Medical Xpress

Mitochondrial dysfunction is the root cause of many diseases

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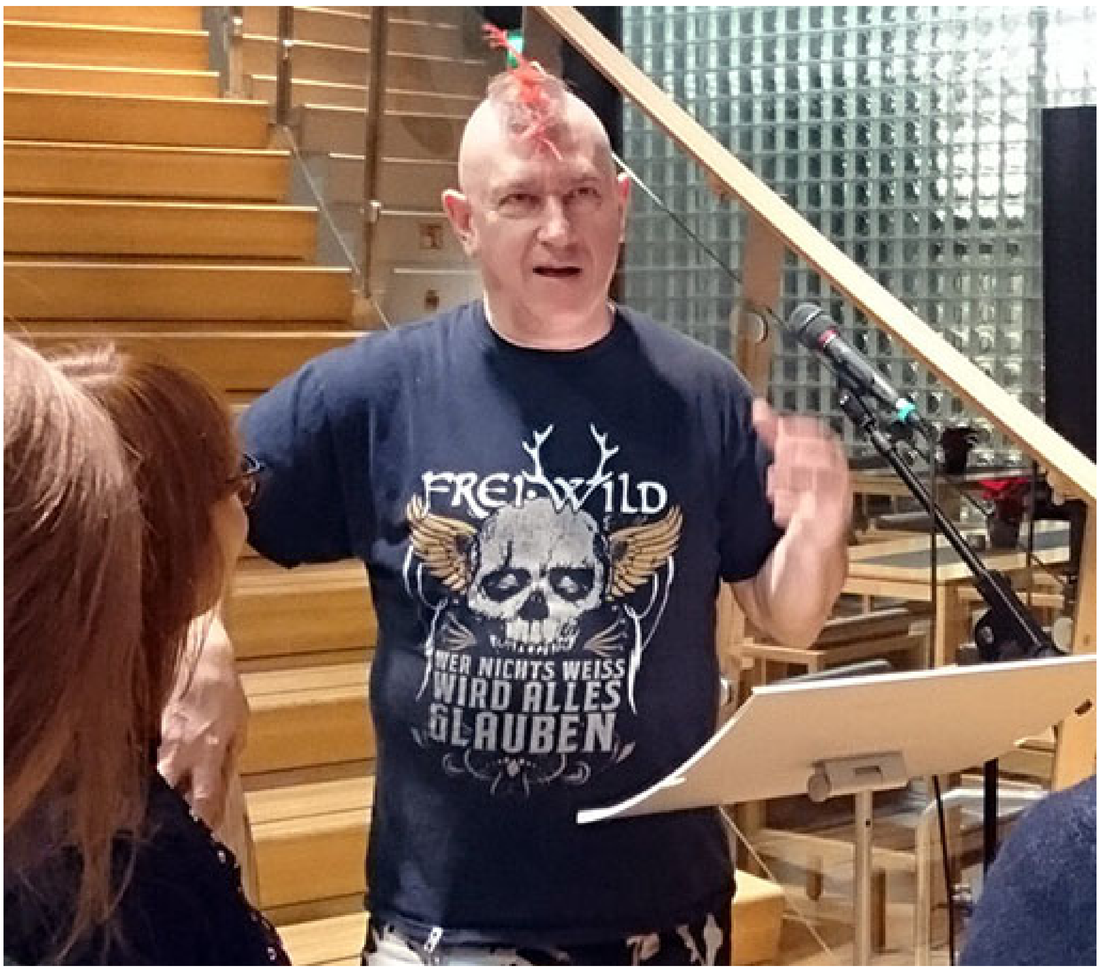

Howy Jacobs, Director of the Institute of Biotechnology . Credit: Helsingin yliopisto (University of Helsinki)

Mitochondrial dysfunction is the root cause of many diseases that are bewildering in their variety and complexity. They include rare genetic disorders in children, some forms of heart disease, and most likely many cases of Parkinson's disease.

Research on mitochondria started already in the late 19th century, but there are still many unsolved issues concerning their composition, their function and their relevance to health and disease. Director Howy Jacobs and his research group at the Institute of Biotechnology are amongst many scientists worldwide who seek to answer the open questions, in their daily work. Their main aim is to understand how mitochondria interact with other cellular components to maintain physiological homeostasis, and how mitochondrial defects lead to pathological states.

"Mitochondria arose as a bacterial intruder in ancient cells, and much of their biology has to be understood in this light. They retain a degree of autonomy, and still manufacture some of their most crucial components, which are encoded by the mitochondrial DNA, a relic of the intruder's original genome. Understanding how mitochondria are put together is important, if we are ever going to be able to intervene to correct their malfunction," explains Jacobs.

"It's of course worthwhile studying mitochondria in order to understand fundamental processes of the cell and of evolution. The disease angle isn't the only motivation. But naturally, I am very happy that our research has turned out to be important for medicine, and could one day lead to new treatments," says Jacobs.

"In any case, at least for me, science is addictive," Jacob states.

A back-up system to protect cells from mitochondrial damage

Since this research been going on for well over a century, it's clear that mitochondria only give up their mysteries rather slowly.

"For the past decade our focus has been on a particular 'back-up' system found in the mitochondria of lower organisms, but which has been lost during the evolution of complex animals such as humans or fruit flies. This back-up system kicks in when the regular energy-generating system of the mitochondria is overloaded, damaged or poisoned, protecting the cell against the harmful stresses of having a malfunctioning 'engine'. Indeed, mitochondria can be thought of rather like a car engine, that burns fuel (food molecules), and recovers the energy in a useful form to drive the processes of life. A malfunctioning engine imparts less energy but also creates toxic by-products as a result of incomplete combustion. Mitochondria are very similar," Jacob clarifies.

Jacob's team has transplanted the back-up or 'alternative' respiratory machinery from the mitochondria of lower organisms to human cells, showing that it can protect against pathological stresses, and even lethal poisons like cyanide, that target the mitochondria.

"This could have medical applications even within the next decade. But part of our work is still focused on very basic processes inside mitochondria. And there are always new surprises, sometimes relating to topics that have been neglected or have been impossible to study until the right tools became available," says Jacobs

An example is Jacob's current work in collaboration with a team in Paris, to try to measure the actual temperature at which the mitochondrial engine operates.

Science at the edge

One issue that scientists will have to grapple with in future is how far they are prepared to go to apply genetic knowledge to human disease.

"Until now, the human genome has been considered sacrosanct, and any direct or permanent manipulation of it has been regarded as unethical. However, the time is gradually approaching when we will acquire the means to prevent disease or reverse disease processes when they occur, by making such changes to the genome," Jacobs predicts.

"This obviously opens a major ethical dilemma," states Jacobs.

Is it ethical to engineer 'improvements' to what has evolved naturally, sometimes without being able to predict all the consequences? But equally, is it ethical to withhold life-saving technologies that can prevent suffering?

Provided by University of Helsinki