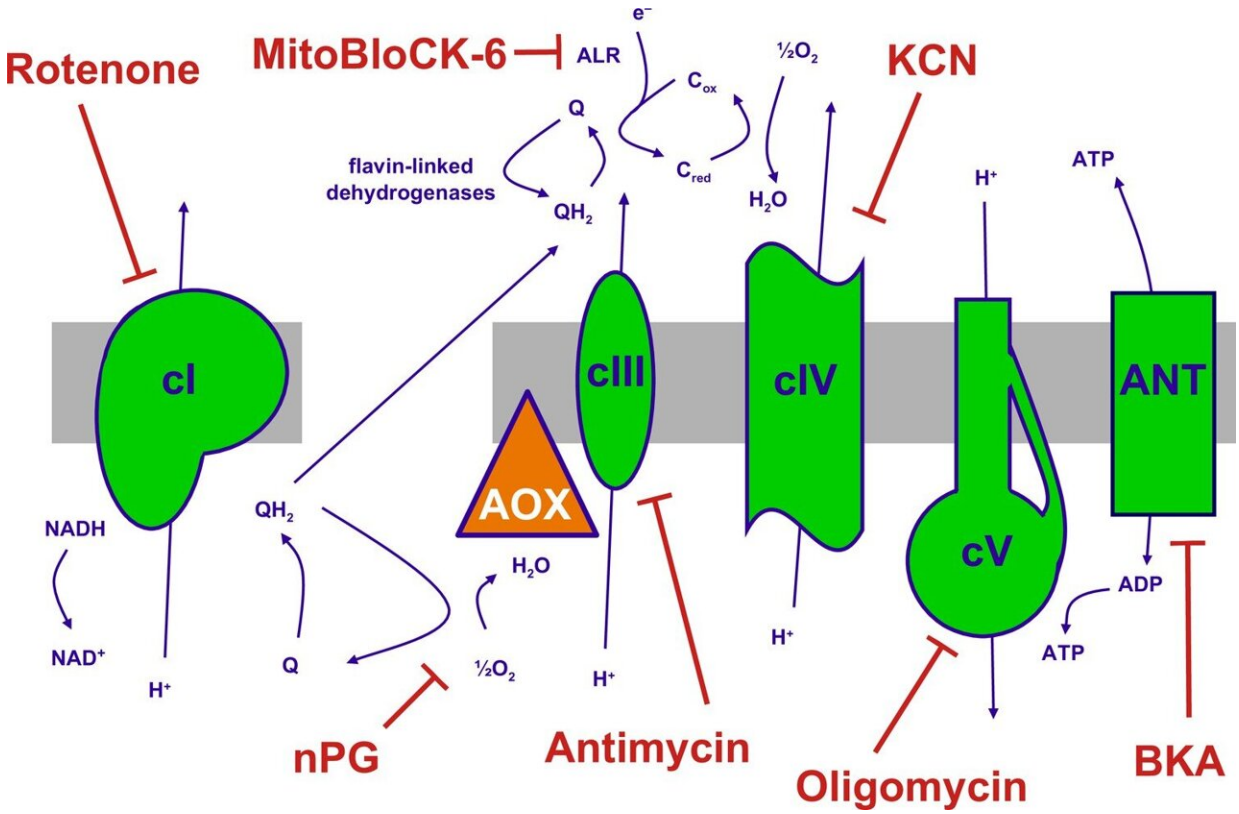
High mitochondrial temperature is maintained in cells subjected to metabolic stress, study shows

December 19 2023



The mitochondrial oxidative phosphorylation (OXPHOS) system and inhibitors. Summary of the major components of the OXPHOS system and classic inhibitors. Protonmotive OXPHOS enzyme complexes (cI, cIII, cIV, cV) shown in green, the non-protonmotive transgenically introduced alternative oxidase (AOX) from *Ciona intestinalis* in orange, the inner mitochondrial membrane in gray. Ions and small molecules indicated in purple, inhibitors in brick-red. BKA—bongkrekic acid, an inhibitor of the adenine nucleotide translocase

(ANT). nPG—*n*-propyl gallate, an inhibitor of AOX, Q—ubiquinone (oxidized coenzyme Q), QH_2—ubiquinol (reduced coenzyme Q), c_{red}, c_{ox}—reduced and oxidized forms of cytochrome *c*, respectively. Complex I (cI), along with a number of flavin-linked dehydrogenases, one of which is succinate dehydrogenase, also described as complex II, each reduce ubiquinone, thus contributing input electrons to complex III (cIII). ALR—'augmenter of liver regeneration', Evr1 in yeast, acts as an additional feeder of electrons to cytochrome *c*, from the oxidation of sulfhydryl groups in proteins destined for the mitochondrial inter-membrane space via the Mia40 pathway and is inhibited by MitoBLloCK-6. Credit: *eLife* (2023). DOI: 10.7554/eLife.89232.3

Mitochondria in human and mammalian cells are maintained at around 52 ºC, significantly warmer than the cell's external environment. A new study shows that even under external metabolic stresses, mitochondrial metabolism is remodeled to maintain this high temperature. The findings have implications for understanding disease processes.

Together with colleagues in four countries, Mügen Terzioglu and Howy Jacobs from Tampere University's Faculty of Medicine and Health Technology have just published a paper in *eLife* reporting extraordinary findings on the temperature of mitochondria in human and animal cells.

Corroborating their own preliminary observations, first published in 2018, that mitochondria are maintained at around 50 ºC, they have now demonstrated this high mitochondrial temperature using two independent methods in a range of different cultured cells from humans, mice, and the fruit-fly Drosophila.

Furthermore, they have shown that when external metabolic stresses are applied to cells, such as by toxins that disrupt cellular energy transactions or by changes in nutrient availability, mitochondrial metabolism is remodeled so as to maintain a temperature about 15 ºC warmer than the

cell's external environment.

To put this in context, while our bodies as a whole are kept at a steady 37 ºC, with even a small increase perceived as fever, the energy factories inside our cells are much hotter, operating at the temperature of a typical cup of freshly made coffee. Radiating heat to the rest of the cell appears to be one of the core functions of mitochondria, which are not just supplying energy for other processes, such as muscle contraction or electrical signaling in nerve cells.

There are huge implications of these findings for understanding disease processes, as well as how cells and organisms cope with fluctuations in the external environment. If the 'heat-work balance' becomes disturbed, many vital physiological functions are likely to suffer.

The next steps in this research are to pinpoint the molecular machinery that monitors mitochondrial temperature and modulates mitochondrial heat output in response to cellular needs.

"This opens a whole new chapter in biochemistry and physiology and may require us to revise a lot of basic 'textbook' knowledge," Howy Jacobs says.

More information: Mügen Terzioglu et al, Mitochondrial temperature homeostasis resists external metabolic stresses, *eLife* (2023). DOI: 10.7554/eLife.89232.3

Provided by Tampere University

https://phys.org/news/2023-12-high-mitochondrial-temperature-cells-subjected.html