Aniridia
The Definitive eye development disorder

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3 months
Shaking eyes
Not seeing well
Unusual pupil

“Family eyes”

Affected

PAX6

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The Central Dogma

Genes: source code

- Transcription
- Translation
- mRNA
- Polypeptide
- Protein

Nonsense-mediated decay

Pan-ocular disorder

- Limbal stem cell deficiency
- Iris hypoplasia
- Cataract
- Spherophakia
- Optic nerve hypoplasia
- Coloboma
- Foveal hypoplasia

Ma, Grigg, Jamieson
Hum Gen 2019
**Title: Aniridia**

**WAGR**
- Aniridia
- Wilms tumour
- Growth retardation

**Gillespie**
- Aniridia
- Intellectual disability
- Cerebellar ataxia

**Syndrome until proven otherwise**

**Treatment**
- Prevention
- Maximise Vision
- Refractive
- Amblyopia
- Keratopathy
- Glaucoma
- Cataract
- Gene Directed

**Prenatal diagnosis**
- Refractive correction
- Photochromic / Tinted glasses
- Occlusion therapy for amblyopia

**Maximise vision**
Keratopathy

Edén et al, Cornea 2010

Critical Diagnoses of Congenital Aniridia

Staging of Aniridia-Associated Keratopathy

Stage 1A: % risk of pupillary block and angle closure

Stage 1B: % risk of postoperative anterior segment fibrosis

Stage 2A: Angle closure

Stage 2B: Anterior segment fibrosis syndrome

Stage 3: Morcher lens implants

Cataract

Congenital anterior and posterior polar

70-80% Late teens –early 20's

Anterior Pyramidal

Surgery – fragile capsule / zonular dehiscence

Anterior segment fibrosis syndrome

Glaucoma

30-67%

Childhood goniodysgenesis

Schlemm’s canal aplasia

Teens onwards Forward rotation of ciliary body

Progressive angle closure

After anterior segment surgery

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**Glaucoma Treatment**

- Congenital - Goniosurgeries
- Topical drops
- Trabeculectomy
  - Success 0-80%
- Shunts / Tubes – success 66-100%
- Cyclodestruction

**Translational read through inducing drugs (TRIDS)**

For nonsense mutations
- Anterior segment disorders
- Retinal dystrophies
- RP2
- REP1
- MERTK
- USH1B

**Ataluren (PTC124)**

- Mouse model of aniridia
  - Inhibited disease progression
  - Reversed corneal and lens opacity
  - Improved retinal development
- Suggests post natal tissue plasticity
- STAR Clinical Trial Phase 2 NCT02647359
  - Feb 2016 - Feb 2022

**Aniridia**

- Pan-Ocular disorder
- Exclude syndromic
- Early diagnosis - family planning
- Maximise vision
- Regular Screening
- Emerging therapies

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