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ERC Synergy Grant has started

The international research project MitoContact is dedicated to investigating how organelles within a cell communicate and interact with other cellular components. Kai Johnsson, Director at the Max Planck Institute for Medical Research, has received funding from the European Research Council (ERC) for this project. Colleagues in Lausanne and Bern are also participating in the project, which has been awarded 10 million euros in funding. The findings are expected to provide new insights into fundamental cellular processes and, in the long term, contribute to a better understanding of various diseases. The research has started with a kick-off event.

Basic research with medical implications

Research into mitochondrial membrane contact sites is part of basic research. Their significance for various diseases is increasingly coming into focus. Changes in the contact sites within these organelles have been linked, among other things, to metabolic diseases such as obesity and type 2 diabetes, as well as to neurodegenerative diseases such as Parkinson's.

"A better understanding of molecular communication between the organelles could, in the long term, enable new therapeutic approaches that directly target the cellular causes of these diseases," explains Kai Johnsson. The project thus opens up prospects for the development of future treatment strategies that go beyond merely alleviating symptoms.

Little is known about contact points

Mitochondria are considered the powerhouses of the cell and ensure the energy supply. The neighboring endoplasmic reticulum (ER) performs important tasks, including calcium storage and lipid production. Both organelles are connected via dynamic membrane contact sites. Among other things, calcium, lipids, and other signaling molecules essential for cellular function are transferred at these sites. Although these contact sites influence numerous cellular processes, little is currently known about when they form, how they are regulated, and which substances are exchanged there.

This is where the *MitoContact* project comes in: It aims to comprehensively investigate the architecture, dynamics, and function of these contact sites. In particular, the project seeks to clarify how the exchange of calcium and lipids is organized and what role these processes play in mitochondrial function.

Sensor proteins shed light on the cell

At the Max Planck Institute for Medical Research (MPIMR) scientists are developing chemical biology tools to track cellular events at membrane contact sites with unprecedented high temporal and spatial resolution. "To do this, we are designing fluorescent sensor proteins that can be specifically deployed at the contact sites," explains Kai Johnsson. To achieve this the so-called "split-HaloTag" platform plays a central role. HaloTag is a protein that can permanently bind to a fluorescent dye. It enables the placement of fluorescent markers where specific proteins are located or where cellular structures interact.

Tools for analyzing cellular processes

In addition, an already established biosensor called "Caprola" is being further developed for use in mitochondria to detect calcium signals. Complementing this, methods will be developed for selecting highly specific antibodies – in particular nanobodies – that serve as precise molecular tools for analyzing cellular processes.

"With the help of these tools, we can investigate when the contact sites in the cell open and close, what passes through them – for example, calcium, lipids, or other signals – or how diseased cells can be brought back into balance," explains doctoral candidate Anja Benderoth.

In the long term, the newly developed sensors will also be combined with genome-wide CRISPR-Cas screenings to identify

genes involved in the regulation of these contact sites.

Close international collaboration

Suliana Manley's research group at the École polytechnique fédérale de Lausanne (EPFL) – where she also serves as the official head of the consortium – contributes also to this European collaborative project. With intelligent microscopy techniques, her group aims to use neural networks to detect biological events in real time and automatically control image acquisition. The research group led by Wanda Kukulski at the University of Bern is using its expertise in cryo-electron microscopy and correlative microscopy to directly visualize the three-dimensional architecture of the contact sites within the cell.

The work at the Max Planck Institute is led by Kai Johnsson and Richard Wombacher; the team also includes Birgit Koch, Jonas Fiebig-Fischer, and Anja Benderoth, as well as other doctoral students and postdocs in Kai Johnsson's Department of Chemical Biology.

To kick off the project, the teams met for a multi-day scientific retreat to present their research approaches and develop joint strategies. Going forward, regular scientific meetings, monthly video conferences, and laboratory visits to Lausanne and Bern will ensure close collaboration between the research groups.

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Further information

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