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H-BRS researches cellular transport mechanisms in DFG consortium to better understand diseases

When transport processes in cells do not function properly, this often results in diseases such as metabolic disorders, high blood pressure, kidney and lung damage or inflammation. In the interdisciplinary DFG research network 'CytoTransport - Mechanisms and Modulation of Cellular Transport Processes', a team of scientists from Hochschule Bonn-Rhein-Sieg (H-BRS) is investigating the underlying processes. A better understanding of the processes is a prerequisite for developing new therapeutic strategies.

Transport processes play a very important role in the function of cells. For example, components that are required for metabolism or the production of proteins must enter the cells, whereas certain waste products must be transported out of the cell. The transport of electrically charged particles, known as ions, is also essential for cells, as they generate tiny electrical membrane voltages that nerve cells use for communication, for example. 'Transport processes are involved in everything that makes us human. There is no biological process that is not associated with transport,' says Professor Mike Althaus, spokesperson for the "CytoTransport" network, which is funded by the German Research Foundation (DFG). One figure illustrates the scale of the project. The human brain consists of 86 billion nerve cells. Every single one of these nerve cells generates electrical voltages that are due to the transport of thousands of ions.

Different types of transport in each cell
Different types of transport can be distinguished. On the one hand, there are ion channels in the cell membrane. These are pores that channel ions such as sodium, potassium or calcium into or out of the cell. Such an ion channel opens and closes like a front door. The process itself is called gating and happens very quickly. But how do you get the door open? How do ion channels open and close, and what happens if the signals are disrupted? As the transported goods are electrically charged particles, the researchers can measure the current through the ion channels using the so-called patch-clamp technique. This makes it possible to characterise the function of the ion channels and, for example, to investigate which structural parts of the ion channels are responsible for the gating mechanisms. Figuratively speaking: Which structure is the door handle? Which is the hinge? Are there keys that keep the door closed for longer or stoppers that keep it open? 'Many of these processes are not yet understood,' says Althaus.
In addition to the doors, i.e. the ion channels, there are so-called transporters in the cell membrane. These can also move larger molecules such as sugar or amino acids into or out of the cell. However, the process is slower than in the ion channels. The transporters play an important role in metabolism or detoxification processes, for example. The researchers are also investigating how these so-called solute carrier transporters work.

But how do the ion channels and transporters get to the places where they are needed? In other words, how do they get to work in a figurative sense? This happens with the help of membrane vesicles, among other things. These are transported along the cytoskeleton, a kind of rail network formed by filamentous proteins inside a cell, via motor proteins, analogous to transport vehicles.

All transport pathways are crucial for many cellular processes, and disruptions can have serious consequences for human health.

The ‘CytoTransport’ project goes beyond a better understanding of the various biological transport processes. ‘We also want to lay the foundations for the production of vehicles that make it possible to transport molecules that modulate transport proteins to their site of action,’ says H-BRS Professor Althaus, explaining this chemical aspect. In the future, methods could be developed to ideally deliver new drugs to the precise location in a cell where they are to be used.

Models and hypotheses using AI-supported methods
Biological issues are at the centre of the research project. However, scientists from other disciplines at the university are also involved in order to broaden the perspective and learn from each other.

For example, a project group from the field of chemistry and materials science is involved, which draws inspiration for technical solutions from biological processes. One example: The production of drinking water is a major problem worldwide and artificial membranes are used to desalinate seawater. While biology has solved the targeted transport of certain salts via cell membranes over billions of years through evolution, researchers still face technical challenges when it comes to the efficiency and selectivity of artificial membranes. Here it is worth taking a look at biology.

Computer scientists at H-BRS are supporting the project with the help of artificial intelligence (AI) methods. They are developing models for biological and chemical transport processes and creating models of protein structures, which will then be tested in the laboratory. This topic is highly topical in science, as demonstrated last year by the award of the Nobel Prize in Chemistry. It was awarded to the scientists John Jumper and Demis Hassabis, who work in the UK, for the development of AI-supported methods for predicting complex protein structures.

Project in the DFG's ‘Forschungsimpulse’ programme
The German Research Foundation (DFG) is funding the joint project ‘CytoTransport’ at the H-BRS and thus the establishment of a centre for biomedical research over a period of five years with a total of around six million euros. The project is part of the new ‘Forschungsimpulse’ programme for universities of applied sciences (HAW). At the end of 2023, H-BRS was selected as one of ten HAWs nationwide for the programme. ‘The long-term goal is to develop a methodological portfolio with which transport processes can be researched from different angles and at different scales of resolution, from the atom to the cell,’ says Professor Mike Althaus.

The research results could also lead to personalised therapies. ‘A lot will happen in medicine if we know which variant of a protein plays a role in faulty transport processes,’ says Althaus with a view to corresponding clinical pictures. For example, drugs and therapies could be used in a more targeted way if we could find out how effectively they work on certain protein variants. Or which gene variants are responsible for the fact that some people react more sensitively than others to an increase in blood pressure in connection with a high-salt diet.

Scientists from nine working groups are conducting research in the ‘CytoTransport’ research network: Professor Mike Althaus, Professor Matthias Preller, Professor Jörn Oliver Sass, Professor Margit Schulze, Professor Christopher Volk and Professor Steffen Witzleben from the Department of Natural Sciences, Professor Dirk Reith (Department of Engineering and Communication), Dr Karl Kirschner (Department of Computer Science) and Dr Katrin Richter from Justus Liebig University Giessen. They belong to the two H-BRS research institutes IFGA (Institute for Functional Gene Analytics) and TREE (Institute of Technology, Resource and Energy-efficient Engineering). The team consists of a total of 26 researchers from twelve countries, including eleven doctoral students. The network is interdisciplinary and international, and the scientists will collaborate with research institutions in Germany, the USA, Denmark, the UK and Israel.

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