Nature: Cells Have a Secret Power Line: Scientists Discover How the Nucleus Gets Its Own Private Energy Supply

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For decades, biologists assumed a cell’s energy simply diffused to wherever it was needed. It turns out the most important destination of all has a private delivery line An international team of

scientists led by Dr. Ivan Menendez-Montes, Assistant Professor at the University of Arizona, and Dr. Hesham A. Sadek, Director of the Sarver Heart Center at the University of Arizona and Group Leader at the Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), has uncovered a previously unknown mechanism through which mitochondria directly supply energy to the cell nucleus.

Published in *Nature*, the study demonstrates that mitochondria, the power house of the cell, physically dock at control center of the cell, the nucleus, though its main gate – the nuclear pore complexes. This creates a highly efficient system for delivering energy and metabolites directly into the nucleus. Turns out that rather than flooding a house with heat and hoping it reaches every room, the system is more like running a dedicated power cable straight to the control center. The findings challenge the long-standing view that mitochondrial products, such as ATP, diffuse freely through the cytoplasm before reaching the nucleus.

Mitochondria and the nucleus are known to maintain a close functional relationship. The nucleus supplies proteins required for mitochondrial function, while mitochondria provide energy and metabolites essential for cellular activities. Until now, it was assumed that these mitochondrial products reached the nucleus through passive diffusion. **The new study reveals that mitochondria and the nucleus have evolved a much more efficient mechanism**.

Using advanced microscopy, proteomics, genetic engineering and animal models, the researchers discovered that mitochondria physically attach to the nuclear pore complex through an interaction between the mitochondrial protein VDAC1 and the nuclear pore protein RANBP2. This contact enables the direct delivery of energy-rich molecules to the nucleus, supporting processes such as gene regulation, chromatin remodeling, transcription and cellular differentiation.

The connection is astonishingly precise. When the researchers nudged the mitochondria just 500 nanometers away from the nucleus — a gap thousands of times thinner than a human hair — the nucleus’s energy supply collapsed almost to zero. Unplug the cable, and the lights go out. To investigate the biological importance of these contacts, the team generated cellular and animal models in which the interaction between mitochondria and nuclear pores was disrupted without affecting the ability of mitochondria to produce energy.

The consequences were dramatic. Cells lacking these contacts failed to differentiate properly into cardiomyocytes, the contractile cells of the heart. Likewise, mouse embryos carrying mutations that disrupted the interaction died before birth and exhibited severe developmental abnormalities affecting both the heart and the nervous system.

“**I think that this is an important discovery, not only for the heart, but across all eukaryotic cell types**. We found that these contacts are present in every cell type we analyzed.” Hesham Sadek said, “The research possibilities that our results represent are huge. Almost every field studying human pathophysiology can apply our results and determine how they interact in the context of their study model”.

“This was a surprising a fascinating result. We started this project trying to find how the mitochondrial oxidants, known as ROS, reached the DNA in the nucleus and stops the innate ability of the heart to repair itself”” Ivan Menendez-Montes add. “What we found here was even bigger. We have seen that the mitochondria and the nucleus have coordinated so much, that have developed a system in which the nucleus gets its own exclusive energy delivery service”.

The study represents eight years of collaborative research involving 38 scientists from more than ten institutions worldwide. In addition to Dr. Sadek, CNIC researchers who participated in the work include **Dr. José Antonio Enríquez, Dr. Miguel Torres, Dr. Jesús Vázquez, Dr. Fátima Sánchez-Cabo, Dr. Consuelo Marín-Vicente, Dr. Manuel José Gómez and Dr. Enrique Calvo**.

The findings establish a new paradigm in cell biology by showing that the nucleus is not fueled solely through passive diffusion but receives energy through direct physical interactions with mitochondria. The researchers believe that understanding how these contacts are regulated could have important implications for developmental biology, regenerative medicine, cardiovascular disease, cancer and

aging. In other words, a connection too small to see may help explain how hearts form, how diseases take hold, and how our cells age — and learning to control it could open doors to new treatments.

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- *Menendez-Montes, I., Marin-Vicente, C., Mukherjee, S., Ahmed, M. S., Gomez, M. J., Anene-Nzelu, C. G., Lee, C. J. M., Koslowski, S., Solmonson, A., Tassin, T., Ali, S. R., Pessoa, P., Elnwasany, A., Lam, N. T., Thet, S., Calvo, E., Cardoso, A. C., Pereira, A. H. M., Xiao, F., Wang, P., Mohamed, A., El-feky, H., Elghamry, A., Gancedo-Alonso, G., Nguyen, N. U. N., Hsu, C.-C., Westfall, A. K., DeBerardinis, R., Foo, R. S.-Y., Kinter, M., Pressé, S., Xing, C., Szweda, L., Aroumougame, A., Sanchez-Cabo, F., Enríquez, J. A., Torres, M., Vázquez, J., & Sadek, H. A. (2026). Mitochondria directly interact with the nuclear pore complex. Nature. https://doi.org/10.1038/s41586-026-10588-3*

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