Research Spotlight, April 2024

Inherited Retinal Dystrophies:

Genetic testing experiences of people living with inherited retinal degenerations (IRDs) - results of a global survey

TLDR*: This study explored patient experiences while seeking genomic services for inherited retinal degenerations (IRDs). IRD patients are caregivers were surveyed in relation to the accessibility, affordability, and timelines of genomic services for IRDs as well as patient perceived awareness of genomic services for IRDs among healthcare professionals.*

An online survey was designed based on a focus group conducted by Retina International and including people affected by IRD and their families living in different regions around the world. The survey was then circulated to 43 Retina International member organizations globally via email newsletters and social networks. A total of 410 respondents (IRD patients and caregivers) from over 30 countries across all continents responded to the survey.

Key findings:

- A considerable number of the patients had to go through a long and arduous journey to access genetic testing and counselling services wherein 40% had to visit more than 5 physicians, 27% had to visit more than 5 clinics and 57% had to wait for more than 3 years before obtaining a genetic diagnosis.
- Furthermore, 46% of respondents reported not receiving genetic counselling prior to undergoing genetic testing and 39% not receiving genetic counselling after undergoing genetic testing.
- Over 3/4th of the participants reported that they did not have to pay for their genomic services for IRD.
- Thirty seven percent of the respondents reported that their eye care professionals were either not aware of genetic testing, remained neutral or did not encourage them to undergo genetic testing.

Some limitations to the study include

- the survey was circulated online and therefore results may not be representative of the broader population including those without internet access,
- the study targeted patients who had already received genetic testing therefore may not fully identify of barriers to genetic testing and the experiences of individuals unable to undergo genetic testing, responses from patients outside Europe and the US were limited

Nevertheless, given the relatively large sample size of the study and the inclusion of participants from multiple diverse geographical regions, the findings of the study provide valuable insights into the experiences of individuals who have undergone GT for IRDs.

What does this mean for patients?

Patients with IRDs do not have equitable access to best practice genetic testing and counselling services. Greater awareness and training regarding inherited retinal degenerations and the benefits of genetic testing and genetic counselling for patients and families is needed among eye care professionals. A best practice model on access to genomic services for IRDs is required

CRB1-associated retinal degeneration is dependent on bacterial translocation from the gut

TLDR*: The study authors investigated the impact of the Crumbs homolog 1 (CRB1) gene, which is known to be expressed in the retina and is crucial to building the blood-retina barrier to regulate what passes in and out of the eye. CRB1 has been associated with Leber congenital amaurosis and retinitis pigmentosa. In this mouse model in eyes with sight loss caused by CRB1, gut bacteria were found within the damaged areas of the eye. Treatment of these bacteria with antimicrobial agents prevented sight loss albeit didn't repair the disrupted cellular barrier. A short video summarizing the study by author Dr Richard Lee can be found via Twitter*

The gut contains trillions of bacteria, many of which are key to healthy digestion. However, they can also be potentially harmful. Using mouse models, the research team discovered the CRB1 gene is key to controlling the integrity of the lower gastrointestinal tract, the first ever such observation. There, it combats pathogens and harmful bacteria by regulating what passed between the contents of the gut and the rest of the body.

Key findings:

- CRB1 is critical to epithelial barrier integrity in both the retina and colon
- *Crb1* mutations permit bacterial translocation from the gut to the eye
- *Crb1*-associated retinal degeneration is dependent on this bacterial translocation
- Germ-free conditions and antibiotics rescue *Crb1*-associated retinal degeneration

Some limitations to the study include:

- This work was carried out in a mouse model future work is required to investigate whether this mechanism and potential treatment applies in humans

What does this mean for patients?

This research could lead to new treatments for CRB1-associated eye conditions and possibly extend to other eye diseases.

Age Related macular Degeneration:

Systemic treatment with cigarette smoke extract affects zebrafish visual behaviour, intraocular vasculature morphology and outer segment phagocytosis

TLDR: Cigarette smoking adversely affects multiple aspects of human health including eye disorders such as age-related macular degeneration, cataracts and dry eye disease. However, there remains a knowledge gap in how constituents of cigarette smoke affect vision and retinal biology. The study authors used the zebrafish model to assess effects of short-term acute exposure to cigarette smoke extract (CSE) on visual behaviour and retinal biology. Zebrafish larvae with a developed visual system display apparent defects in visual behaviour and retinal biology after acute exposure to CSE

The paper authors used zebrafish as a vertebrate animal model to explore the effects of cigarette smoke on visual behaviour and retinal biology. The use of zebrafish as an animal model to identify environmental substances impairing vision has increased considerably in recent years. Advantages of zebrafish include the similarity in eye structure with the human eye, accessibility of the model to handling and manipulation, the ability to efficiently perform systemic drug administration and rapid advances in visual behaviour assays

Key findings:

- CSE disrupts visual behaviour, visual acuity and contrast sensitivity in larval zebrafish
- Zebrafish eyes showed increased oxidative stress and abnormal hyaloid vessels
- CSE induced axial length elongation, lens thickness increase and a disruption of photoreceptor outer segment phagocytosis.
- Zebrafish larvae can be used as a valuable model to investigate ocular disorders related to cigarette smoke.

What does this mean for patients?

Second-hand smoke is a strong risk factor for developing dry or neovascular types of age-related macular degeneration (AMD) in Europe. The zebrafish model can be used to further examine the effects of cigarette smoke in AMD disease pathogenesis.