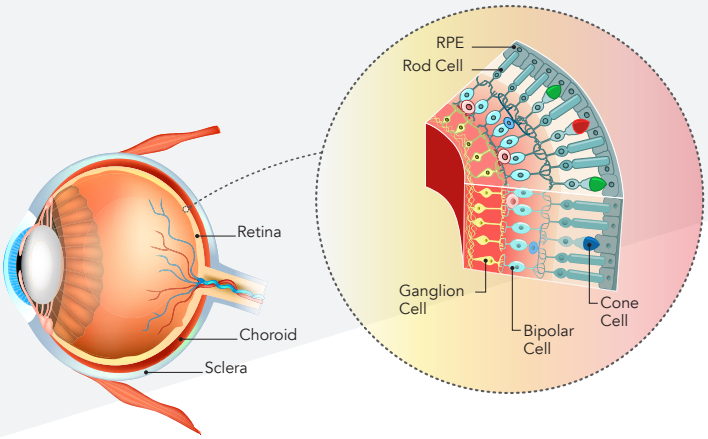
Autosomal Dominant Optic Atrophy Fact Sheet

What is Autosomal Dominant Optic Atrophy (ADOA)?

- Autosomal dominant optic atrophy is a rare disease that causes progressive and irreversible vision loss in both eyes starting in the first decade of life. Many children progress to blindness.[1,2,3]
- ADOA is the most common inherited optic nerve disorder seen in clinical practice.[2]
- 80% of patients experience symptoms before age 10, typically beginning between the ages of 4 and 6.[1,4]
- Characteristic features of ADOA include reduced color vision and central field defects.[1]
- The severity of the disease can vary greatly – even within families – with visual acuity and rate of vision loss being difficult to predict.[1,2,5,6]
- ADOA was first described by two British ophthalmologists, Frederick Batten and Simeon Snell, at the end of the 19th century. It was later named Kjer's optic neuropathy, after Danish ophthalmologist Poul Kjer, who studied 19 families with the disease in the 1950s.[3]



Mutations of the *OPA1* Gene: The Most Common Cause of Autosomal Dominant Optic Atrophy

- *OPA1* is the most common gene mutated in ADOA and is responsible for several distinct clinical presentations of the disease.[3]
  - Approximately 20% of patients have a more severe form of ADOA called ADOA "plus" syndrome. In addition to vision loss, these patients experience significant non-visual effects such as permanent hearing loss or other more severe conditions affecting the body's nervous system and skeletal muscles.[5]
- Approximately 65-90% of dominant optic atrophy cases are caused by a mutation of the *OPA1* gene.[6] – More than 400 different *OPA1* mutations have been reported in people diagnosed with dominant optic atrophy.[7]
- OPA1 protein is found inside of mitochondria, which are the energy- producing centers of cells.[4]
  - OPA1 is ubiquitous and strongly expressed in retinal ganglion cells (RGCs). RGCs have particularly high-energy requirements due to the role they play in visual signal transmission.[3]
- Most mutations in the *OPA1* gene result in a severe decrease – up to 50% – of the normal amount of OPA1 protein. This is known as a haploinsufficiency because there is only one functional copy of the gene and is the leading cause of ADOA.[5,6]
- When a person with a mutation of the *OPA1* gene has children, each child has a 50% chance of inheriting the mutation, and it affects males and females equally. The mutation can occur spontaneously (de novo).[1,3]

Symptoms and Effects

- Affected individuals first experience a progressive loss of nerve cells within the retina. The loss of these retinal ganglion cells is followed by the degeneration (atrophy) of the optic nerve. The optic nerve is partly made up of specialized extensions of retinal ganglion cells called axons. When the retinal ganglion cells die, the optic nerve cannot transmit visual information to the brain normally.[1,4]
- Simultaneous involvement of the two optic nerves typically results in bilateral, symmetric vision loss.[3,4,5]
- The severity of the condition by adolescence reflects the overall level of visual function to be expected throughout most of the patient's adult life.[4]
- About half of people with dominant optic atrophy do not meet driving standards and up to 46% are registered as legally blind.[1]

Diagnosis

- Most patients are diagnosed when entering school or only incidentally during the examination of other affected members of the family.[3]
- Diagnosis is usually made by an ophthalmologist based on a combination of family history and clinical findings, such as the presence of optic disc pallor, an abnormal coloration of the optic disc.
- Genetic testing is typically performed to confirm diagnosis.

A Rare Disease with No Approved Treatment Options

- Autosomal dominant optic atrophy is a rare disease, although it is a relatively common inherited optic atrophy. ADOA affects 1/30,000 people globally with a higher incidence of approximately 1/10,000 in Denmark due to a founder effect.[5,7]
- Since ADOA causes deterioration of the optic nerves, glasses or contacts do not help improve vision lost to the disease.
- While there are currently no available treatments for dominant optic atrophy, supportive services and low-vision aids are offered for patients with severely decreased visual acuity.

A Potential New Way to Treat OPA1 Deficiency

- STK-002 is a proprietary antisense oligonucleotide (ASO) designed to upregulate OPA1 protein expression. The goal of our approach is to stop or slow vision loss in patients with ADOA. We believe STK-002 has the potential to be the first disease-modifying therapy for people living with ADOA.
- Preclinical studies for STK-002 are ongoing.

More Resources

- For more information about dominant optic atrophy, visit:
  - Autosomal Dominant Optic Atrophy Association: https://www.adoaa.org/.
  - National Institutes of Health – Genetic and Rare Diseases Information Center: https://rarediseases.info.nih.gov/diseases/11972/dominant-optic-atrophy

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