

International Research on Bioengineering of the Mitochondrial Genome

Novel genetic engineering approaches are to enable targeted interventions in the genome of mitochondria – that is the research goal of Prof. Dr. Nora Vögtle and Prof. Dr. Michael Knop, for which they are receiving funding from the Advanced Research + Innovation Agency (ARIA). The two scientists from the Center for Molecular Biology of Heidelberg University form one of 19 project teams that are working in the Precision Mitochondria Programme to develop a tool box for engineering mitochondrial genomes and will be testing new approaches. ARIA is allocating around 710,000 pounds sterling (approximately 825,000 euros) to fund the Heidelberg studies for a period of three years.

While the cell nucleus contains almost all of the genome, the mitochondria – the powerhouses of the cell – have their own small genetic code. It consists of only 37 genes, which are organized in circular DNA – mtDNA, for short. Defects in the mitochondrial genome are related to incurable neurodegenerative and metabolic diseases, cancer and also aging processes. They have, however, not yet been understood in detail, as Prof. Vögtle explains. While processes such as CRISPR – known as genetic scissors – enable interventions in bacterial or nuclear DNA, with the result that scientists can edit and examine a huge variety of such genomes, there is so far no comparable process for mtDNA.

The purpose of the Precision Mitochondria Programme is to develop and test novel genetic engineering approaches that bridge this gap. One question is how genetic instructions can be imported into a mitochondrion and read there, for example, to synthesize proteins. The studies aim to transfer successfully tested approaches to a living model system. While the aim of the programme is to unlock the technological capability to engineer mitochondria, Prof. Knop underlines that this could empower researchers to ultimately study and treat diseases caused by changes in the mitochondrial genome. “Some day we want to be able not only to treat the symptoms but also, by repairing the mitochondrial genome, to eliminate their actual cause,” says the Heidelberg molecular biologist. In order to realize the vision of an mtDNA that can be intentionally edited and programmed, 19 project teams, known as R&D creators, are collaborating in the ARIA-funded programme.

In this context, Michael Knop and Nora Vögtle will test a novel bioengineering approach on yeast as a model system. “Yeast is ideal for this as mitochondria are highly conserved in evolution. That means that findings can be transferred directly to higher eukaryotes, and specifically to human cells,” Prof. Vögtle explains, who conducts research on mitochondria, for example on mitochondrial protein import. “Yeast stands out as an established model system enabling fast and efficient experimental implementation,” Prof. Knop adds, whose research is on questions in systems biology and bioengineering. Their joint approach is based on the hypothesis that transporting DNA into the mitochondria has failed so far due to a mechanical obstacle – unlike importing proteins, channeling DNA into the mitochondria requires more energy. To remedy this, Prof. Knop and Prof. Vögtle want to equip the protein import machinery with additional “engines”.

The Advanced Research and Invention Agency (ARIA) is sponsored by the UK’s Department for Business, Innovation, Science and Trade. The agency funds teams of scientists and engineers to pursue research at the edge of what is scientifically and technologically possible. It supports high-risk projects with disruptive potential and, in special cases, is also open to applications from outside the United Kingdom to involve global expertise and so raise the chances of scientific and technological breakthroughs. For the research studies in the Precision Mitochondria Program ARIA is providing funding worth up to 66 million pounds sterling (approximately 77 million euros) over a period of up to five years.

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