Study reveals possible treatment for diseases caused by Mitofusin 2 deficiency

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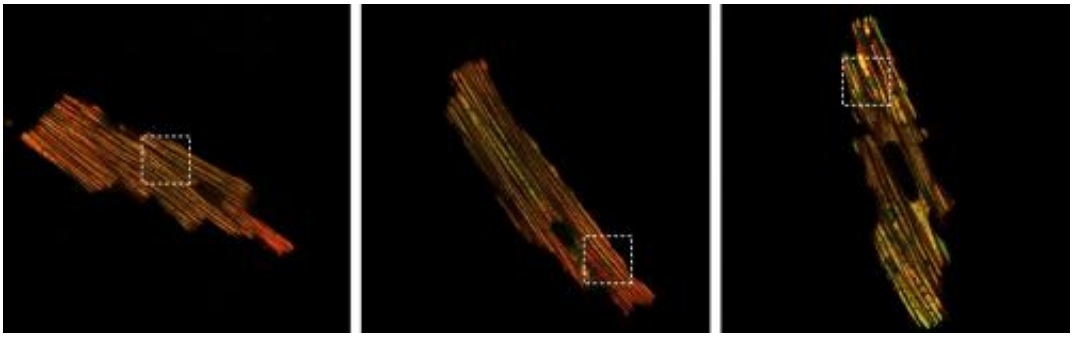

In mice, mitochondria (green) in healthy (left) and *Mfn1*-deficient heart muscle cells (center) are organized in a linear arrangement, but the organelles are enlarged and disorganized in *Mfn2*-deficient cells (right). Credit: Mourier et al., 2015

Researchers have discovered a novel role for Mitofusin 2, and the findings may point to a new treatment for patients with diseases caused by loss of the mitochondrial protein. The study appears in *The Journal of Cell Biology* .

Mitofusin 2 and its closely related counterpart, Mitofusin 1, are located in the outer membrane of mitochondria. Both proteins are required for mitochondrial fusion, an important maintenance function in which adjacent organelles join together and exchange contents. Mice lacking the *Mfn1* gene, which encodes Mitofusin 1, nevertheless seem perfectly healthy, but *Mfn2*-deficient mice die soon after birth. Moreover,

mutations in the *Mfn2* gene are known to cause human diseases, including the peripheral neuropathy Charcot-Marie-Tooth type 2A. Lack of Mitofusin 2 therefore seems to affect mitochondrial function in other ways besides membrane fusion, but researchers have been unclear how.

To find out, Max Planck Institute scientist Nils-Göran Larsson and colleagues investigated mouse heart muscle cells lacking *Mfn2*. They found that energy metabolism in the cells was impaired compared with healthy and *Mfn1*-deficient cells. They determined that the process was stalled because of reduced levels of coenzyme Q, a key component of the mitochondrial respiratory chain that generates cellular energy in the form of ATP. In the absence of Mitofusin 2, many of the enzymes and molecules involved in the pathway that generates precursors of coenzyme Q were decreased, indicating that Mitofusin 2 is required for coenzyme Q production.

By supplementing *Mfn2*-deficient cells with coenzyme Q, Larsson and colleagues were able to partially restore respiratory chain function. They therefore think that coenzyme Q supplements might help treat patients with diseases caused by *Mfn2* mutations.

More information: Mourier, A., et al. 2015. *J. Cell Biol*. DOI: 10.1083/jcb.201411100

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