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MITOCHONDRIA AT WORK

Mitochondria combine hydrogen derived from dietary carbohydrates and fats with oxygen to generate heat and ATP. Electrons flowing through the electron transport chain, made up of OXPHOS complexes I through V, are used to pump protons out of the mitochondrial inner membrane. This creates an electrical charge used to generate ATP, which powers most of the cell's biochemical reactions. As a toxic by-product of OXPHOS, mitochondria generate reactive oxygen species (ROS), called free radicals. At high levels, free radicals damage mtDNA, nuclear DNA, proteins, lipids, and other molecules in the cell. As the percentage of mutated mtDNA in a cell increases, mitochondrial energy output declines, ROS production increases, and the likelihood of cell death increases. Through the work of Wallace and others, energy deficiency caused by these factors, as well as inherited mtDNA mutations, have been linked to numerous diseases.

mtDNA MUTATIONS

Mutations in the mtDNA genes can result in a wide range of symptoms. Several single-base changes in the complex I genes predispose to a person to Leber hereditary optic neuropathy (LHON), a form of inherited vision loss. Mutations in the complex V ATP synthase 6 gene can cause retinal problems when few mtDNA in a cell harbor the mutation, but can cause the lethal Leigh syndrome when many mtDNA in a cell have the mutation. Mutations in the ribosomal and transfer RNA genes in the mtDNA can predispose to deafness, muscle and heart disease, strokes, diabetes, Alzheimer's and Parkinson's. For example, a mutation in the tRNA(Lys) gene can cause a form of epilepsy together with muscle symptoms known as myoclonic epilepsy and ragged-red fiber disease (MERRF).