MYOCLONIC EPILEPSY WITH RAGGED RED FIBERS (MERRF)

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MERRF is a rare panethnic mitochondrial disease which is caused by mutations in the mtDNA. It mainly affects the muscle tissue and the nervous system. Onset can range from childhood to adulthood, but typically symptoms show after a normal early development. As one ages, symptoms start progressing. Because MERRF is a heteroplasmic disease, phenotypes may vary from person to person. Myoclonus is usually the first symptom. It is later followed by epilepsy, ataxia, physical weakness, and dementia. Other characteristics include difficulty speaking, short stature, hearing loss, peripheral neuropathy, and optic atrophy. When muscle cells of an affected individual are stained and viewed under a microscope, the cells appear as ragged-red fibers making the cells abnormal.
MERRF is a mitochondrial disease—meaning that its pathway is matrilineal.

- It is caused by point mutations in the mtDNA.

- Mutations typically occur in the MT-TK (Mitochondrially encoded tRNA lysine), MT-TL1 (Mitochondrially encoded tRNA leucine 1), MT-TH (Mitochondrially encoded tRNA histidine), and MT-TS1 (Mitochondrially encoded tRNA serine 1) genes which are contained in mitochondrial DNA.

- More than ninety percent of the patients have a point mutation on MT-TK gene which codes for tRNA\text{\text{_{lys}}}

- This is an A-to-G transition at nucleotide 8344.

- The tRNA\text{\text{_{lys}}} helps in the assembly of proteins for oxidative phosphorylation.

- These mutations make the mitochondria incapable of using oxygen, producing energy, and making proteins—because there’s a lack of energy production, organs and tissues that use a lot of energy, like the brain and the muscles, fail to function adequately.
CURRENT TREATMENTS AND LIMITS

- Currently there is no cure and there are a few treatments available
- Treatments are symptomatic and palliative
- Prenatal testing can be done, but it won’t give too much information
- Valproic Acid- Used to treat myoclonic epilepsy; causes secondary carnitine deficiency which can impair the functioning of the mitochondria; it is strongly advised to avoid using this, but if needed, to use it with L-Carnitine supplements
- Other treatments for myoclonic epilepsy include levetiracetam, clonazepam, and zonisamide
- Vitamin supplements that help optimize the activity of the OXPHOS complexes
- Coenzyme Q and L-Carnitine Supplements- Help to improve mitochondrial functioning
- Antiepileptic drugs are used to treat seizures
- Physical therapy and aerobic exercise are used to improve impaired motor ability
- Over ninety percent of MERRF patients have a point mutation on the MT-TK gene, so cloning and inserting the MT-TK gene would be the most effective cure.

- To do this, the wild-type MT-TK gene would be inserted into a plasmid, made into recombinant DNA, and then inserted into the patient.

- When recombinant DNA has been inserted into the patient, the DNA can replicate and code for the wild type tRNA\textsubscript{lys} codon.

- While the current treatments are mainly symptomatic and can only treat one manifestation of MERRF disease at a time, using a plasmid to deliver the insert of the MT-TK gene into the affected individual may be able to treat many of the manifestations of the disease.

- Because of the heteroplasmic nature of the disease—inserting the wild type MT-TK into a patient can treat it efficiently since it will be able to treat it no matter what phenotype a patient exhibits.

- However, one limitation to this is that in some rare circumstances, an individual may have more than one mutated gene, making it harder to treat the disease like this.
REFERENCES


