MERRF (myoclonic epilepsy with ragged red fibers)

Genetics

-Genes: MT-TK (90%, encoding tRNALys; 80% m.8344A>G); MT-TF, MT-TL1, MT-TI, MT-TP

Clinical findings/Dysmorphic features

-Multisystem disorder: onset in childhood, after normal early development; myoclonus (quick, involuntary muscle jerk, i.e. hiccups) often the first symptom --> generalized epilepsy, ataxia, weakness, dementia

-Common findings: HL, short stature, optic atrophy, cardiomyopathy

Etiology

-Prevalence of the m.8344A>G: <1:100,000

Pathogenesis

-MT-TK pathogenic variant directly inhibits protein synthesis --> cell cultures containing >85% mutated mtDNA with decreased translation (mainly proteins with large numbers of lysines)

-Cells with m.8344A>G contain low levels of tRNALys and aminoacylated tRNALys

Genetic testing/diagnosis

-Diagnosis: 4 "canonic" features: myoclonus, generalized epilepsy, ataxia, ragged red fibers