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Bursts of Power

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Mitochondria fire oxidants to communicate with organelles nearby, a communication that could be important in various diseases.

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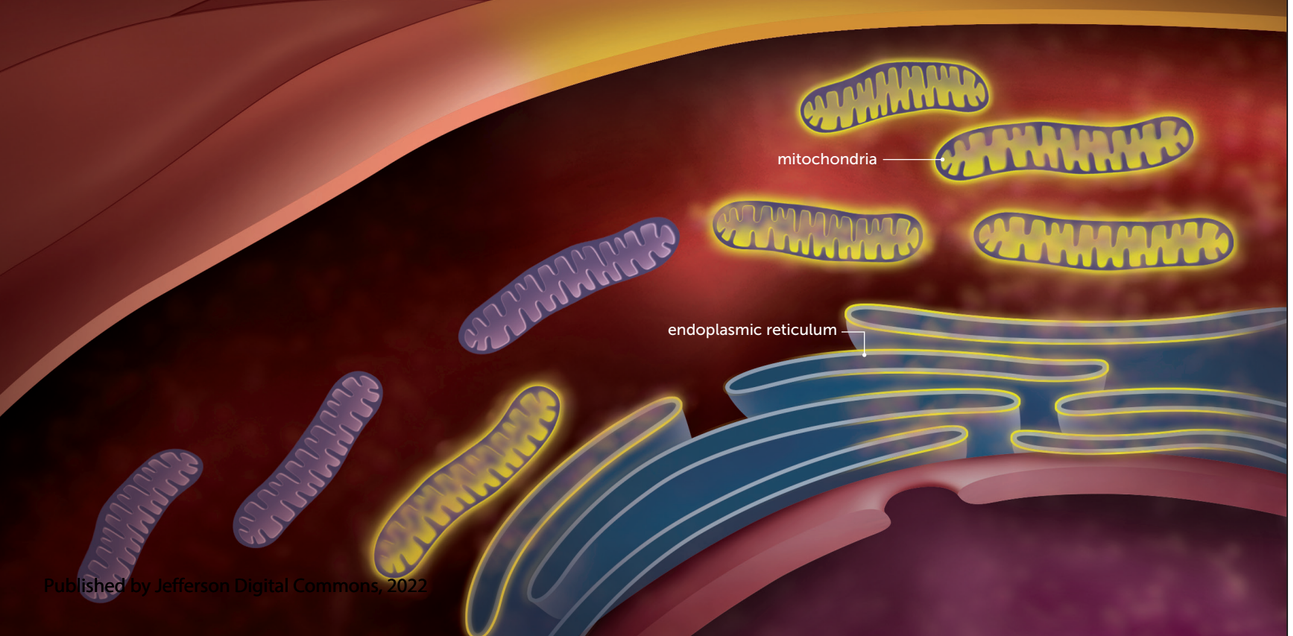
For a few years now, researchers have noticed that clusters of mitochondria abruptly change their activity inside the cell: a smattering firework here, a few there, all seemingly random. When at rest, only a few light up. But when the cell is stressed, it's like a meadow full of fireflies at dusk. What do these fireworks mean for the cells? Gyorgy Hajnoczky, MD, PhD, the Raphael Rubin, MD, Professor of Pathology, Anatomy and Cell Biology, and his team at the Jefferson MitoCare Center developed a toolkit of ultra-resolution instruments and fluorescent tags to find out what was happening at the individual-mitochondrion level, and discovered a mechanism for messages whispered only to the closest of neighbors. While oxidation drives energy production, it may also be involved in a new and highly specific kind of communication.

In recent years, researchers from fields as far flung as neurology, genetics and ophthalmology have found a role for mitochondria in disease. More than 3500 papers, including work from Dr. Hajnoczky, have linked mitochondria to Alzheimer's disease alone, and the organelle likely plays a role in nearly every other neurodegenerative disease. Although many researchers agree the mitochondria are involved, they don't yet know exactly how.

A recent study published by Dave Booth, PhD, Dr. Hajnoczky and collaborators in the high-impact journal *Molecular Cell*, uncovered a means of specific communication that could explain how mitochondria is involved in disease. The researchers show that mitochondria send messages to neighboring organelles, usually the endoplasmic reticulum — the site of protein and phospholipid production and calcium storage in the cell — and the organelles answer back. Mitochondria discharge oxidants that trigger the endoplasmic reticulum to release calcium. Rather than broadcast to the entire cell, however, these missives are only meant for organelles in closest proximity. The rest stay in the dark. But when the cell becomes stressed, the mitochondria amplify the whisper into a full-scale broadcast meant for the entire cell.

What is the use of the messaging for the mitochondrion and for the cell? Mitochondria are clearly initiating a conversation, and the Hajnoczky lab is working to find out whether these signals help to maintain the local status quo and whether the amplification and expansion of the signals could be involved in diseases like neurodegeneration. ■



Mitochondrial Whispers and Shouts
A single mitochondrion flickers on with an oxidative burst (bottom left). It sends a signal to its closest neighbor — the endoplasmic reticulum, which answers back, without alerting other organelles. But under stress (right), as in disease states, these same oxidative messages are amplified and broadcast to the entire cell in a global alert.