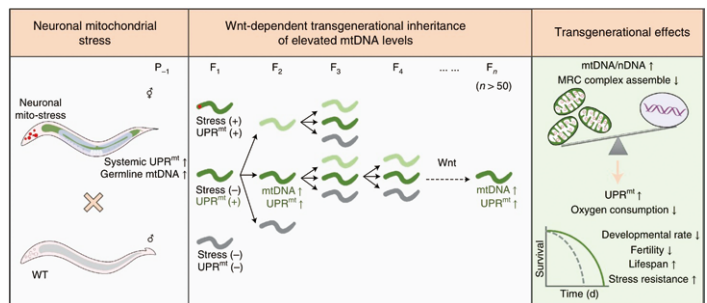


The Memory of Neuronal Mitochondrial Stress is Passed on to Their Descendants

The impact of the parental experiences has been observed to extend over multiple generations in various organisms. It is therefore of significant scientific interest to determine what environmental and physical conditions could induce transgenerational effects.

In a cover study of *Nature Cell Biology*, Dr. TIAN Ye's group from the Institute of Genetics and Developmental Biology, the Chinese Academy of Sciences, revealed that neuronal mitochondrial stress can be sensed and reacted to by the mitochondria in the germline to potentially promote the maternal inheritance of elevated mtDNA levels across many generations in a Wnt signaling-dependent manner. This study entitled "The memory of neuronal mitochondrial stress is inherited transgenerationally via elevated mtDNA levels" has been published on August 2.

In this study, the authors described a discovery stemmed from a serendipitous observation that neuronal mitochondrial stresses elicit a global induction of the UPR^{mt} that can be transmitted to offspring for multiple generations (>50) in *Caenorhabditis elegans* even after the original stress signal has been gone. The transgenerational induction of UPR^{mt} was caused by the elevated mtDNA inherited maternally, which disturbed the balance between mitochondrial oxidative phosphorylation subunits encoded by the mtDNA and the nuclear DNA to induce mitochondrial proteostasis stress. Wnt signaling is required for the propagation



Model for the transgenerational inheritance of increased mtDNA levels and the UPR^{mt}. (Image by IGDB)

of elevated mtDNA levels across generations via transgenerational regulation of the mtDNA polymerase *polg-1*.

The transgenerational inheritance of the elevated mtDNA levels and the UPR^{mt} enable their descendants to live longer and confer increased stress tolerance. However, there is clearly a cost of transgenerational UPR^{mt}, animals with these transgenerational effects take a longer time to sexually mature and will produce less progeny. The presence of such a trade-off implies a fitness cost of inheritance of elevated mtDNA levels if stress conditions are not experienced in the near future.

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Reference

Q. Zhang, Z. Wang, W. Zhang, Q. Wen, X. Li, J. Zhou, . . . Y. Tian, (2021) The memory of neuronal mitochondrial stress is inherited transgenerationally via elevated mitochondrial DNA levels. *Nature Cell Biology* 23, 870. doi: 10.1038/s41556-021-00724-8.