Bad mitochondria may actually be good for you

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Mice with a defective mitochondrial protein called MCLK1 produce elevated amounts of reactive oxygen when young; that should spell disaster, yet according to a study in this week's JBC these mice actually age at a slower rate and live longer than normal mice.

Mitochondrial oxidative stress is a popular theory explaining the aging process; over time, reactive oxygen species produced by mitochondria while they make energy slowly accumulate and begin damaging cells, including the mitochondria. Several recent studies have begun to question this theory, though, and to get some more direct answers, Siegfried Hekimi and colleagues at McGill University examined the mitochondria of MCLK1-defective mice, a strain known for its longevity, at various ages.

What they found was that in young (3 month old) MCLK1-defective mice, mitochondria were quite energy inefficient and produced a lot of harmful oxygen radicals; yet surprisingly, when these mice were 23 months old, their mitochondria were working better than normal mice. So, despite the oxidative stress, these mice experienced less deterioration than normal.

To confirm whether MCLK1-defiency could be somehow protective, the researchers crossed MCLK1-defective mice with those lacking SOD2, a major protein antioxidant. Normally, SOD2-defective mice accumulate cellular damage quickly, yet when combined with MCLK1-defiency, they exhibited less damage and oxidative stress.

In explaining this seeming paradox, Hekimi and colleagues suggest that while MCLK1-defective mice produce more oxygen radicals from their mitochondria, their overall inefficiency results in less energy and fewer oxygen radicals being produced in other parts of a cell. Thus while these mice may have some higher risks of damage while young, they accumulate less damage as they age -a finding that seems to indicate the mitochondrial stress theory may not be correct.

More information: "Reversal of the Mitochondrial Phenotype and Slow Development of oxidative biomarkers of aging in long-lived Mclk1+/- mice" Jerome Lapointe, Zaruhi Stepanyan, Eve Bigras and Siegfried Hekimi. *Journal of Biological Chemistry*. Article link: www.jbc.org/cgi/content/abstract/284/30/20364

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