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Spying On Subcellular Structures

Microfluidics: Tiny channels trap individual mitochondria, allowing scientists to watch the organelles' behavior

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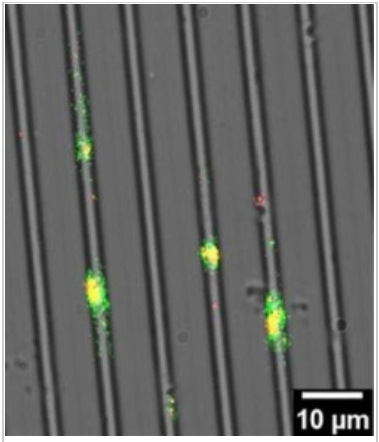

Caught In A Trap
Single mitochondria stained with fluorescent dye are trapped in nanometer-sized channels. The organelles glow green because they have low membrane potentials.
Credit: *Anal. Chem.*

Mitochondria act as the power plants for our cells. Biologists think that dysfunctional mitochondria could be linked to conditions such as diabetes, cancer, and aging. To study the differences between healthy and unhealthy mitochondria and better understand the structures' role in disease, researchers developed **a new nanofluidic device that can trap individual mitochondria** for spectroscopic analysis (*Anal. Chem.* 2013, DOI: **10.1021/ac4010088**).

Mitochondria synthesize the molecule ATP, which fuels many of the cell's biochemical processes. To drive ATP synthesis, mitochondria pump protons across a pleated inner membrane, building up an energy potential. **Peter J. Burke** at the **University of California, Irvine**, and his colleagues wanted to study single mitochondria to get better insight into the conditions that disrupt this membrane potential. For example, if the potential drops significantly, it triggers cell death, or apoptosis. Cells that resist apoptosis can lead to tumors.

Burke's team used soft lithography to etch a silicon chip that served as a mold to make a nanofluidics device out of the polymer polydimethylsiloxane. "The hardest part was to design a chip with a channel that was small enough to trap one—and only one—mitochondrion," Burke says. The device had channels 500 nm high and 2 µm wide.

To monitor the membrane potential of mitochondria trapped in the channels, the researchers first stained the organelles with fluorescent dye molecules. The charged dyes make the organelles glow different colors depending on the membrane potential: High potentials lead to a reddish glow, and low potentials create a green color.

The team pumped a solution of the dyed mitochondria into their device and measured each organelle's fluorescence. The organelles' potentials responded as predicted when the researchers added chemicals known to affect mitochondria function. For example, spiking the solution with pyruvate and malate, both involved in the metabolic pathway mitochondria use to make ATP, caused the membrane potential to increase.

Burke thinks the technique could help scientists screen the effect of drugs for cancer and other conditions on mitochondria.

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