

MitoInsights

Bringing mitochondrial science closer to the people it matters to most

Science moves fastest when everyone can take part. That's why MitoCanada is committed to empowering our community with knowledge. By translating cutting-edge mitochondrial research into clear, easy-to-understand summaries, we aim to nurture curiosity, strengthen understanding, and build confidence in the science driving hope and progress.

Lay Summary: Silencing Mitochondrial Gene Expression in Living Cells

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What's this research about?

Mitochondria are often called the “powerhouses” of our cells because they produce the energy that keeps every tissue and organ working. To do this, mitochondria rely on tiny instructions written in their own set of genes, separate from the genomic DNA in the cell's nucleus. These mitochondrial genes encode a small number of essential proteins that help the cell turn oxygen and nutrients into usable energy.

For years, scientists have wanted to study what happens when specific mitochondrial genes are turned off, but this has been nearly impossible to do inside living cells. Traditional gene-editing tools, like CRISPR, don't easily work in mitochondria. This has made it hard to understand how mitochondrial genes interact with the rest of the cell, and what goes wrong when they stop working properly.

In this study, led by Luis D. Cruz-Zaragoza, Peter Rehling, and colleagues, researchers developed a new way to temporarily “silence” or switch off individual mitochondrial genes inside living cells, giving researchers a powerful new tool to study mitochondrial function in real time.

Why is this important?

Understanding how mitochondria regulate their own genes is crucial for comprehending many human diseases. Issues with mitochondrial gene expression, the process where genes produce the proteins vital for energy generation, are associated with serious conditions that can impact the brain, muscles, heart, and other organs.

Until now, researchers could only study mitochondrial genes indirectly, often using isolated mitochondria or models that didn't entirely reflect how cells work in real life. This new method allows researchers to study the process *as it happens in living cells*, offering a more accurate view of how mitochondria communicate with the rest of the cell and respond when things go wrong.

By helping researchers look closely at the timing, coordination, and response of cells when mitochondrial genes are disrupted, this approach brings research a step closer to understanding the biological roots of mitochondrial disorders.

How did they study this?

The researchers designed small, custom-built molecules called **peptide-morpholino chimeras**. A chimera refers to entities that have components from two or more different sources. For example, in research, scientists create cellular and molecular chimeras.

In this study, each chimera combines two parts: a “delivery tag” that helps it enter mitochondria, and a genetic “message blocker” that attaches to a specific piece of mitochondrial RNA, the molecule that carries genetic instructions from DNA to make proteins.

When these chimeras were introduced into human cells grown in the lab, they successfully traveled into the mitochondria and attached to their target RNAs. This prevented the selected gene from producing its protein, effectively silencing that gene. The researchers could then observe how the cell responded over time.

They tested the tool on several mitochondrial genes that are part of the oxidative phosphorylation (OXPHOS) system, the machinery responsible for producing energy. By switching off these genes one at a time, they tracked how each change affected the cell's metabolism, protein production, and communication between mitochondria and the nucleus.

What did they find?

The new tool worked reliably and specifically. It could silence targeted mitochondrial genes within hours, and the effect lasted for several days. When certain genes were turned off, the researchers observed clear changes in the mitochondria's ability to produce energy. Importantly, the tool only affected the targeted genes, it didn't interfere with unrelated parts of the cell.

When the team silenced genes responsible for the energy-producing complexes (called complexes I, III, IV, and V), they observed a decrease in activity in those complexes, confirming that the silencing was accurate. They also discovered that when one mitochondrial gene stopped functioning, it triggered specific responses in the nucleus, showing how closely connected these two genetic systems are.

Over time, they were able to watch how mitochondria adjusted to the loss of certain proteins and even identified new helper proteins that may assist in assembling and maintaining the energy complexes.

What does this mean for mitochondrial disease research?

This study doesn't present a therapy or treatment, but it offers a powerful new research tool. By making it possible to silence specific mitochondrial genes in living cells, scientists can now explore how mutations or defects in these genes lead to disease.

This could enhance how researchers model mitochondrial diseases in the lab, assist them in studying how cells respond to mitochondrial stress, and identify new molecular players involved in energy production. Over time, these insights could influence future strategies for understanding and eventually treating mitochondrial dysfunction.

The research in simple terms

The researchers found a way to temporarily turn off single mitochondrial genes inside living cells. This lets them see what happens when specific genes stop working, helping to uncover how each one contributes to making cellular energy. It's a bit like being able to unplug one wire in a complex electrical system to see exactly what that wire controls.

Why this matters to the mito community

For people and families affected by mitochondrial disease, this kind of research builds the foundation for future progress. By improving the tools used to study mitochondria, researchers can make faster, more accurate discoveries about how these tiny energy producers function and fail. While this research doesn't directly lead to a treatment, it makes the science more precise, and that precision is what helps move the field forward. Every step that helps researchers understand the "how" and "why" behind mitochondrial function brings us closer to better diagnostics, improved disease models, and, someday, targeted therapies.

Acknowledgment

This research was led by Luis D. Cruz-Zaragoza (Université de Sherbrooke) and Peter Rehling (University Medical Center Göttingen) in collaboration with the research groups of Michael Lidschreiber (Max Planck Institute for Multidisciplinary Sciences, MPI-MS), Stefan Jakobs (MPI-MS and Fraunhofer Institute for Translational Medicine and Pharmacology), and Bettina Warscheid (University of Würzburg). Together, their work represents a major collaborative effort to expand the scientific tools available for studying mitochondrial gene function in living cells.