INSTITUTE OF OPHTHALMOLOGY
THE FRANCIS CRICK INSTITUTE

DYRK1A and ocular diseases

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How does it start?

“Do eye defects observed in my son are related to his *DYRK1A*-associated intellectual disability?”

Contact families

DYRK1A Syndrome International Association (DSIA)

- 26 patients from DYRK1A Syndrome International Association (DSIA)
    - Ocular defects? Yes, for 26 patients
    - Genetic details? Yes, for 14 patients

Contact families

UK Genomics England 100,000 Genomes Project

- Sequencing ~85,000 NHS patients with rare disease or cancer and their families

→19 patients with *DYRK1A* mutations

Genomics england

Contact families
Published cases

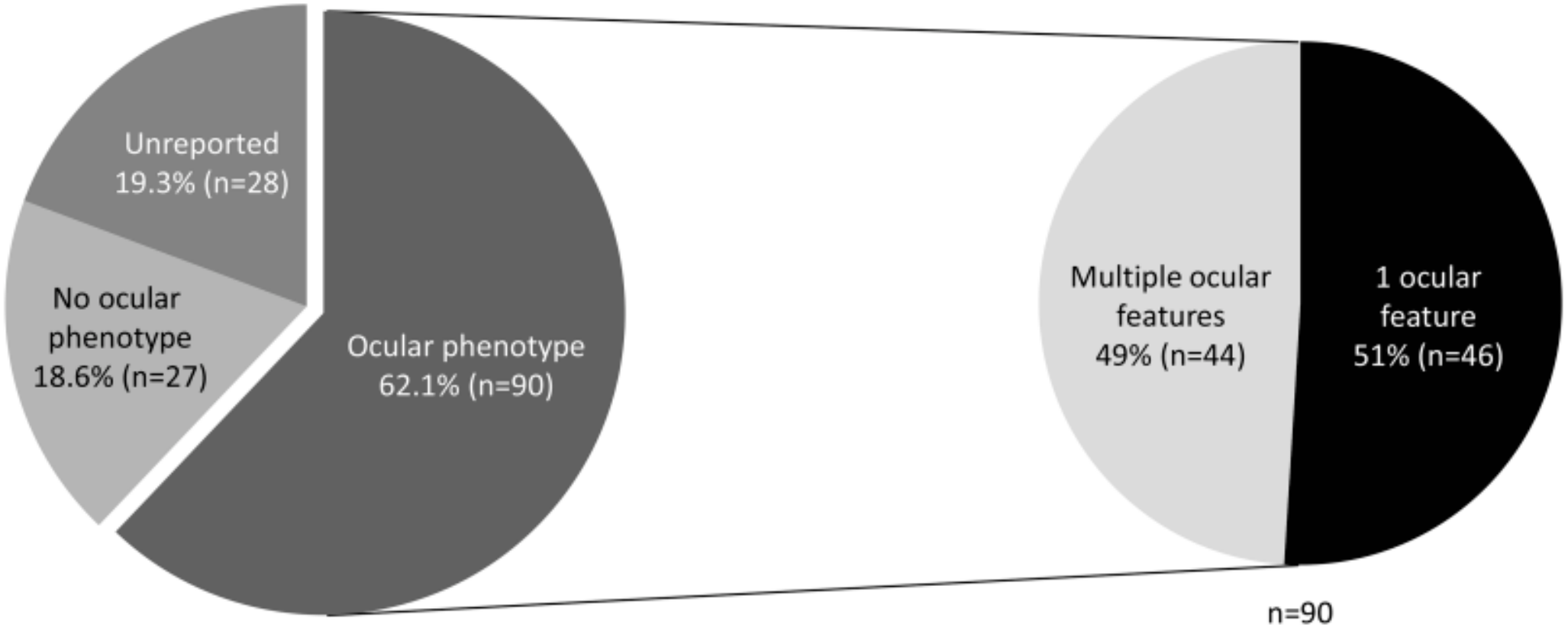
- 112 patients with *DYRK1A* mutations reported in the literature

Contact families

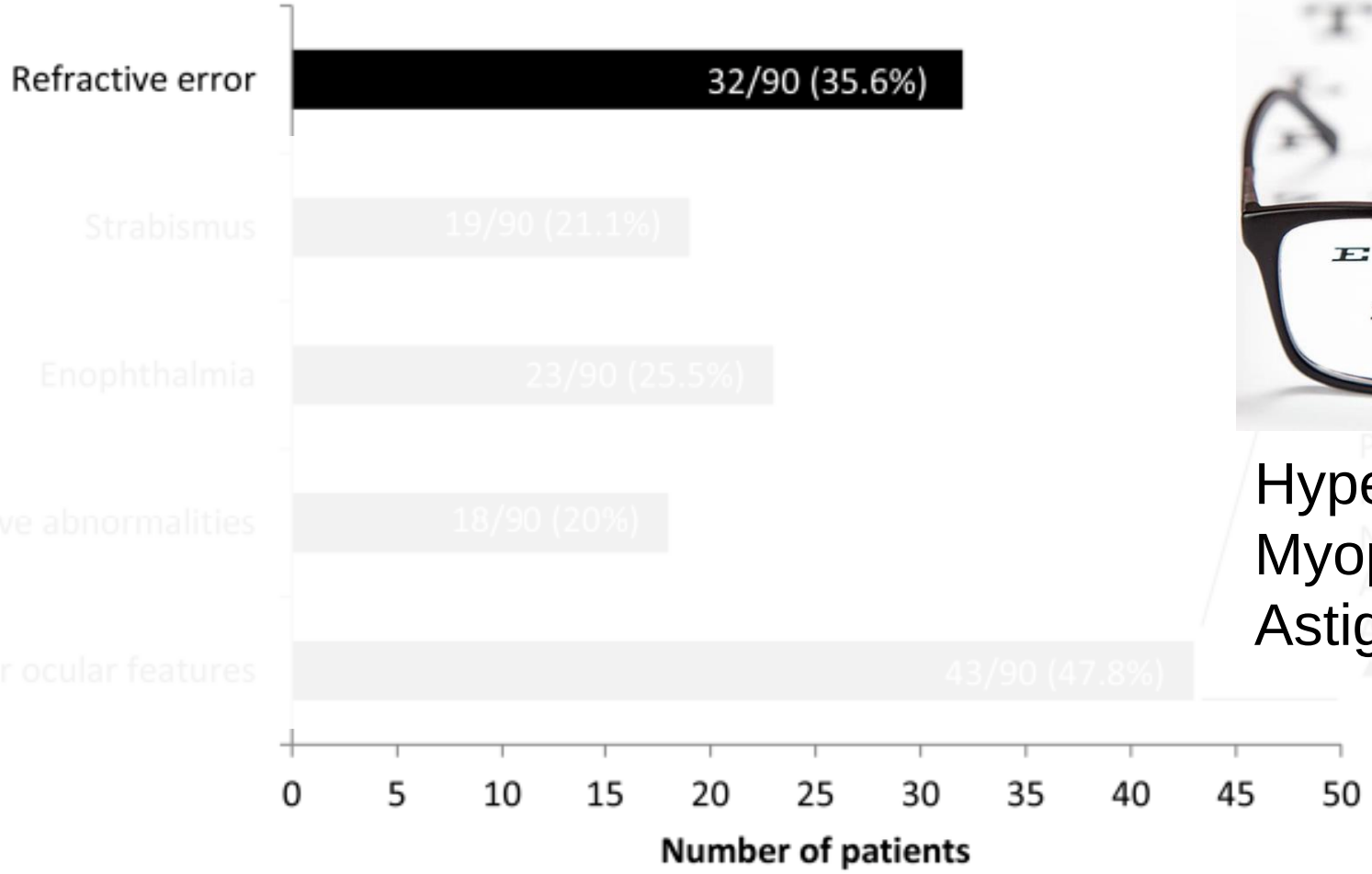
- 14 patients with genetic details from DYRK1A Syndrome International Association (DSIA)
- 19 patients from the UK Genomics England 100,000 Genomes Project
- 112 patients reported in the literature

➔ **145 patients from 144 unrelated families**

62.1% of patients have ocular features

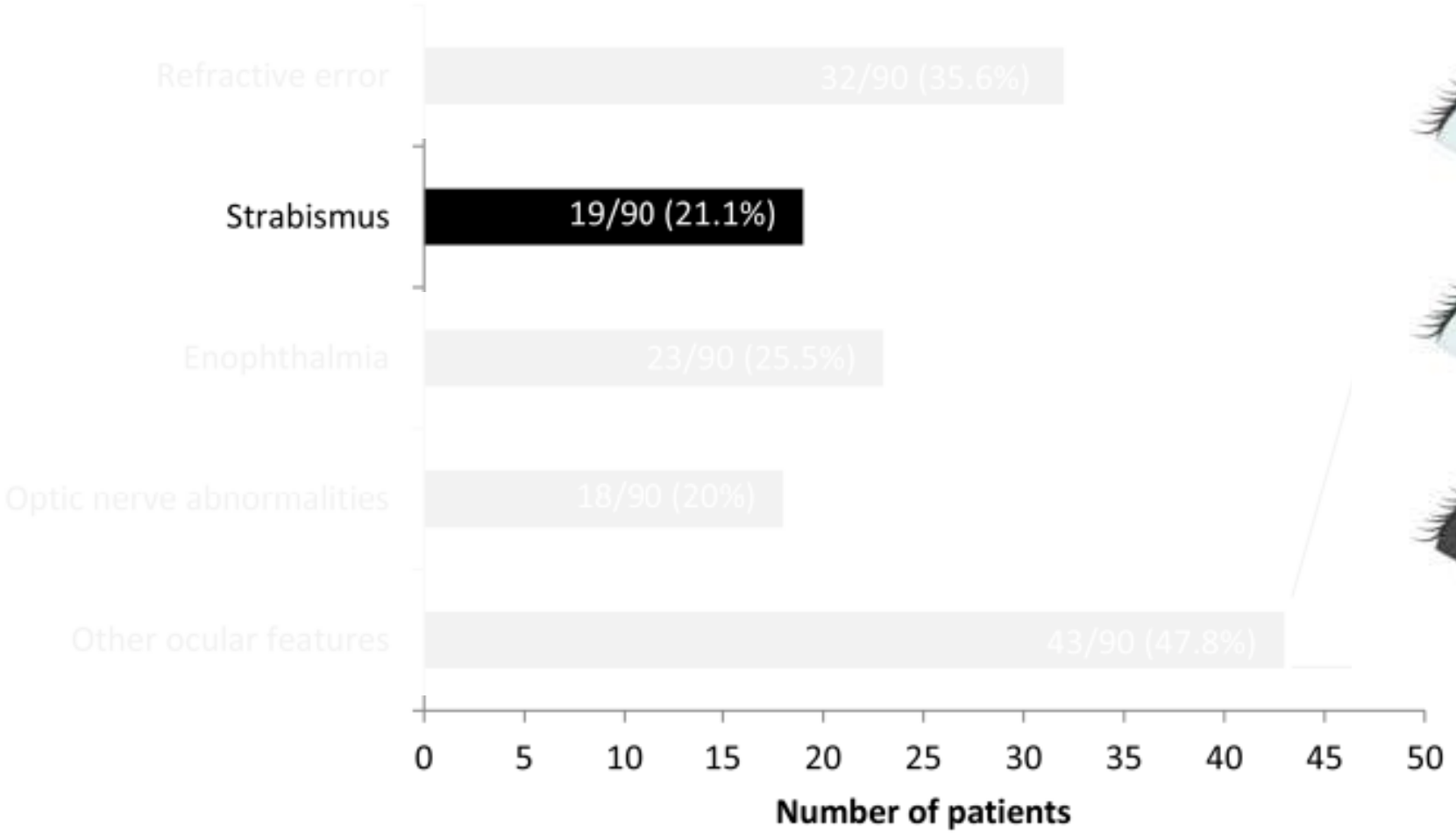


35.6% of patients have refractive error

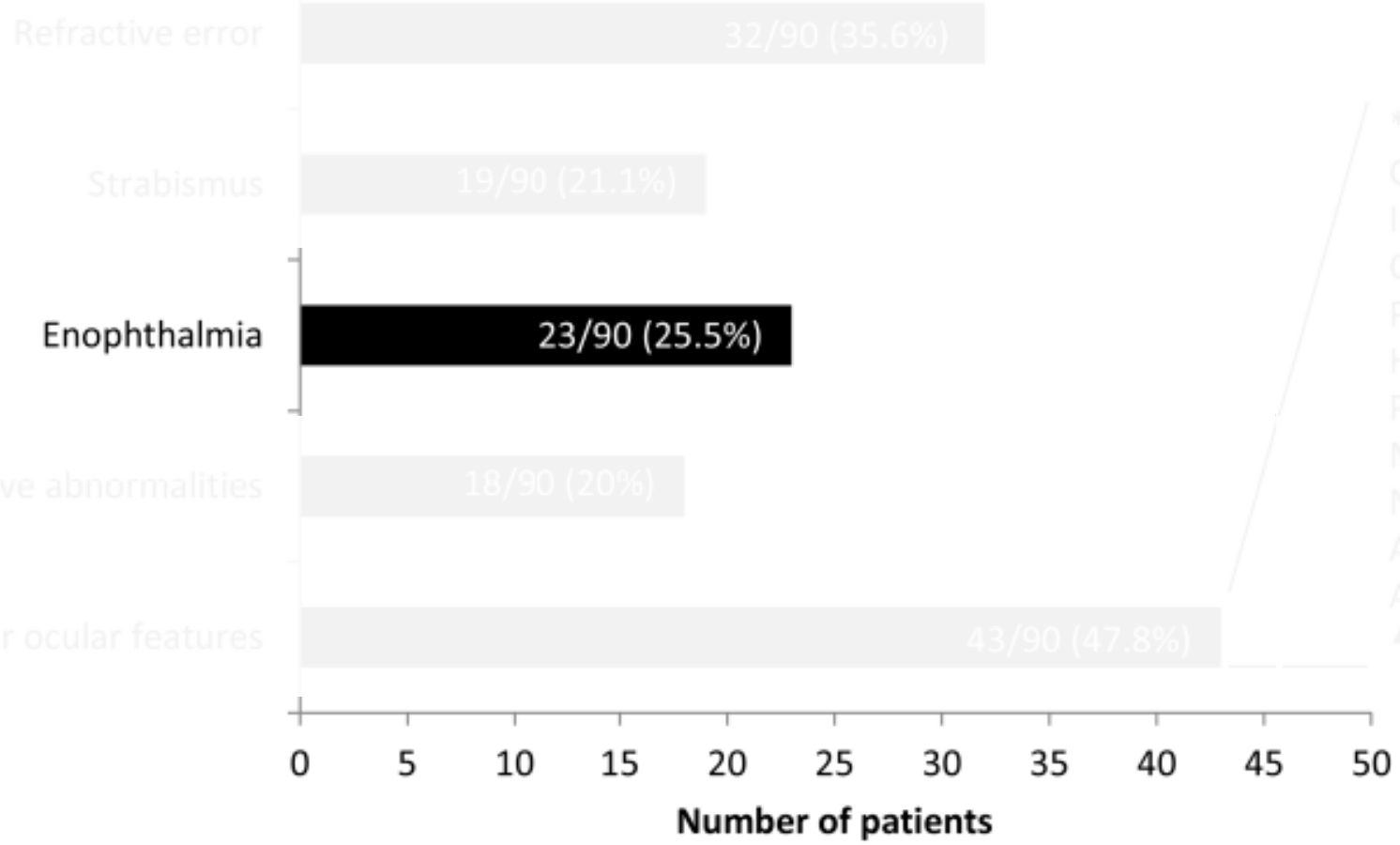


Hyperopia/hypermetropia
Myopia
Astigmatism

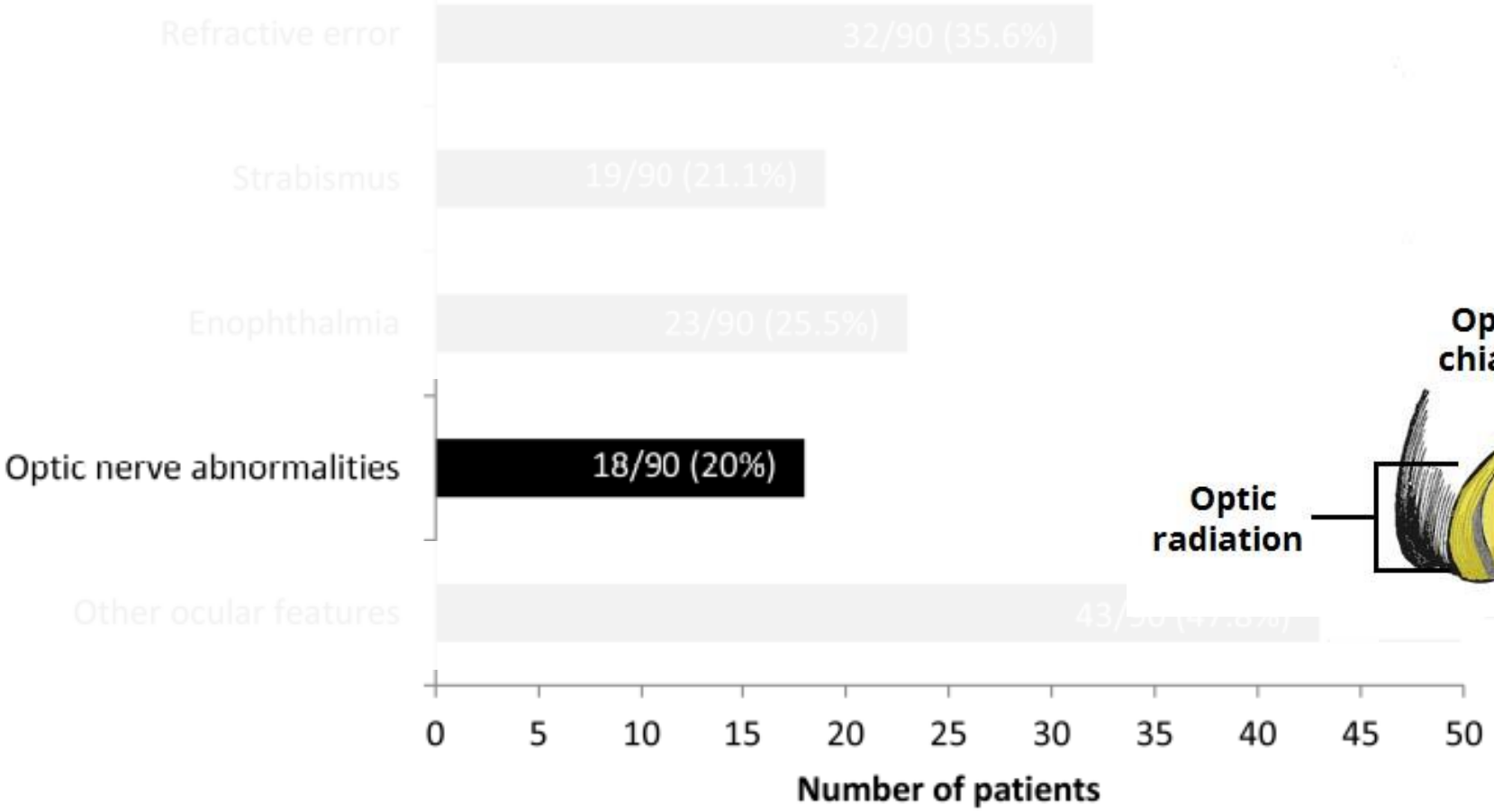
21.1% of patients have strabismus

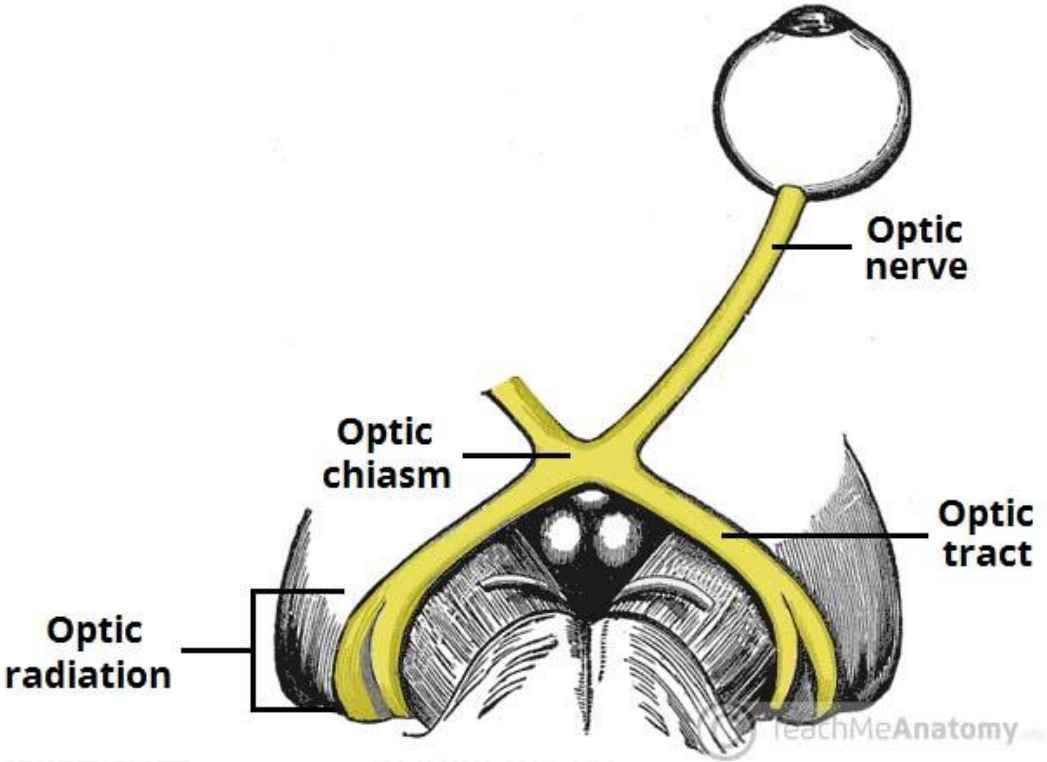


25.5% of patients have enophthalmia or deep-set eyes

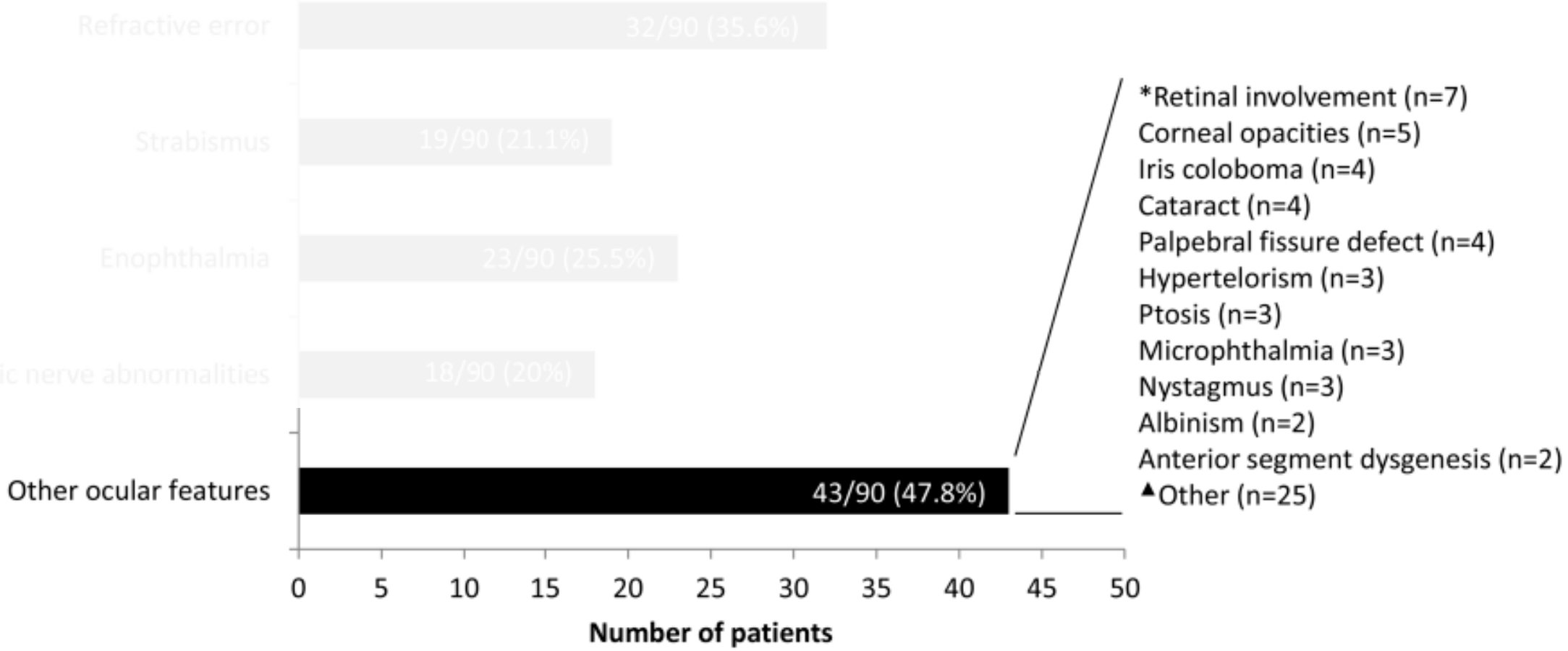


20% of patients have optic nerve abnormalities





47.8% of patients have other ocular features

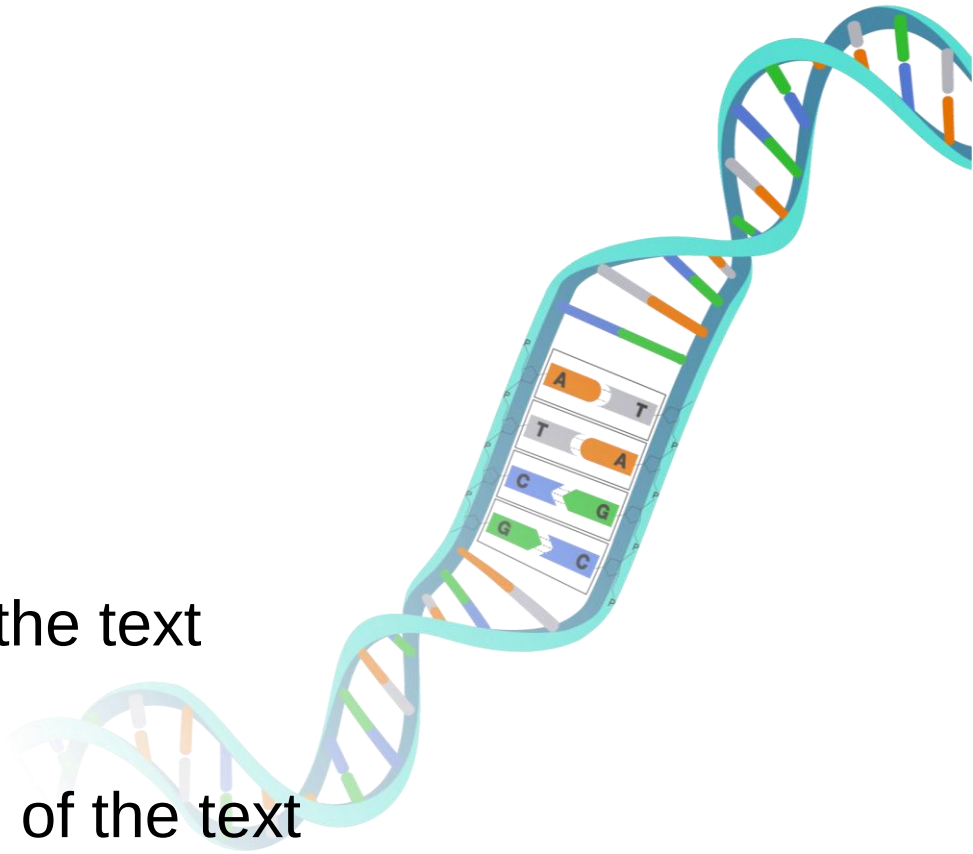


DYRK1A and brain development

- *DYRK1A* is expressed in developing and adult brain and optic nerve development
- DYRK1A influences neural development
- Mouse model mimics patient diseases (including optic nerve abnormalities)

DYRK1A syndrome,
a genetic disease

- DNA is like a text, in two copies
- Important to have two clear copies
- A misspelling, an insertion or a deletion can modify the text
- Some misspellings do not modify the understanding of the text



Specific mutations lead to specific ocular defects?

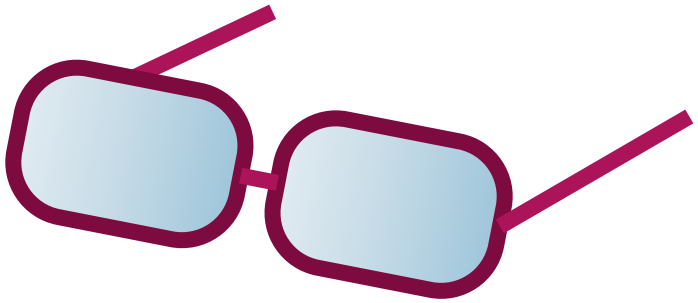
- 108 mutations in *DYRK1A* associated with intellectual disability
  - Large deletions
  - Misspelling (81 mutations)

- Similar ocular diseases between patient groups with or without large deletions
- Large deletion affect several genes which may contribute to extra-*DYRK1A*-related features

Specific mutations lead to specific ocular defects?

- Same misspellings showed a variable ocular features
- We are unique, with misspellings in other genes
- Numerous ocular features were ambiguous

Conclusions



- Increased risk of ocular pathology compared to the general population
  - Optic nerve defect
  - Refractive error (x2)
  - Strabismus (x6.7)
- Recommend to refer to ophthalmology after genetic diagnosis is confirmed
- The treatment of any preventable vision loss may reduce the social and behavioural difficulties seen in these patients

Thank you!

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DYRK1A SYNDROME INTERNATIONAL ASSOCIATION

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