TK2 Gene

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Contributor: Rui Liu

Thymidine kinase 2, mitochondrial: The TK2 gene provides instructions for making an enzyme called thymidine kinase 2 that functions within cell structures called mitochondria, which are found in all tissues.

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1. Normal Function

The *TK2* gene provides instructions for making an enzyme called thymidine kinase 2 that functions within cell structures called mitochondria, which are found in all tissues. Mitochondria are involved in a wide variety of cellular activities, including energy production; chemical signaling; and regulation of cell growth, cell division, and cell death. Mitochondria contain their own genetic material, known as mitochondrial DNA (mtDNA), which is essential for the normal function of these structures. Thymidine kinase 2 is involved in the production and maintenance of mtDNA. Specifically, this enzyme plays a role in recycling mtDNA building blocks (nucleotides) so that errors in mtDNA sequencing can be repaired and new mtDNA molecules can be produced.

2. Health Conditions Related to Genetic Changes

2.1. TK2-related mitochondrial DNA depletion syndrome, myopathic form

More than 30 mutations in the *TK2* gene have been found to cause *TK2*-related mitochondrial DNA depletion syndrome, myopathic form (*TK2*-MDS). *TK2*-MDS is an inherited condition that causes progressive muscle weakness (myopathy), typically beginning in early childhood. About two-thirds of the mutations that cause this condition change single protein building blocks (amino acids) in thymidine kinase 2. All *TK2* gene mutations result in a decrease of enzyme activity, which impairs recycling of mtDNA nucleotides. A shortage of nucleotides available for the repair and production of mtDNA molecules leads to a reduction in the amount of mtDNA (known as mtDNA depletion) and impairs mitochondrial function. Greater mtDNA depletion tends to cause more severe signs and symptoms. The muscle cells of people with *TK2*-MDS have very low amounts of mtDNA, ranging from 5 to 30 percent of normal. Other tissues can have 60 percent of normal to normal amounts of mtDNA. The cause for the variability in the amount of mtDNA lost among affected individuals, even those with the same mutations, is unknown.

It is unclear why *TK2* gene mutations typically affect only muscle tissue, but the high energy demands of muscle cells may make them the most susceptible to cell death when mtDNA is lost and less energy is produced in cells.

Progressive external ophthalmoplegia

3. Other Names for This Gene

- KITM_HUMAN
- mt-TK
- MTDPS2
- MTTK

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