Researchers develop new tool to check cells' 'batteries'

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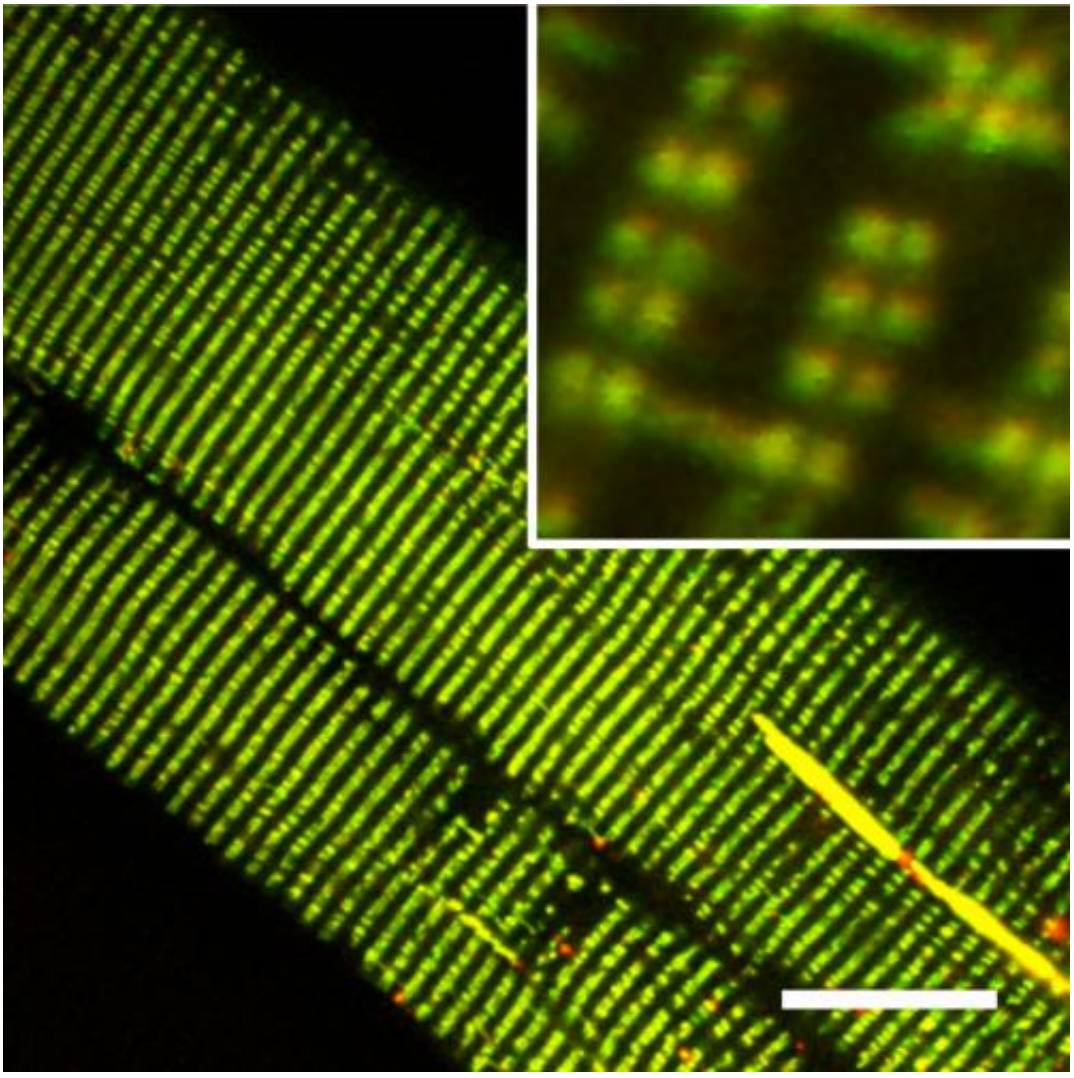

Researchers at U.Va.'s School of Medicine have created a method to illuminate and understand mitochondria in living creatures like never before.

(Medical Xpress)—Under the microscope, they glow like streetlights, forming tidy rows that follow the striations of muscle tissue. They are mitochondria – the powerhouses of cells – and researchers at the University of Virginia School of Medicine have created a method to illuminate and understand them in living creatures like never before.

Not only can the researchers make the mitochondria glow for the microscope, but they also can discern from that fluorescence the mitochondria's age, their health, even their stress level. And ultimately that glow, in its soft reds and greens, will shed light on human health and a massive array of illnesses, from diabetes to Parkinson's disease to cancer.

"Mitochondrial health is important for physiology and disease. That is well-known," said researcher Zhen Yan of U.Va.'s Cardiovascular Research Center. "However, the whole field of mitochondrial health is largely unexplored, in large part because of the lack of useful tools. This has hindered the understanding of the importance of mitochondria in disease development.

"With this study we have, for the first time, shown that we can use a reporter gene to measure mitochondrial health robustly in vivo. We believe this tool will allow us to get into the field of mitochondrial biology like never before. Before, we could see the mitochondria under an electron microscope. That showed us only what they looked like. Now we can measure the health of millions of mitochondria at the click of a button."

The reporter gene on which Yan and his team based the new tool is a type of gene used in scientific research to determine the activity and function of other genes. The reporter gene produces a protein that glows green when newly made; the protein then transitions to red as it ages. By giving the reporter gene specific targeting directions, the researchers

were able to instruct the protein to enter the mitochondria, setting them aglow.

"So now we have fluorescent mitochondria, which are fluorescent green initially and then, as the mitochondria age or become oxidized, they transition to red, so that we can assess the oxidation status," said Rhianna Laker, a postdoctoral fellow in Yan's lab and the lead author of a new paper detailing the work.

The researchers have put their tool to the test in flies, worms and mice. They found that mice fed a high-fat diet had more red mitochondria, meaning the mitochondria were stressed or oxidized, while mice that exercised had more green mitochondria, Laker said. That finding speaks both to the importance of exercise and to the potential diagnostic power of the new tool, dubbed the MitoTimer.

Yan's lab collaborated with Jeff Saucerman of the Department of Biomedical Engineering to take the work to the next level. Saucerman's team has developed a computer program that can analyze the degree of mitochondrial fluorescence to assess both individual mitochondria and the overall ratio of red to green in a particular area. That ratio speaks to the health of the cells.

The mitochondria are also a sensor of metabolic state and stress, Yan said.

The findings have been published online in the *Journal of Biological Chemistry* and will appear in a forthcoming print edition.

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