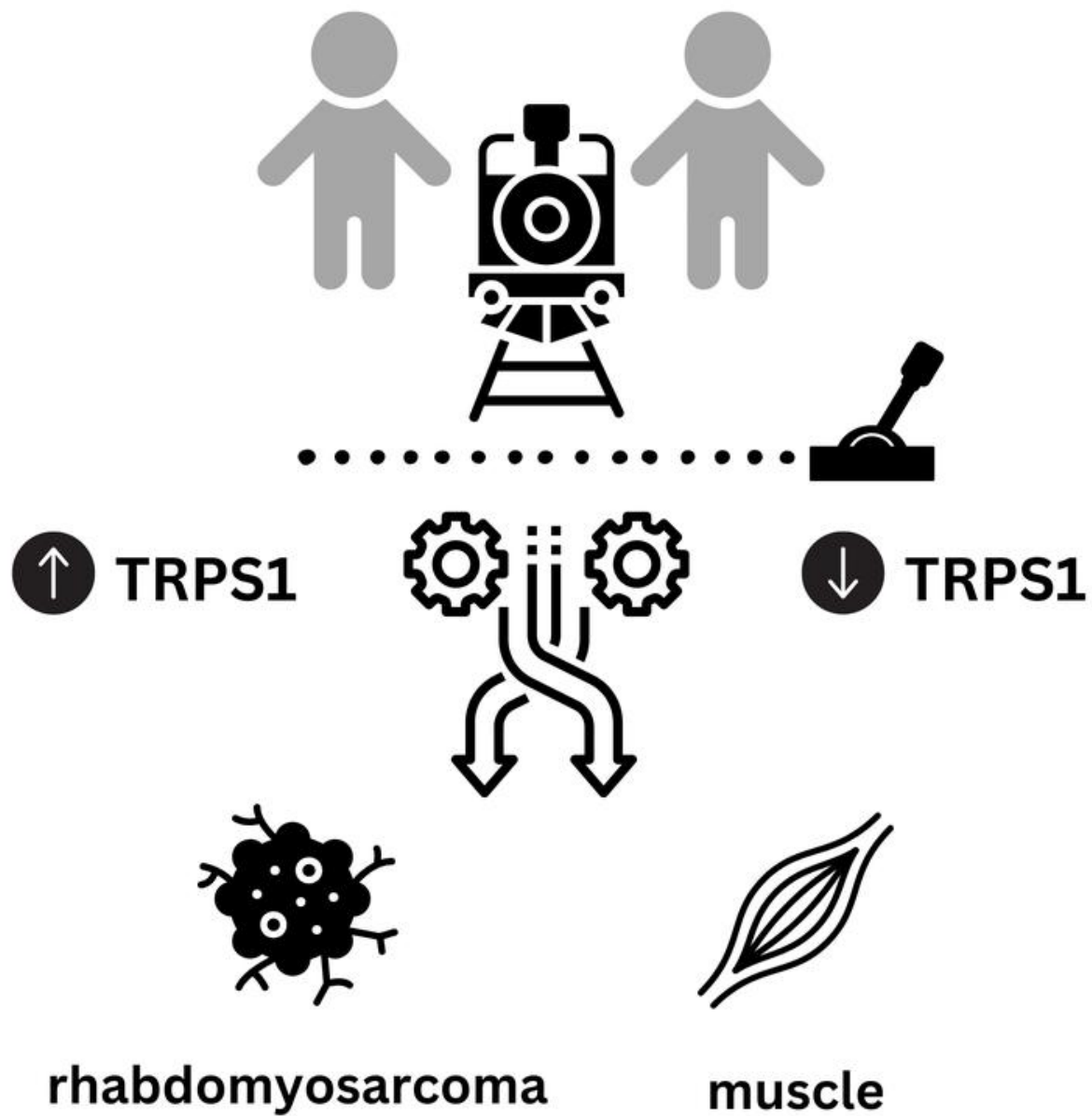
Anhang FLI Press release (pdf) <http://idw-online.de/de/attachment99055>



Induction of myogenic differentiation and reduction of cell division in rhabdomyosarcoma cells after reducing of the amount of TRPS₁ via siRNA, in red: myosin heavy chain (marker for differentiated muscle cells), in green: Ki67 (marker for dividing) ...

BTU / Julia von Maltzahn

BTU



The protein TRPS1 prevents the transcription of genes which are important for the muscle development. In soft tissue tumors (rhabdomyosarcomas), TRPS1 levels set the path how tumor cells can transform into muscle cells.

(Graphic: FLI / Kerstin Wagner)

FLI