Mitochondrial disease: cause

- Many mitochondrial disorders, resulting from mutations in both nuclear and mitochondrial DNA, have been characterised
- Here, we focus on some of the diseases caused by mutations to mitochondrial DNA

**LHON (Leber’s hereditary optic neuropathy)**
- **Mutations:** 3460G>A (complex I: ND1) 11778G>A (complex I: ND4) 14484T>C (complex I: ND6)
- **Affects:** Rentinal ganglion cells
- **Symptoms:** Sudden, painless loss of central vision, initially in one eye; second eye affected after 2 – 3 months

**MELAS (Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes)**
- **Mutations:** 3243A>G (transfer RNA: leu) 3271T>C (transfer RNA: leu)
- **Affects:** Brain and nervous system
- **Symptoms:** Stroke-like episodes in the brain, migraines, vomiting, seizures; muscle weakness, exercise intolerance

**MERFF (Myoclonic Epilepsy with Ragged Red Fibers)**
- **Mutations:** 8344A>G (transfer RNA: lys) 8356T>C (transfer RNA: lys)
- **Affects:** Muscles and nervous system
- **Symptoms:** Myoclonus (muscle jerks), seizures, ataxia and muscle weakness; deafness and short stature

**NARP (Neuropathy, ataxia, and retinitis pigmentosa)**
- **Mutation:** 8993T>G (ATP synthase: ATP6)
- **Affects:** Nervous system
- **Symptoms:** NARP causes retinitis pigmentosa (blindness), neuropathy and ataxia

- Other mitochondrial diseases involve large deletions of the mitochondrial genome:
  - Kearns-Sayre syndrome: myopathy, ophthalmoplegia, cardiomyopathy
  - CPEO: paralysis of eye movement