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ABSTRACT

"A Mitochondrial Paradigm for Metabolic and Degenerative Disease, Cancer and Aging: Why Do We Still Have a Mitochondrial DNA?"

The human cell is assembled from two different organisms: the nucleo-cytosol organism which specializes in cellular and tissue structure and whose genes are Mendelian and the mitochondrial organism which specializes in energy and whose genes are maternal and stochastic. Inherited pathogenic mitochondrial DNA (mtDNA) mutations have been linked to a wide range of metabolic and degenerative diseases. Somatic mtDNA mutations accumulate with age in a broad spectrum of organisms, introduction of catalase into the mouse mitochondrial matrix reduces the mtDNA somatic mutation rate and extends life span, increasing *Drosophila* cAMP levels reduces mitochondrial reactive oxygen species (ROS) and extends life span, and treating short-lived *Drosophila* mutants with mitochondrially-targeted antioxidants can restore the life span. Ancient adaptive mtDNA polymorphisms have been associated with altered risk for metabolic and neurodegenerative diseases, such as Parkinson disease, and somatic mtDNA mutations are elevated in the brains of Alzheimer Disease patients. Finally, both germline and somatic mtDNA mutations are associated with various cancers including prostate cancer. Therefore, diseases which appear “complex” when viewed exclusively from the nucleo-cytosol perspective might be more readily understood if the contribution of the mitochondrial organism were also considered.

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