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ISGEDR Quarterly

Members Newsletter

Former fellows of ISGEDR founder Irene Hussels Maumenee, MD, pose with her after her keynote at the 2025 ISGEDR meeting in Oslo, Norway

The Inaugural Newsletter

Hello Colleagues

---------- ARLENE V. DRACK, MD

Welcome to the inaugural ISGEDR Newsletter! This quarterly publication is intended to keep members informed, engaged, and connected to the International Society for Genetic Eye Diseases and Retinoblastoma (ISGEDR). Each newsletter will feature concise updates on current topics in genetic eye disease, authored by members of the ISGEDR Board, along with information on the biannual meetings and other items of interest.

A small, dedicated group of specialists founded ISGEDR at a time when genetic eye disease represented a small subspecialty within ophthalmology. With the advent of transformative treatments and an expanding landscape of clinical trials—many driven by the work of ISGEDR members—interest in this field has grown and so has ISGEDR.

The 2025 meeting in Oslo, Norway, hosted by Josephine Prener Holtan and her outstanding team, was a huge success, welcoming attendees from countries literally all around the world. I was honored to assume the Presidency of ISGEDR at that meeting.

One of my priorities is to strengthen our professional community through this quarterly newsletter. We welcome your feedback regarding topics you would like to see featured to support your clinical practice, professional development, and research efforts.

Sincerely,

Arlene

ISGEDR

First Meeting, 1975 Oxford, England

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Designed by El Traboulsi

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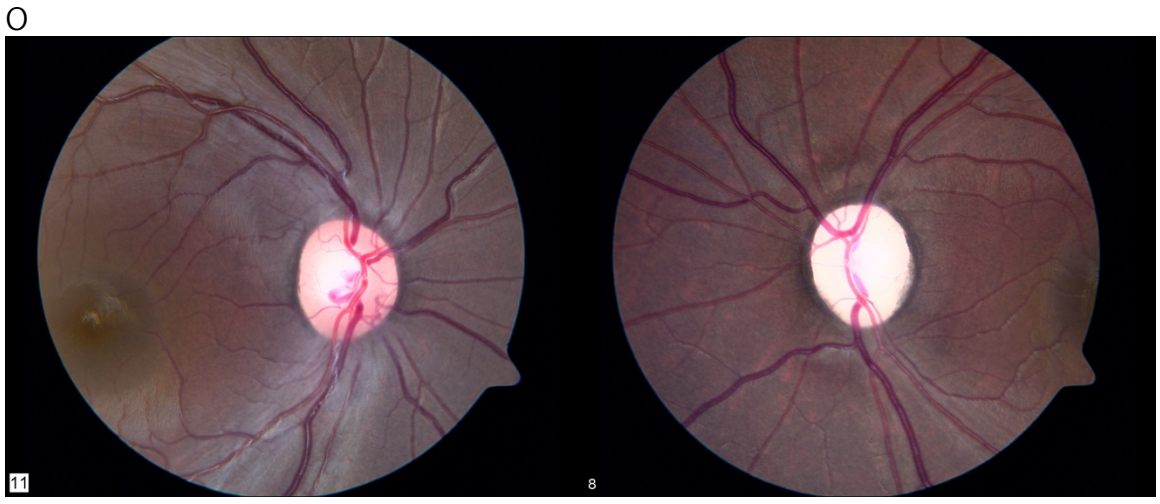

Left optic atrophy in a patient with Leber hereditary optic neuropathy

Do mutations in Inherited Optic Neuropathy and IRD-associated genes always cause disease?

BART LEROY, MD, PHD

Two interesting studies published in the AJHG in 2021 and 2026 shed light on whether the burden of disease is as high as commonly assumed when looking through the lens of inherited retinal and optic nerve disease practices, rather than from a population-based perspective. Through an epidemiological and penetrance study using a clinical register covering the entire Australian population, Lopez Sanchez and co-authors show that the risk of developing Leber hereditary optic neuropathy for both male and female carriers of any of the three classic mitochondrial mutations is significantly lower than generally assumed. These lower risks are important as overestimating the risk of developing disease has significant consequences for the individuals involved.
In a second study,

T Zaslavsky and coworkers suggest that traditional disease-causing variant identification for IRDs based on populations identified through phenotypic ascertainment may also overestimate the risk of disease in individuals with variants in inherited retinal disease related genes. Using large biobanks with linked genomic and clinical data, they show a significantly higher than previously assumed frequency of IRD genotypes with lower penetrance than expected. Those two papers make an interesting read for all of those involved in genetic counseling and treatment of inherited ocular diseases as they show the power of perspective to identify and mitigate common effects of ascertainment bias. These studies suggest that factors other than the traditional genotypes play a role in the manifestation of disease. It is important that the findings need confirmation with solid, individual gene-specific analysis.
But both these studies are certainly thought-provoking.

References

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https://www.cell.com/ajhg/pdfExtended/S0002-9297(25)00466-5

Member News

ISGEDR 2027 Meeting

Applications from sites worldwide interested in hosting ISGEDR 2027 were accepted through January 31, 2026. The membership will receive a ballot email, with a presentation by each site. All ISGEDR members in good standing with Dues paid for 2026 should receive an email ballot by mid-March.

Current Topics in Ophthalmic Genetics

Miglustat for CLN3

ARLENE V. DRACK, MD

One of the most devastating disorders we diagnose in Ophthalmic Genetics is CLN3 Batten Disease, caused by biallelic mutations in the *CLN3* gene. Typical presentation is a healthy child 5-7 years old with a failed vision screen which proceeds to rapidly progressive vision loss often resulting in light perception vision. This is typically followed by seizures and inexorable neurologic deterioration culminating in premature death. There is no approved treatment. Of note, there are some reported cases of isolated retinal degeneration without other systemic disorders due to biallelic mutations in the *CLN3* gene. CLN3 protein function is not fully understood, but it plays a role in lysosomal enzyme trafficking.

Miglustat is a substrate reduction therapy which inhibits glucosylceramide synthase and which crosses the blood-brain barrier. It has demonstrated efficacy in patients with Gaucher, Nieman Pick and Pompe Disease. A clinical trial in patients with CLN3 is ongoing; unpublished data from the NCL2023 meeting reported a decline in biomarkers of neurodegeneration. An open label study by Pietrafusa et al. reported 6 patients, median age 20 yrs, treated for 4 years who had worsening Batten Scale of 1.96/year compared to historical controls showing 2.25-2.86/year. Grigg's group reported 2 sisters with stabilized Batten Scale and improved visual acuity over 18 months after starting Miglustat at younger ages. The company that manufactures a liquid formulation of Miglustat, THXPharma, has recently established a partnership with Biocodex, a company with longstanding commitment to rare neurological diseases. THXPharma and Biocodex plan to test Miglustat in CLN3 patients in a clinical trial in the EU and in the United States. An expanded access program may also be put in place by Biocodex in the US for some patients.

References

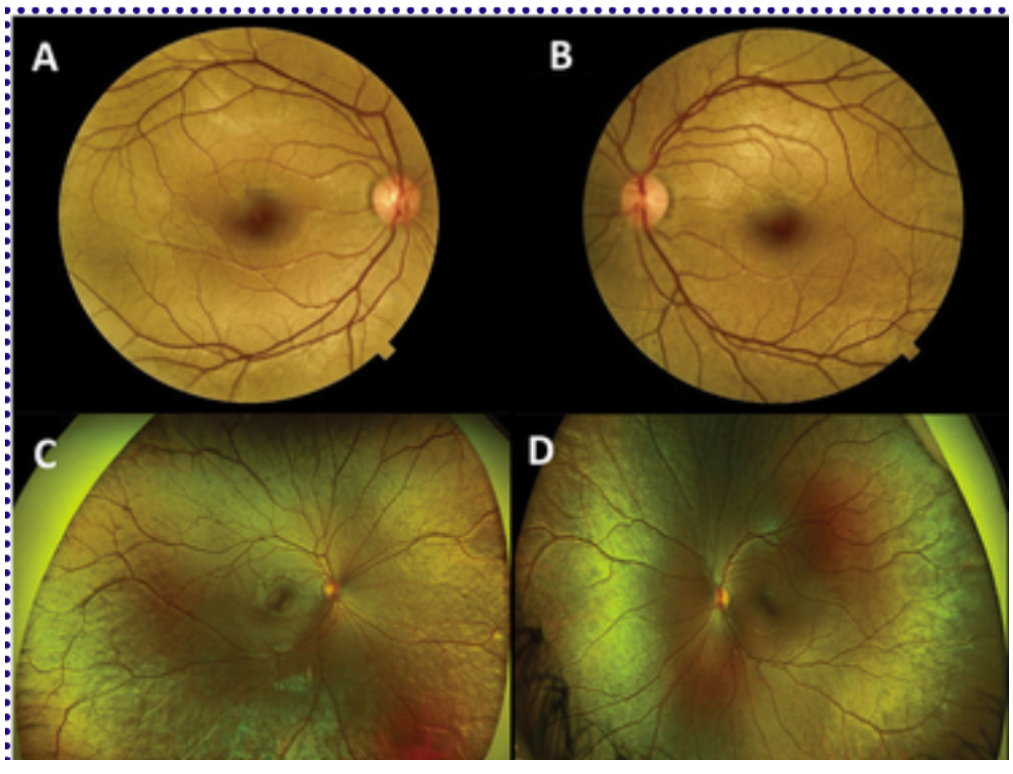
https://pmc.ncbi.nlm.nih.gov/articles/PMC12424071/pdf/WNL-2025-200773.pdf

https://journals.sagepub.com/doi/epub/10.1177/08830738251374538

https://link.springer.com/article/10.1007/s00431-025-06669-6

Clinical Images from *Ophthalmic Genetics*

ARIF O. KHAN, MD



The retinal golden-yellow discoloration with dark-appearing vessels and metallic sheen in this 5-year-old boy with *GRK1*-related Oguchi disease are classic for the condition in the light-adapted state and disappear after prolonged dark adaptation (not shown). Fathy, N., Elbagoury, N. M., Abdel-Hamid, M. S., ElKitkat, R. S., & Shehab, A. A. (2026). A novel variant in the G-

protein receptor kinase (GRK1) causes Oguchi syndrome, type II, in an Egyptian family. *Ophthalmic Genetics*, 1–8. https://doi.org/10.1080/13816810.2025.2612272.

Philately and Medicine

From the philatelic collection of Elias I. Traboulsi, Cleveland Clinic, Cleveland, OH, USA

This is a fascinating stamp from Egypt!. It beautifully merges ancient Egyptian symbolism with a modern global health theme.
Country: Egypt
Year of Issue: 1976
Theme: This stamp was issued to commemorate a campaign related to blindness prevention or World Sight Day (which is suggested by the philatelic records and the theme of the image). The Arabic text at the bottom (mukafaḥat faqadān al-baṣar), which translates to "Combating the Loss of Sight" or "Combat Blindness."
Value: 20 Milliemes (20M).

The stamp features the logo of the WHO (World Health Organization). The stamp's design is highly symbolic, featuring one of the most iconic images from ancient Egyptian mythology: the Eye of Horus (or Udjat/Wedjat Eye).

The Eye of Horus is a powerful ancient Egyptian symbol representing protection, healing, royal power, and good health.

The symbol is rooted in the myth of the god Horus, who lost his left eye during a battle with his rival, the god Set (who murdered Horus's father, Osiris). The eye was miraculously restored (often by the god Thoth). The restored eye became a symbol of regeneration, restoration, and making whole—specifically linked to healing and physical well-being.

Using the Eye of Horus on a stamp dedicated to "Combating the Loss of Sight" is a powerful and very direct visual metaphor. It draws on Egypt's ancient history to symbolize restored sight and good health in a modern medical context, aligning perfectly with the stamp's purpose.

ELIAS I. TRABOULSI, MD, MED
PAST PRESIDENT, PAST EXECUTIVE VP AND CURRENT TREASURER OF ISGEDR