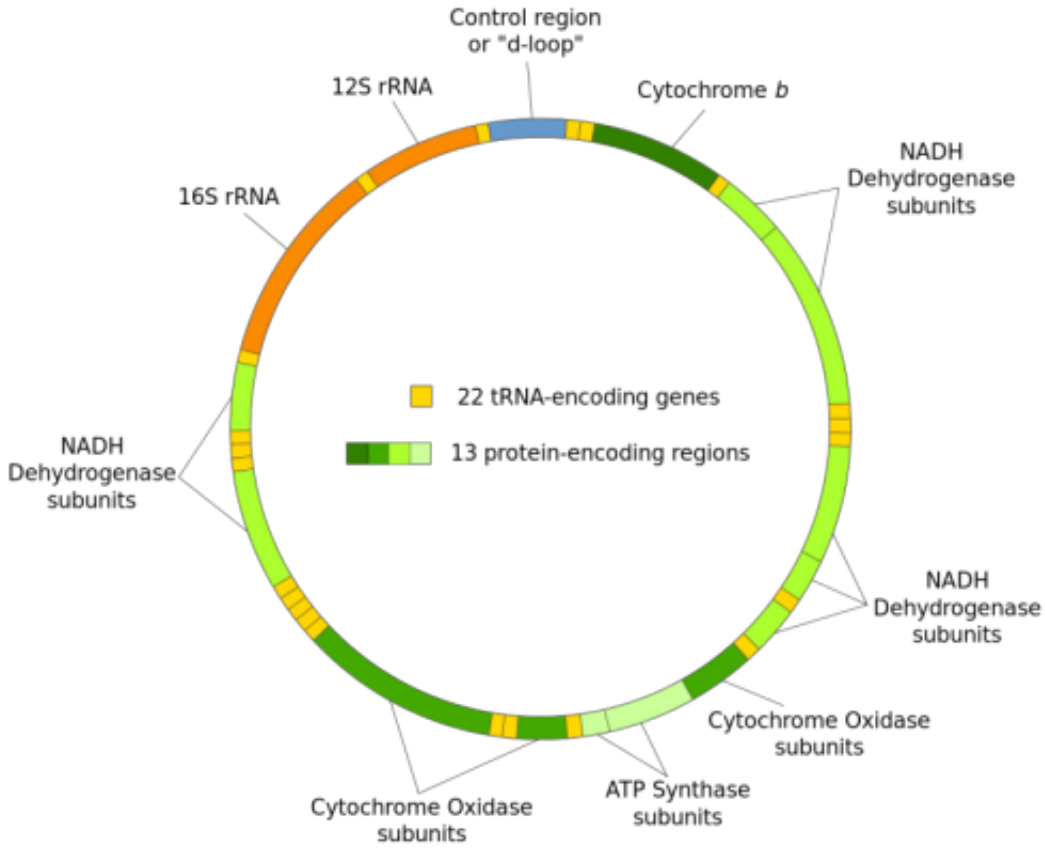
How to protect cells from selfish mitochondrial DNA

April 20 2017



Structure of the human mitochondrial genome. Credit: Wikipedia/CC BY-SA 3.0

Using yeast cells as a model, scientists from the A.N. Belozersky Institute of Physico-Chemical Biology, Lomonosov Moscow State University investigated the mechanisms that allow cells to protect

themselves from invasion of selfish mitochondrial DNA molecules. The findings were published in the *Journal of Cell Science*.

The information on the structure and functioning of a cell is encoded in its DNA. While most of this information is encoded in nuclear DNA, a small but essential part is stored separately in mitochondrial DNA (mtDNA). The main role of mitochondria is to convert energy into ATP—the "molecular currency" of a cell. Mitochondrial DNA encodes some of the proteins involved in mitochondrial function. Selfish mitochondrial DNA molecules emerge as a result of mutations. Such mtDNA molecules usually contain large deletions. These mtDNA molecules do not contain information necessary for mitochondrial operation, but have a competitive advantage over functional mtDNA molecules—being shorter than the normal mtDNA, selfish mtDNA molecules are able to replicate faster than the normal ones. As a result, eventually selfish mtDNAs replace functional mtDNA molecules. The accumulation of selfish mtDNA molecules in the cells can impair mitochondria functioning and induce pathologies. In their work the scientists investigated potential strategies to protect cells from selfish mtDNA clonal expansion.

Dmitry Knorre, a senior researcher at the A.N. Belozersky Institute of Physico-Chemical Biology, the corresponding author of the study shares: "We have crossed yeast cells containing different (normal and selfish) variants of mtDNA and observed the results of their "competition". This experiment was possible because diploid yeast cells, in contrast to mammalian zygotes, inherit mtDNAs from both gametes (parents)."

The biologists have found out that the uncouplers of oxidative phosphorylation (namely, compounds, which decrease the efficiency of mitochondrial energy conversion) change the results of this "competition" in favor of functional mtDNA. Notably, this effect of uncouplers could be observed only in those cells, where mitochondria

could divide into separate fragments and undergo intracellular digestion.

Dmitry Knorre says: "We've found that uncouplers stimulate the mitochondrial turnover in the cells. However, this effect is well pronounced only in zygotes but not in haploid yeast cells. Perhaps, the digestion of non-functional mitochondria is an evolutionary conserved mechanism protecting organisms from invasion of selfish mtDNA during sexual reproduction."

In their research, the scientists have used fluorescence microscopy and electron microscopy and also molecular biology techniques.

The biologists are going to continue studying mitochondria degradation mechanisms at different stages of the yeast life cycle. They want to find out how the cellular molecular machinery of "mitochondria digestion" recognizes bad mtDNAs hidden by two membrane layers and how the cell decides whether to eliminate this mitochondrion or not.

More information: Iuliia E. Karavaeva et al, Mitochondrial depolarization in yeast zygotes inhibits clonal expansion of selfish mtDNA, *Journal of Cell Science* (2017). DOI: 10.1242/jcs.197269

Provided by Lomonosov Moscow State University