

FRAUNHOFER INSTITUTE FOR TRANSLATIONAL MEDICINE AND PHARMACOLOGY ITMP

PRESS RELEASE

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Pharmaceutical research pioneers succeed in Clusters4Future competition

Fraunhofer ITMP is pioneering the development of a new class of active substances in the PROXIDRUGS project together with seven regional partners, under the leadership of the Goethe University Frankfurt am Main. The project has now been designated as a cluster for future by the German Federal Ministry of Education and Research (BMBF) and will be funded with up to 15 million euros.

FRANKFURT. Most of the drugs available today are small molecules that develop their efficacy by binding to specific proteins associated with a disease. However, only about 20 percent of proteins have defined binding sites for drugs, which are able to produce the necessary blocking or inhibition of protein function. The remaining 80% of disease-related proteins are inaccessible to therapeutically relevant modulation by classical small molecules. This situation is now set to change through the development of active substances that have two functional binding arms, with which they grab two intracellular players in order to bring them into close spatial proximity: on one side the disease-related protein, on the other an enzyme that marks this protein for targeted degradation by the cellular "disposal system". An advantage of this principle of action is its high specificity. Following the reaction, the active substance is reusable and thus can be dosed at low levels with the promise of lower potential side effects.

Fraunhofer ITMP is involved in seven out of eleven planned subprojects of the PROXIDRUGS cluster, which aim at discovering targeted protein degradation-based agents with the potential to be eventually developed into clinical treatments. Together with several industrial partners, it will develop innovative high-throughput test systems for the identification of proximity-inducing molecules that cause degradation of target proteins, for example by autophagy. In addition, scientists from Fraunhofer ITMP are involved in research into how such drugs can be delivered to where they are needed in the body. This includes using stem cell-based models of the blood-brain barrier to better understand how these type of drugs enter the brain - an essential step for the treatment of neurodegenerative diseases. Fraunhofer ITMP is also involved in innovation and data management in order to make the results of the consortium sustainably usable.

Worldwide, only a few representatives of the targeted protein degradation based drugs, the so-called PROTACS (PROteolysis Targeting Chimeric Molecules) – are in the clinical development for prostate and breast cancer. "PROXIDRUGS intends to extend the scope of this promising class of active substances to other indications, such as neurodegenerative diseases, infectious diseases and immunological diseases," explains PD Dr. Aimo Kannt, Head of Drug Discovery at Fraunhofer ITMP. "The multidisciplinary expertise in our network of basic and applied research institutions, pharmaceutical and

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technology companies will significantly accelerate the translation of our findings into clinical application." Prof. Dr. Ivan Đikić, spokesman of the PROXIDRUGS consortium, added: "Our bodies have a sophisticated system to dispose of defective, superfluous or harmful proteins. We will use this system to specifically break down disease-related proteins."

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PROXIDRUGS is one of only two biomedically-oriented selected by the BMBF in the first round of its Clusters4Future competition for funding of an initial three-year period. "This decision speaks for the exceptional innovation strength of the Rhine-Main region in pharmaceutical research and builds on strong traditions," says Prof. Dr. Dr. Gerd Geißlinger, deputy spokesman of PROXIDRUGS and head of Fraunhofer ITMP, which became an independent Fraunhofer Institute in 2021 with the help of the Hessian State Offensive for the Development of Scientific and Economic Excellence (LOEWE). "Proxidrugs are one of the most promising new drug classes in pharmacology. We are proud to help drive medical progress in this first-class environment."

As part of the High-Tech Strategy 2025, the Clusters4Future competition was launched in summer 2019 with the aim of promoting knowledge and technology transfer in scientific hotspots. Out of 137 proposals, 16 finalists were initially selected for a concept development phase that began in May 2020, from which a total of seven clusters have now emerged as winners.

Partners:

Goethe University Frankfurt am Main (leadership)
TU Darmstadt
University of Heidelberg
Fraunhofer Institute for Translational Medicine and Pharmacology ITMP
Max-Planck Institute of Biophysics
Pharmaceutical and biotechnology companies in the Rhine-Main area