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Target validation for drug development against aggressive breast cancer cells

Breast cancer is the most common form of cancer among women. Triple-negative breast cancer is a particularly aggressive form of tumors for which treatment options are poor. Important receptors are missing here, which serve as targets for possible treatments. Researchers of the Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) in Jena and the Friedrich Schiller University Jena, Germany now start a project to validate the protein TRPS1, which is commonly overexpressed in these tumors, as target for treatment. The researchers aim at developing therapeutics to treat this aggressive form of breast cancer. Their project is funded by BMBF with 832K Euro for two years.

Jena. At around 30.5 percent, breast cancer is the most common cancer among women in countries of the industrialized world. The number of cases has doubled since the 1980s: about 69,000 times a year women are diagnosed with breast cancer. Triple-negative breast cancer is a particularly aggressive form of breast cancer. As important receptors are missing here, treatment options and prognosis for such tumors are very poor.

Researchers around Dr. Björn von Eyss, junior group leader at the Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) in Jena, Germany reported 2018 in their study in *Nature Communications* that the protein TRPS1 (*Trichorhinophalangeal Syndrome 1*) plays an important role in such tumors. They showed that TRPS1 is increased in tumors, as they occur in triple-negative breast cancer, and found out that a downregulation of TRPS1 results in better survival prognosis of breast cancer patients.

Independent studies in Harvard and at Novartis confirmed, that a decrease of TRPS1 inhibits cell division in other cell types. This shows that TRPS1 could be a promising new drug target in breast cancer. It is hypothesized that new therapeutics for inhibiting this protein would have few side effects on the body, because TRPS1 mainly occurs in cells of breast tissue.

Dr. von Eyss pursued this potential therapeutic approach at FLI and got support by the internal SPARK@FLI program to continue his research for two more years. SPARK@FLI supports researchers to develop their results from basic biomedical research towards possible applications in therapeutics or diagnostics, bringing them from bench to bedside. Thus, research at FLI can contribute to a better health of our society. "The first important step towards drug development was the development of a mouse model to investigate the newly discovered mechanism of TRPS1 regulation", says Dr. von Eyss about his research.

"With the newly launched project funded by the BMBF, we can continue our research and further work on the validation of targets for the development of pharmaceutical drugs", he further explains. The project "Targeting TRPS1 in breast cancer" is funded by the Federal Ministry of Education and Research (BMBF) for the next two years with 832K Euro. The researchers aim at finding highly effective tailor-made therapies for the inhibition of this novel oncogene, which can be applied in future for the treatment of triple-negative breast cancer.



The researchers use high-throughput screening for target validation to identify chemical substances that successfully inhibit the TRPS1 protein. The team is supported by Prof. Dr. Hans-Dieter Arndt from the Institute of Organic Chemistry and Macromolecular Chemistry at the Friedrich Schiller University Jena (FSU), an expert in the synthesis and design of peptide and non-peptide natural products. His research group at FSU, will study how to improve the biological activity of the newly discovered inhibitors.

External industry mentor Dr. Hélène Chéry Hernandez complements the existing expertise of this project team. She will contribute to the implementation of guidelines for industry-based target validation in academic research. "This will significantly increase the chances of success of this project", says Dr. Sonja Schätzlein, coordinator of the SPARK@FLI program, who accompanies the research project from the idea to its implementation. "The advice of our industry advisors was just as crucial to the development process as the seed-funding from the SPARK@FLI Program."

BMBF funding is provided under the federal "Health Research" framework program in the guideline for funding of projects on "Target validation for pharmaceutical drug development" and is part of the "National Drug Initiative" with the aim of strengthening drug research and promoting the development of new drugs. Two postdoc positions in the von Eyss research group at FLI and one at FSU in the Arndt research group are associated with the funding.

The project is funded by the Federal Ministry of Education and Research (BMBF), funding code 16GW0271K.



Picture:

The protein TRPS1 is overexpressed in triple-negative breast cancer. A new project aims at developing highly effective tailor-made treatments for the inhibition of this novel oncogene, which can be applied in future for the treatment of this aggressive form of breast cancer. (Graphic: Kerstin Wagner / FLI; Source: www.pixabay.com)



Publications

TRPS1 shapes YAP/TEAD-dependent transcription in breast cancer cells. Elster D, Tollot M, Schlegelmilch K, Ori A, Rosenwald A, Sahai E, von Eyss B, *Nature Communication* 2018, 9, 3115. DOI: 10.1038/s41467-018-05370-7. <u>https://www.nature.com/articles/s41467-018-05370-7</u>

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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 <u>www.leibniz-fli.de</u>.

The **Leibniz Association** connects 96 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 20,000 people, including 10,000 researchers. The financial volume amounts to 1.9 billion euros. See https://www.leibniz-gemeinschaft.de/en/ for more information.