Vol. 2 No. 3 (2025)
ONLINE ISSN :3007-309X
PRINT ISSN :3007-3081
Journal of Medical & Health Sciences Review

GENE THERAPY FOR INHERITED RETINAL DYSTROPHIES: CURRENT ADVANCES AND FUTURE PERSPECTIVES"

Muhammad Umer[1], Tooba Javaid[2], Nisha Jameel[3], Moaz Imran[4], Hafsa Bhatti[5], Muhammad Maaz Qamar[6]

[1] Final Year MBBS Student, Pakistan, Email: mu1247536@gmail.com ,
ORCID: https://orcid.org/0009-0008-9990-4857
[2] Final Year MBBS Student, Pakistan, Email: toobajavaid01@gmail.com ,
ORCID: https://orcid.org/0009-0002-7406-340
[3] MBBS, FCPS-1 (Surgery & Allied), Pakistan, Email: nishajameel040@gmail.com ,
ORCID: https://orcid.org/0009-0009-2101-4018
[4] MBBS, House Officer, HIT Hospital, Pakistan, Email: moazimran58@gmail.com ,
ORCID: https://orcid.org/0009-0006-1174-0348
[5] BS Biotechnology, Graduate, University of Veterinary and Animal Sciences (UVAS), Lahore, Pakistan,
Email: hb.learning53@gmail.com
[6] MBBS, District Layyah, Pakistan, Email: muhammadmaaz783@gmail.com ,
ORCID: https://orcid.org/0009-0004-7253-2097

ARTICLE INFO:

Keywords:
Retinal Dystrophies, Hereditary, Gene Therapy, Photoreceptor Cells, Vertebrate, Retinal Pigment Epithelium, CRISPR-Cas Systems, RNA, Therapeutic, Optogenetics, Adeno-Associated Virus, Retinal Diseases/genetics, Vision, Ocular

Corresponding Author:
Muhammad Umer,
Final Year MBBS Student, Pakistan,
Email: mu1247536@gmail.com ,
ORCID: https://orcid.org/0009-0008-9990-4857

Article History:
Published on 22 August 2025

ABSTRACT

Background: Inherited retinal dystrophies (IRDs) are a group of genetically diverse disorders that are manifested by progressive degeneration of photoreceptors and consequently, vision loss and in many cases irreversible blindness. Up until now, there have been relatively few treatment options available for IRDs, and they have thus remained a substantial burden for both patients and the medical community.
Purpose: This narrative review endeavours to offer an updated summary of the state-of-the art and future prospects of gene therapy for IRDs, including recent advances, active clinical trials, emerging gene delivery systems and also ethical implications.
Summary of Advances: Gene replacement has become a revolutionary approach for treating the genetic causes of IRD. *voretigene neparvovec*-rzyl (Luxturna) being approved for RPE65-related retinal dystrophy has already underscored the potentiality of gene replacement strategies in a clinical context. Several ongoing clinical trials are deploying, using vectors including adeno-associated virus (AAV) and lentivirus, directed to genes including RPGR, ABCA4, and CHM. Novel approaches to drug delivery, such as intravitreal and subretinal injections, have significantly progressed the field. Although the advances have been significant, challenges still persist, such as vector restriction, host immune response, expense, and long-term safety.
Future Directions: New strategies like CRISPR-Cas9 gene editing, therapies based on RNA, optogenetics and combination therapies (e.g. gene + cell therapies) are being developed that are changing the therapeutic landscape. Personalized treatment based on early diagnosis and genetic characterization will be the key to achieving the best therapeutic results and extending access.

INTRODUCTION

Inherited retinal dystrophies (IRDs) are a heterogeneous collection of genetically inherited progressive diseases which cause alterations in the structure and function of the retina, leading to either visual impairment or blindness (1,2). These diseases are characterized by the dysfunction or degeneration of photoreceptor cells or the retinal pigment epithelium (RPE), essential for light capture and visual processing (3–6). IRDs include a heterogeneous group of disorders such as retinitis pigmentosa (RP), Leber congenital amaurosis (LCA), Stargardt disease, and choroideremia, among others (1,7–10).

Globally, IRDs are a leading cause of inherited blindness, estimated to affect around 1 in 3,000-4,000 people in all populations (11,12). The genetic complexity of IRDs is remarkable, with more than 270 IRD-causative genes discovered so far (13). These entities may have autosomal dominant, autosomal recessive, or X-linked inheritance, and the range of phenotypes even in those with the same mutation presents a substantial diagnostic and therapeutic dilemma (4,7). To date, there is no cure for the majority of IRDs, despite having available diagnostic modalities and palliative treatment (14,15). Current treatments are predominantly palliative consisting of symptomatic control, low vision care, and slowing disease progression (6,16,17). This treatment gap highlights the critical requirement for novel, disease-modifying therapies that can address the underlying genetic defect (18,19).

Gene therapy has become a revolutionary intervention in the management of monogenic retinal disorders (20–22). Gene therapy may have the power to stop, and in some cases reverse vision loss by providing functional copies of a defective gene or editing the faulty sequence directly within retinal cells (23). Anatomical and immunological characteristics of the eye, including its relatively small size, immune privilege, and ease of access, render it to be an excellent target organ for gene-based therapies (24,25). This overview aims to present a contemporary summary of the state of gene therapy for IRDs by reviewing key clinical achievements, the efficacy and shortcoming of current therapy, and prospective directions. The review also highlights the eminence of gene therapy in translation of vision and life quality for patients.

Pathophysiology and Genetics of Inherited Retinal Dystrophies (IRDs)

The retina is a layered, complex neural tissue that lines the back of the eye and is responsible for transforming light into neural signals that ultimately are used for visual processing (26,27). The photoreceptor cells (rods and cones) and the retinal pigment epithelium (RPE) are two important elements of the retina (12,28,29). Photoreceptors transduce light and initiate visual signals whereas the RPE contributes surviving of the photoreceptor cells through recycling of visual pigments, absorption of excessive light, and blood-retina barrier maintenance (30)(27).

Genetic mutations in inherited retinal dystrophies (IRDs) interfere with the normal development, function, or life span of these cells of the retina (31–34). The consequence is a gradual destruction of the retina, starting at the level of either photoreceptors or RPE, and culminating in a slow vision loss (21,35). The phenotype of IRDs is highly variable, based on the underlying mutated gene, mode of inheritance, and age of onset (33,36).

Common IRDs

Retinitis Pigmentosa (RP) is the most common IRD, which presents as night blindness and loss of peripheral vision due to a gradual loss of rod photoreceptors (19,26,31,32). Cone photoreceptors are affected later with resulting complete blindness (14). RP can be inherited in an

autosomal dominant, autosomal recessive, or X-linked manner(4). Leber Congenital Amaurosis (LCA) is a childhood-onset IRD, typically manifesting early in life with profound visual impairment or blindness (37–39). Mutations in genes including RPE65 and CEP290 are frequently involved (40,41). Patient presentation may include nystagmus, slow pupillary response, and absent ERG electroretinogram responses (42,43). Stargardt disease is the juvenile forms of macular dystrophy is due mainly to mutations in the ABCA4 gene (9,19,34,44). It causes gradual central visual loss as the function of the macular degenerates with relative sparing of peripheral vision that can be preserved until late in the disease (45,46).

Key Mutated Genes and Modes of Inheritance

There are over 270 genes that are linked with different IRDs, and each gene contributes to different cellular pathways that are essential for retinal function. Some of the best-studied genes are RPE65, ABCA4, USH2A, CEP290, CRB1, and RPGR (9,38,47,48). **RPE65** is linked with autosomal recessive RP and LCA (33,38). This gene is encodes the enzyme of the visual cycle in the RPE (49). **ABCA4** is associated with Stargardt disease, cone-rod dystrophy and certain forms of RP (9,44). It encodes a protein associated with transport that is important in removing toxic retinal byproducts (34). **USH2A** is responsible for Usher syndrome type II and nonsyndromic RP. It causes retinal degeneration and sensorineural hearing loss (50). Mutation of **CEP290**, **CRB1**, and **RPGR** genes occurs in severe early-onset retinal dystrophies and in syndromic forms (13,38,51,52). Common patterns of inheritance of IRDs are, Autosomal dominant where only one mutated gene is needed (e.g. some RP cases) (53). Autosomal recessive with two abnormal alleles are necessary (RPE65 LCA for example) to cause mutation (54). X-Linked mutations are on the X chromosome lead to higher prevalence of disease in males (such as RPGR-related RP) (48,54). Due to the genetic and phenotypic heterogenenities of IRDs, it is hard to diagnosm and treat them (55–58). Yet, such diversity also represents a fertile playground for gene-specific approaches designed to correct the underlying molecular defects (15,42,54,58).

Principles of Gene Therapy

Gene therapy's goal is to repair or replace genes that don't work so properly or that are at fault and can cause the onset of a disease(21,53). Gene therapy has the potential in the treatment of IRD to arrest or even reverse the progression of vision loss by targeting the molecular basis of the disease (41,59). Given the immune-privileged status of the eye, its small size, and compartmentalized structure, gene therapy to the retina is well suited for targeted gene therapy applications (13,44,60).

Mechanisms of Gene Therapy

Gene replacement therapy is the oldest treatment method, most established especially in autosomal recessive IRDs where a loss-of-function mutation results with the absence or dysfunctional protein (50,61–63). A normal gene copy is introduced with the help of a viral vector into troubled retinal cells to enable them make functional protein. Example: RPE65 gene therapy for LCA (37,64,65). With **gene editing** tools such as CRISPR/Cas9, doctors can now modify a patient's own DNA accurately (28,32,56,66). This method can fix point mutations, replace lost genetic material or deactivate buttons of genetic activity that harm our health (41,67). Compared with gene-replacement therapy, gene editing seeks to make permanent correction of the endogenous gene (62). The **gene silencing** approach has been used in autosomal dominant IRDs due to gain-of-function mutations, or from the production and deposition of a toxic protein, where gene silencing by RNA interference (RNAi) or antisense oligonucleotides (ASOs) have

been used (4,26,68). In these methods the expression of the mutated gene is at least partially silenced, resulting in reduced toxic protein accumulation (26).

Vectors Used for Gene Delivery

Efficiency of gene therapy critically depends on the choice of the vector to deliver the therapeutic gene into target cells (66,69). Adeno-Associated Virus (AAVs) are the most commonly used vectors for retinal gene therapy because they are safe, cause few adverse immune responses, and lead to persistent gene expression (12,41,70,71). However, these vectors have a relatively low capacity for packaging (~4.7 kb), limiting their applicability for larger genes (72). Lentivirus are lentiviral vectors can accommodate larger genes (~8 kb) and are integrate in the host genome providing long-term expression (34,73). They have been employed in diseases such as Stargardt disease, but there is the theoretical concern of insertional mutagenesis (10). In CRISPR-based systems because of their size, CRISPR/Cas9 systems are typically divided into two AAV packaging vectors (63,74). Delivery strategies are continuously being improved, to enhance the editing efficiency with decreased in off-target impact (22,53,75).

Routes of Administration

Subretinal injection is the approach which allows delivery of the vector subretinally to the space between the photoreceptors and RPE (12,29,58,68). This has the advantage of precise targeting of affected cells, and has been the most commonly employed approach for most clinical trials, including FDA-approved therapy with voretigene neparvovec (Luxturna) to treat RPE65-related LCA (75–77). However, it is surgically invasive, and complications, such as retinal detachment, can arise (41,78). **Intravitreal injection** is the less invasive approach is an intravitreuse delivery of the vector (12,30,64). It is extensively used in the clinic of ophthalmology (e.g., anti-VEGF therapies), but in the inner and outer retina, the transduction efficiency is much lower, particularly in photoreceptors and RPE (10,58,64). Efforts to modify AAV capsids to enhance cellular transduction through this pathway are being pursued (79). The selection of the therapeutic mechanism, the vector, and the route of administration, among other factors, is influenced by target cell type, gene size, mode of inheritance, and stage of the disease. Collectively, these principles constitute the foundation of creating successful gene therapies for IRDs (34,80).

Current Approved Therapies and Clinical Trials

Gene therapy for inherited retinal dystrophies (IRDs) has reached the point that the field has advanced beyond preclinical study and into the clinic with notable accomplishments along the way (34,81,82). The first gene therapy to treat an inherited eye disorder has been approved by the FDA (12,31,64,75,83). Its most recent notable success is the drug voretigene neparvovec (brand name Luxturna), which treats a rare form of inherited blindness (75). Moreover, there are several clinical trials targeting other IRD genes, and this is a testament to the potential and complexity of this promising therapeutic landscape (64).

Luxturna (Voretigene Neparvovec): First FDA-Approved Gene Therapy

Luxturna is a milestone in eye gene therapy. It is FDA and EMA approved for the treatment of IRDs due to biallelic RPE65 mutation, e.g., Leber Congenital Amaurosis type 2 (LCA2) and early onset severe retinal dystrophy (12,64,75). Luxturna uses an AAV2 vector to introduce a functioning copy of the RPE65 gene by subretinal injection (41,57). Clinical trials showed significant gains in functional vision, such as light sensitivity and ability to navigate in dim light, as well as longer-term preservation of visual function for a duration of up to four years (41,65). Most side effects were mild to

moderate in severity including those reported by some participants of temporary ocular inflammation, with few serious adverse events. The approval of Luxturna has established proof of principle and durability of gene therapy in IRDs, and serves as a regulatory precedent (84,85).

Gene Therapies in the Clinic Trials

Several promising treatments for other causative genes are currently in clinical trials in phase I–III (17,37,53). RPGR (X-linked Retinitis Pigmentosa) is X-linked RP (XLRP), commonly caused by mutations in RPGR, it is a severe and early-onset IRD (48). Initial improvements in visual acuity and retinal sensitivity have been demonstrated in clinical trials testing AAV8-RPGR vectors (e.g., NSR-RPGR, now in the hands of Biogen) (29). Nevertheless, acute inflammation, alongside dose-limiting toxicity concerns are under scrutiny (49). ABCA4 (Stargardt Disease), the large size and overcapacity of AAV prevent a direct insertion into the ABCA4 gene, a common mutation of Stargardt's disease, which makes it a challenge (9,44). Both lentiviral vectors and dual AAV approaches are under investigation. Safety and dose tolerance are under investigation in phase I studies (e.g., SAR422459) (49). CHM (Choroideremia), an X-linked IRD, is attributed to mutations in the CHM gene (57). AAV2-REP1 has been administered subretinally in a number of trials producing modest improvements to stabilisation of vision, particularly in early disease (57). The Nightstar/CHM trial was among the first to show long-term safety data, yet results were mixed for functional efficacy (19,86).

Discussion of Safety, Efficacy and Trial Outcomes

Majority of clinical trials have reported positive safety profiles and minimal inflammatory response controlled by corticosteroids (49,65). Effectiveness is determined by stage of disease, mutation type, vector-dose and surgical precision (34,87,88). In general, younger age of onset and presence of persistent photoreceptor layers are associated with better outcome, supporting an early therapeutic approach (59,89). Challenges to this include, immunological responses to viral vectors, limitation of gene carrying capacity of AAVs, challenge to reach deep retinal layers using less invasive approaches, differential long-term stability of gene expression (60,90).

Limitations and Patient Selection Criteria

Gene therapy works ideally for alive recipient cells (91). For that reason patients with advanced retinal degeneration could be disqualified because of the irreversibility of cell loss (17,67,92). Commonly applied selection criteria includes, the documented biallelic mutation in the disease gene, OCT with remaining retinal structure, stable systemic health condition, there was no ongoing ocular inflammation or infection (42,49). Cost and accessibility are, however, major barriers. As example, the high price of Luxturna (~$850,000 USD per treatment) has driven questions of ethics and sustainability into discussions of insurance coverage, equity and global crimes (42,93).

Challenges and Limitations

Despite an unprecedented success of gene therapy in inherited retinal dystrophies (IRDs), technical, biological, and socioeconomic barriers preclude its widespread application (25,66). Such constraints have implications for the effectiveness, safety, scalability and sustainability of these treatments, highlighting the ongoing requirement for innovation and improvement (43,60,66).

Vector-Related Issues

Size limitation is one drawback, the limited payload capability of the most popular ocular gene therapy vectors, adeno-associated viruses (AAVs) (60,94). AAVs have a packaging capacity of approximately 4.7 kb of genetic material, and are therefore unable to accommodate larger genes such as ABCA4

(Stargardt disease), USH2A, or CEP290 (19,72). This requires other approaches like, dual AAV vectors (splitting the gene between two vectors), lentiviral vectors which can accommodate larger cargo but safety issues are higher, or non-viral delivery, which are still in experimental phase (34,51,72,74,95).

Despite the fact that the eye is defined as an immune-privileged site, systemic administration of viral vectors or repeated dosing might activate both innate and adaptive immune reactions (29,43). These may lead to unconjugated catalyst and reduced therapeutic efficacy as a consequence of neutralizing antibodies, Inflammation of ocular tissues, and long-term potential complications in need of cautious immunosuppressive control (30,49,93).

Delivery Technique Complications

Retinal gene transfer commonly uses subretinal or intravitreal injection (10,12,58,73). Both methods have their own drawback. Subretinal injection, although it is accurate, is an invasive and surgically difficult procedure (30,52). It can include the dangers of retinal detachment, haemorrhage or the photoreceptor layer injury (52). However, intravitreal injection is less invasive, but vector is difficult to penetrate through thin inner limiting membrane and infect photoreceptors is inefficient (12,30). In addition, targeting to central retina/ macula is particularly challenging because of the functional importance of the region and the desirability to minimize trauma.

Variability in Outcomes

Gene therapy has yielded heterogeneous results in the context of clinical trials between patients sharing the same genotype (7,96). This inconsistency may be due to time of treatment in the disease course (i.e. the earlier, the better), variation of vector dose (application method, and immune status), modifiers of response (genetic and epigenetic modifiers) that affect response, inadequate or partial expression of the transgene (38,45,61,97). It is such unpredictability that has prevented the formulation of standardized protocols, and the reliable prediction of therapeutic success.

Cost and Accessibility

One of the major challenges is the expense of gene therapy (42,98). For example, Luxturna costs about $850,000 per patient, putting nonsurgical interventions out of reach (41,99). Causing challenges for the LMIC health systems, uninsured patients, and public healthcare funding arrangements (4,100). Furthermore, the expense of the production of vectors, specialized surgical instruments, and trained clinical teams restrict the worldwide application of such therapies (52,91,99).

Longevity and Monitoring

Although initial gene therapy trial results are promising, the extent of long-term durability is unknown (42,65). How durable are the effects of the therapeutic gene expression in the body? Will patients need to be re-dosed, and if so, will immune memory prevent it? Do vector integration or persistent transgene expression cause long-term effects? In addition, standard post-treatment surveillance protocols are not established, making it difficult to obtain long-term follow-up and safety data (65,68). Creating patient registries and international databases is essential in enabling a long-term assessment of efficacy, possible side effects, and disease progress (7).

Future Directions and Innovations

Regulation of gene therapy for inherited retinal dystrophies (IRDs) is evolving, driven by technological advancements that seek to address limitations and expand the clinical scope of applicability (25). These novel techniques are intent on broadening treatable genotypes, enhancing delivery efficiency, and personalized therapy (25,90,99,101–103). From gene-editing tools to optogenetics, the future of retinal gene therapy is brighter than ever (64,80,83,85).

Traditional gene supplementation is most appropriate for recessive loss-of-function mutations while gene **editing** or **silencing** strategies are required for dominant-negative mutations as in the case of autosomal dominant retinitis adRP (4,26,53). The discovery and development of CRISPR-Cas systems has transformed this field by allowing accurate correction of mutations in disease-causing genes at the level of DNA, suppression of mutant alleles while leaving the wild-type intact, and base editing and prime editing, with increased specificity and less off-target non-homologous-end-joining (NHEJ) compared to standard double-strand breaks (13,15,24,41,101). The first clinical trials, including EDIT-101 for CEP290 mutations in Leber Congenital Amaurosis 10, are at the forefront of translating CRISPR technology to the clinic for retinal disease (13,41).

For such complicated IRDs with the destruction of a significant number of the photoreceptor cells, traditional gene therapy is in limited benefit. **Optogenetics** provides a new alternative through, Incorporating light-sensitive proteins (for example, channelrhodopsins) into residual inner retinal neurons, such as bipolar or ganglion cells (22,70,104),The cells are responsive to light, and manage to restore a crude form of vision, gene-impartial, helpful for late-stage blindness no matter underlying mutation (70,94). Clinical trials are currently underway (e.g., Bionic Sight3, GenSight Biologics4) to assess the safety and efficacy of this approach, and early findings suggest that visual perception in the previously blind can be achieved (38,40,43).

Another hopeful avenue is **RNA-based therapies** which is modulation at the level of RNA, with usage of techniques like antisense oligonucleotides (ASOs) – short sequences of RNA or DNA that can bind to mutant mRNA and normalize splicing errors (e.g. QR-110 for CEP290), and RNA interference (RNAi) technology – silences mutant transcripts in dominant diseases (31,50,54,63,78). mRNA replacement therapies provide a temporary expression with less immunogenicity compared to the viral vectors (64). These therapies are typically non-integrating, are reversible, and are potentially safer for repeat dosing. They also serve as a platform for correcting mutations in bigger genes that cannot be accommodated by conventional vectors (60,64,79,105).

Several studies confirmed that combining gene and cell therapy contributed significant in the field of regenerative medicine. A multidisciplinary approach in complicated or end-stage IRDs may be required to achieve a clinically significant outcome (60). **Combination treatment** methods include, gene therapy to fix the genetic mutation, and cell therapy (e.g., Induced Pluripotent Stem Cells, Retinal Progenitor Cells) for degenerate cell replacement agents (60,68). For instance, gene-corrected stem cell-derived RPE or photoreceptors can be transplanted into the subretinal space for function and structure replacement. Technically demanding, these techniques are designed to restore as well as regenerate the retina (38,60,64,91).

With the increasing application of next-generation sequencing, the era of **personalized medicine** is currently inevitable in ophthalmology (99,102). Future directions like vectors and promoters tailored for optimal expression as a function of a patient's genotype and disease state, AI-driven algorithms for prediction of therapeutic response, patient-specific organoids and retinal models to screen drugs in vitro at the bedside, and decentralized genomic databases and biobanks to facilitate patient selection and trial recruitment (25,43,102). Such personalized treatment designs should not only improve the efficacy of treatments, but also reduce unproductive risks and financial costs.

Ethical and regulatory Considerations

The pace of development of gene therapy for inherited retinal dystrophies (IRDs) presents research and clinical challenges and significant ethical and regulatory considerations (33,40). Since these interventions result in permanent genetic changes, and may be used in children, it is critical to have adequate ethical review, patient autonomy, and access (64,89). Also necessary is the need for regulatory standards that evolve while seeking the balance among innovation, safety, and national and international perspectives (33,40,103).

Because gene therapy is a complex and sometimes risky process, informed consent must be strong (91). Patients and their families should be aware of the mode of action, therapeutic uses and limit actions (such as immune responses, insertional mutagenesis, efficacy) (106). The irreversibility of some disruptions, experimental nature of some of the treatments or clinical studies should be known by the patient (31,103). Especially in pediatric cohorts, where many IRDs already show a phenotype at an early age, obtaining consent from legal guardians while respecting assent of the child (where applicable) can further complicate the picture (37,64,89,103). Pre-treatment genetic counseling is also essential for describing the patterns of inheritance, find family members who are at risk, and aide in decision making about treatment eligibility or reproductive planning (36). Genetic counselors with the requisite qualifications should be included in multidisciplinary teams that are providing these therapies to ensure consent is informed, voluntary, and continuous as treatment occurs (33,37).

Though gene addition is reasonably accepted, gene manipulation, especially through CRISPR-Cas9, raises new ethical issues like, germline editing (not currently applicable to IRDs) – genetic material which could be passed on to future generations, off-target activities and the lasting effect of DNA changes, and the therapeutic benefit-versus-unintended harm balance (15,24,37,63). There is a consensus across the world – and certainly in the statements issued by the World Health Organization and UNESCO – that editing the human germline should not be pursued until we have arrived at a layout of ethical, legal and scientific parameters (18,37). For the moment, somatic editing, which is aimed at non-reproductive cells such as retinal neurons, is permitted ethically in the context of strict research guidelines and oversight (16).

The discovery, validation, and regulatory submission of gene therapies require extensive regulation and oversight that differs by region in the U.S., gene therapies are regulated by the U.S. Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER) (9,83). Luxturna was the first ocular gene therapy approved by FDA after preclinical and clinical testing (64). In Europe, it is the European Medicines Agency (EMD) which manages approval the Advanced Therapy Medicinal Products (ATMPs) (63,64). Japan, Canada and China have established fast tracks for gene therapy — but the criteria diverge, particularly on how trials are designed and what counts as safety endpoints and manufacturing standards (107,108).

Cross boarder regulatory harmonization is still a challenge, especially in the context of international clinical trials. The harmonization of ethical requirements, data sharing and post-market surveillance are important to foster trust and international collaboration (108). With the widespread adoption of gene therapies from clinical trials to standard care, ongoing ethical oversight and regulatory adaptation are critical. All constituencies need to be vigilant in advancing the patient perspective, public input and independent, long-term oversight, so that these revolutionary treatments are

delivered safely, equitably and responsibly (33,37,40,103).

CONCLUSION

Inherited retinal dystrophies (IRDs) are a group of disorders estimated to affect more than two million people worldwide with no effective therapy, but gene therapy has moved from concept to clinic with great promise to change the vision of patients with these debilitating diseases. The approval of Luxturna for RPE65-mediated retinal dystrophy was a landmark moment in time heralding a new era of gene-based treatments to restore or halt the loss of sight. With the additional knowledge of disease genetics, there are current and upcoming trials for other causative genes including RPGR, ABCA4, and CHM, which are going to continue to further develop the therapeutic landscape for the many individuals affected by a wide variety of IRDs. Early diagnosis and extended genetic testing are essential. Accurate determination of causative mutation not only determines prognosis and 'therapeutic eligibility' (to gene-based therapies - or soon to be), but it is also essential for timely intervention- itself a critical variable in disease where progressive and irreversible loss of photoreceptors occurs. The Inclusion of genetic counseling is required for ethical clarity and informed consent, not only for the patient, but also his/her relatives.

In the future, the prospects of retinal gene therapy are bright and changing quickly. Advances in the gene-editing technologies such as CRISPR, optogenetics and RNA-based therapies may now be on the horizon to address these challenges, treating dominant mutations and advanced disease stages. Furthermore, the arrival of the era of personalized medicine and combination strategies should tailor treatments to be more definitive, durable, and broadly available. Continuous research efforts, ethical management and equal healthcare provision are needed for the potential of these advances to be realised. Multidiscipline-based cooperation and personalized medicine are making the dream of saving or returning the vision to millions of people with IRDs come true.

Authors' Contributions

Muhammad Umer – Conceptualization, study design, manuscript drafting, reviewing, editing, supervision, final approval, accountability

Tooba Javaid – Drafting, study design, manuscript writing, proofreading, critical revisions, final approval, accountability

Nisha Jameel – Drafting significant sections of the manuscript, critical revisions, consistency check, final approval, accountability

Moaz Imran – Drafting significant sections of the manuscript, critical revisions, consistency check, final approval, accountability

Hafsa Bhatti – Drafting significant sections of the manuscript, critical revisions, consistency check, final approval, accountability

Muhammad Maaz Qamar – Drafting significant sections of the manuscript, critical revisions, consistency check, final approval, accountability

REFERENCES

Dharmaraj S. Gene Therapy for Inherited Retinal Disease. Cutting-edge Vitreoretin Surg. 2021 Jan 1;379–87.

Orenburkina OI, Babushkin AE. State-of-the-art gene therapy for inherited retinal disorders. Russ J Clin Ophthalmol. 2024;24(1):41–5.

Stingl K, Priglinger C. RPE65 -retinal Dystrophies: From the Spectrum of the Clinical Picture to Gene Therapy. Klin Monbl Augenheilkd. 2024 Mar 20;241(3):257–8.

Liu Y, Zong X, Cao W, Zhang W, Zhang N, Yang N. Gene Therapy for Retinitis Pigmentosa: Current Challenges and New

Progress. Biomolecules. 2024 Aug 1;14(8).
5. Huang D, Fletcher S, Wilton SD, Palmer N, McLenachan S, Mackey DA, et al. Inherited retinal disease therapies targeting precursor messenger ribonucleic acid. Vis. 2017 Sep 1;1(3).
6. Livingston CA, Weng CY, Chancellor JR. Retinitis Pigmentosa and Therapeutic Candidates. Int Ophthalmol Clin. 2025 Jan 1;65(1):17–21.
7. Confalonieri F, La Rosa A, Ottonelli G, Barone G, Ferraro V, Di Maria A, et al. Retinitis Pigmentosa and Therapeutic Approaches: A Systematic Review. J Clin Med. 2024 Aug 1;13(16).
8. Dhooge PPA, Valkenburg D, Hoyng CB. Gene therapy for inherited retinal diseases. Genet Genomics Eye Dis Adv to Precis Med. 2019 Jan 1;279–95.
9. Bakall B, Klein K, Mears K. Emerging gene therapy approaches under clinical investigation for retinal degenerative diseases. Top Med Chem. 2020;35:257–72.
10. Battu R, Ratra D, Gopal L. Newer therapeutic options for inherited retinal diseases: Gene and cell replacement therapy. Indian J Ophthalmol. 2022 Jul 1;70(7):2316–25.
11. Chew LA, Iannaccone A. Gene-agnostic approaches to treating inherited retinal degenerations. Front Cell Dev Biol. 2023;11.
12. Hu ML, Edwards TL, O'Hare F, Hickey DG, Wang JH, Liu Z, et al. Gene therapy for inherited retinal diseases: progress and possibilities. Clin Exp Optom [Internet]. 2021 [cited 2025 May 13];104(4):444–54. Available from: https://www.tandfonline.com/doi/pdf/10.1080/08164622.2021.1880863
13. Quinn J, Musa A, Kantor A, McClements ME, Cehajic-Kapetanovic J, MacLaren RE, et al. Genome-Editing Strategies for Treating Human Retinal Degenerations. Hum Gene Ther. 2021 Mar 1;32(5–6):247–59.
14. Takahashi VKL, Takiuti JT, Jauregui R, Tsang SH. Gene therapy in inherited retinal degenerative diseases, a review. Ophthalmic Genet. 2018 Sep 3;39(5):560–8.

Diakatou M, Manes G, Bocquet B, Meunier I, Kalatzis V. Genome editing as a treatment for the most prevalent causative genes of autosomal dominant retinitis pigmentosa. Int J Mol Sci. 2019 May 2;20(10).

Bacci GM, Becherucci V, Marziali E, Sodi A, Bambi F, Caputo R. Treatment of Inherited Retinal Dystrophies with Somatic Cell Therapy Medicinal Product: A Review. Life. 2022 May 1;12(5).

Simunovic MP, Mack HG, Ayton LN, Hassall MM. Gene Therapy, Diet and Drug Approaches to Treating Inherited Retinal Disease. Compr Pharmacol. 2022 Jan 1;3:662–92.

Williams KA, Irani YD. Gene Therapy and Gene Editing for the Corneal Dystrophies. Asia-Pacific J Ophthalmol. 2016 Jul 1;5(4):312–6.

Hafler BP. Clinical progress in inherited retinal degenerations: Gene therapy clinical trials and advances in genetic sequencing. Retina. 2017;37(3):417–23.

Kantor A, McClements ME, Peddle CF, Fry LE, Salman A, Cehajic-Kapetanovic J, et al. CRISPR genome engineering for retinal diseases. Prog Mol Biol Transl Sci. 2021 Jan 1;182:29–79.

Bellingrath JS, Fischer MD. Gentherapie als Behandlungskonzept für erbliche Netzhauterkrankungen. Ophthalmologe. 2015 Sep 13;112(9):720–7.

De Silva SR, Moore AT. Optogenetic approaches to therapy for inherited retinal degenerations. J Physiol. 2022 Nov 1;600(21):4623–32.

Kannabiran C, Mariappan I. Therapeutic avenues for hereditary forms of retinal blindness. J Genet. 2018 Mar 1;97(1):341–52.

Bonillo M, Pfromm J, Fischer MD. Challenges to Gene Editing Approaches in the Retina. Klin Monbl Augenheilkd. 2022 Mar 1;239(3):275–83.

Sanjurjo-Soriano C, Kalatzis V. Guiding Lights in Genome Editing for Inherited

Retinal Disorders: Implications for Gene and Cell Therapy. Neural Plast. 2018;2018.
26. Öner A. Recent advancements in gene therapy for hereditary retinal dystrophies. Turkish J Ophthalmol. 2017 Dec 1;47(6):338–43.
27. Beltran WA, Cideciyan A V., Lewin AS, Iwabe S, Khanna H, Sumaroka A, et al. Gene therapy rescues photoreceptor blindness in dogs and paves the way for treating human X-linked retinitis pigmentosa. Proc Natl Acad Sci U S A. 2012 Feb 7;109(6):2132–7.
28. Chang AY. Challenges of Treatment Methodologies and the Future of Gene Therapy and Stem Cell Therapy to Treat Retinitis Pigmentosa. Methods Mol Biol. 2023;2560:363–74.
29. Colella P, Auricchio A. Gene therapy of inherited retinopathies: A long and successful road from viral vectors to patients. Hum Gene Ther. 2012 Aug 1;23(8):796–807.
30. Moore NA, Morral N, Ciulla TA, Bracha P. Gene therapy for inherited retinal and optic nerve degenerations. Expert Opin Biol Ther. 2018 Jan 2;18(1):37–49.
31. Chiu W, Lin TY, Chang YC, Lai HIAM, Lin SC, Ma C, et al. An update on gene therapy for inherited retinal dystrophy: Experience in leber congenital amaurosis clinical trials. Int J Mol Sci. 2021 May 1;22(9).
32. Jain R, Daigavane S. Advances and Challenges in Gene Therapy for Inherited Retinal Dystrophies: A Comprehensive Review. Cureus [Internet]. 2024 Sep [cited 2025 May 13];16(9):e69895. Available from: http://www.ncbi.nlm.nih.gov/pubmed/39439625
33. Côco M, Han SW, Sallum JMF. Gene therapy for inherited retinal dystrophiesies. Arq Bras Oftalmol. 2009;72(4):560–6.
34. Hohman TC. Hereditary retinal dystrophy. Handb Exp Pharmacol. 2017;242:337–67.
35. Sundaramurthi H, Moran A, Perpetuini AC, Reynolds A, Kennedy B. Emerging Drug Therapies for Inherited Retinal Dystrophies. Adv Exp Med Biol. 2019;1185:263–7.
36. Kohl S, Biskup S. Genetische Diagnostik bei erblichen Netzhautdystrophien. Klin Monbl Augenheilkd. 2013;230(3):243–6.
Chung DC, Drack A V. RPE65-related inherited retinal degeneration gene therapy trials: background and current status, need for genetic testing, and future gene therapies for other retinal dystrophies. J Am Assoc Pediatr Ophthalmol Strabismus. 2015 Aug;19(4):e70.
Boon N, Wijnholds J, Pellissier LP. Research Models and Gene Augmentation Therapy for CRB1 Retinal Dystrophies. Front Neurosci. 2020 Aug 14;14.
Zaneveld SA, Eblimit A, Liang Q, Bertrand R, Wu N, Liu H, et al. Gene therapy rescues retinal degeneration in receptor expression-enhancing protein 6 mutant mice. Hum Gene Ther. 2019 Mar 1;30(3):302–15.
Ducloyer JB, Le Meur G, Cronin T, Adjali O, Weber M. Gene therapy for retinitis pigmentosa. Medecine/Sciences. 2020 Jun 1;36(6–7):607–15.
Costa BL da, Levi SR, Eulau E, Tsai YT, Quinn PMJ. Prime Editing for Inherited Retinal Diseases. Front Genome Ed. 2021;3.
Malvasi M, Casillo L, Avogaro F, Abbouda A, Vingolo EM. Gene Therapy in Hereditary Retinal Dystrophies: The Usefulness of Diagnostic Tools in Candidate Patient Selections. Int J Mol Sci. 2023 Sep 1;24(18).
Bansal M. Clustered Regularly Interspersed Short Palindromic Repeats Gene Editing: Precision Medicine and Newer Therapies for Retinal Dystrophies. Delhi J Ophthalmol [Internet]. 2023 Jan [cited 2025 May 13];33(1):76–8. Available from: https://journals.lww.com/10.4103/DLJO.DLJO_16_23
Chuprov AD, Pidodniy EA. Inherited retinal dystrophies associated with ABCA4 mutation. Mod Technol Ophtalmol. 2023 Oct 6;(5):82–7.
Rolling F. Recombinant AAV-mediated gene transfer to the retina: Gene therapy perspectives. Gene Ther. 2004;11:S26–32.
Weber BHF. Recent advances in the molecular genetics of hereditary retinal dystrophies with primary involvement of the

macula. Acta Anat (Basel). 1998;162(2–3):65–74.
47. Tiwari A, Lemke J, Altmueller J, Thiele H, Glaus E, Fleischhauer J, et al. Identification of novel and recurrent disease-causing mutations in retinal dystrophies using whole exome sequencing (WES): Benefits and limitations. PLoS One. 2016 Jul 1;11(7).
48. Pechnikova NA, Poimenidou M, Iliadis I, Zafeiriou-Chatziefraimidou M, Iaremenko A V., Yaremenko T V., et al. Pre-Clinical and Clinical Advances in Gene Therapy of X-Linked Retinitis Pigmentosa: Hope on the Horizon. J Clin Med. 2025 Feb 1;14(3).
49. Kvanta A, Rangaswamy N, Holopigian K, Watters C, Jennings N, Liew MSH, et al. Interim safety and efficacy of gene therapy for RLBP1-associated retinal dystrophy: a phase 1/2 trial. Nat Commun . 2024 Dec 1;15(1).
50. Li W, Sui R. Advances on gene therapy for USH2A exon 13 related inherited retinal dystrophy. Chinese J Ophthalmol. 2023 Dec 1;59(12):1058–64.
51. Den Hollander AI, Davis J, Van Der Velde-Visser SD, Zonneveld MN, Pierrottet CO, Koenekoop RK, et al. CRB1 mutation spectrum in inherited retinal dystrophies. Hum Mutat. 2004;24(5):355–69.
52. Davis JL, Gregori NZ, Maclaren RE, Lam BL. Surgical Technique for Subretinal Gene Therapy in Humans with Inherited Retinal Degeneration. Retina. 2019 Oct 1;39:S2–8.
53. Daich Varela M, Georgiadis A, Michaelides M. Genetic treatment for autosomal dominant inherited retinal dystrophies: Approaches, challenges and targeted genotypes. Br J Ophthalmol. 2023 Sep 1;107(9):1223–30.
54. Michalakis S, Gerhardt M, Rudolph G, Priglinger S, Priglinger C. Gene Therapy for Inherited Retinal Disorders: Update on Clinical Trials. Klin Monbl Augenheilkd. 2021 Mar 1;238(3):272–81.
55. Gerard X, Garanto A, Rozet JM, Collin RWJ. Antisense oligonucleotide therapy for inherited retinal dystrophies. Adv Exp Med Biol. 2016 Oct 1;854:517–24.
Benati D, Patrizi C, Recchia A. Gene editing prospects for treating inherited retinal diseases. J Med Genet. 2020 Jul 1;57(7):437–44.
Ong T, Pennesi ME, Birch DG, Lam BL, Tsang SH. Adeno-Associated Viral Gene Therapy for Inherited Retinal Disease. Pharm Res. 2019 Feb 1;36(2).
Kovacs KD, Ciulla TA, Kiss S. Advancements in ocular gene therapy delivery: vectors and subretinal, intravitreal, and suprachoroidal techniques. Expert Opin Biol Ther. 2022;22(9):1193–208.
Smith AJ, Bainbridge JWB, Ali RR. Gene supplementation therapy for recessive forms of inherited retinal dystrophies. Gene Ther. 2012 Feb;19(2):154–61.
Alsalloum A, Gornostal E, Mingaleva N, Pavlov R, Kuznetsova E, Antonova E, et al. A Comparative Analysis of Models for AAV-Mediated Gene Therapy for Inherited Retinal Diseases. Cells. 2024 Oct 1;13(20).
Bainbridge JWB. Prospects for gene therapy of inherited retinal disease. Eye. 2009;23(10):1898–903.
Ballios BG, Pierce EA, Huckfeldt RM. Gene editing technology: Towards precision medicine in inherited retinal diseases. Semin Ophthalmol. 2021;36(4):176–84.
Fenner BJ, Tan TE, Barathi AV, Tun SBB, Yeo SW, Tsai ASH, et al. Gene-Based Therapeutics for Inherited Retinal Diseases. Front Genet. 2022 Jan 7;12.
Bremond-Gignac D, Robert MP, Daruich A. Update on gene therapies in pediatric ophthalmology. Arch Pediatr. 2023 Nov 1;30(8):8S41–5.
Leroy BP, Fischer MD, Flannery JG, Maclaren RE, Dalkara D, Scholl HPN, et al. Gene Therapy for Inherited Retinal Disease: Long-Term Durability of Effect. Ophthalmic Res. 2023 Sep 14;66(1):179–96.
Hernández-Juárez J, Rodríguez-Uribe G, Borooah S. Toward the Treatment of Inherited Diseases of the Retina Using

CRISPR-Based Gene Editing. Front Med. 2021 Oct 1;8.
67. Vagni P, Perlini LE, Chenais NAL, Marchetti T, Parrini M, Contestabile A, et al. Gene Editing Preserves Visual Functions in a Mouse Model of Retinal Degeneration. Front Neurosci. 2019 Sep 10;13.
68. Cideciyan A V., Sudharsan R, Dufour VL, Massengill MT, Iwabe S, Swider M, et al. Mutation-independent rhodopsin gene therapy by knockdown and replacement with a single AAV vector. Proc Natl Acad Sci U S A. 2018 Sep 4;115(36):E8547–56.
69. Mühlfriedel R, Sothilingam V, Tanimoto N, Seeliger MW. Genersatztherapie bei hereditären Netzhauterkrankungen. Klin Monbl Augenheilkd. 2017 Mar 1;234(3):320–8.
70. Fortuny C, Flannery JG. Mutation-independent gene therapies for rod-cone dystrophies. Adv Exp Med Biol. 2018;1074:75–81.
71. Dinculescu A, Estreicher J, Zenteno JC, Aleman TS, Schwartz SB, Huang WC, et al. Gene therapy for retinitis pigmentosa caused by MFRP mutations: Human phenotype and preliminary proof of concept. Hum Gene Ther. 2011 Dec 20;23(4):367–76.
72. Toualbi L, Toms M, Moosajee M. The landscape of non-viral gene augmentation strategies for inherited retinal diseases. Int J Mol Sci. 2021 Mar 1;22(5):1–14.
73. Garoon RB, Stout JT. Update on ocular gene therapy and advances in treatment of inherited retinal diseases and exudative macular degeneration. Curr Opin Ophthalmol. 2016;27(3):268–73.
74. Jiang D, Xu CL, Tsang SH. Revolution in Gene Medicine Therapy and Genome Therapy. 2018 Oct 1 [cited 2025 May 13]; Available from: https://www.preprints.org/manuscript/201810.0010/v1
75. Priglinger CS, Gerhardt MJ, Rudolph G, Priglinger SG, Michalakis S. Gene therapy in ophthalmology. Ophthalmologie. 2023 Aug 1;120(8):867–82.
Eszter V, Lilla S, Ágnes J, Máté Oh L, Márta J, Edit TM. Gene therapy treatment based on an ophthalmic indication in hereditary retinal dystrophy caused by RPE65 biallelic gene mutation. Treatment of the first two Hungarian patients. Orv Hetil. 2022 Nov 27;163(48):1923–31.
Daruich A, Boinet R, Falcou C, Cotteret C, Magassa A, Schlatter J, et al. Implementation of a new gene therapy in ophthalmology: Regulatory and organizational issues. J Fr Ophtalmol. 2021 May 1;44(5):730–7.
Garanto A. RNA-Based Therapeutic Strategies for Inherited Retinal Dystrophies. Adv Exp Med Biol. 2019;1185:71–7.
McClements ME, MacLaren RE. Gene Therapy for Retinal Disease. Transl Gene Ther to Clin Tech Approaches. 2015;173–89.
Vázquez-Domínguez I, Garanto A, Collin RWJ. Molecular therapies for inherited retinal diseases—current standing, opportunities and challenges. Genes (Basel). 2019 Sep 1;10(9).
Ku CA, Pennesi ME. The new landscape of retinal gene therapy. Am J Med Genet Part C Semin Med Genet. 2020 Sep 1;184(3):846–59.
Jony MJ, Joshi A, Dash A, Shukla S. Non-Viral Delivery Systems to Transport Nucleic Acids for Inherited Retinal Disorders. Pharmaceuticals. 2025 Jan 1;18(1).
Martinez Velazquez LA, Ballios BG. The next generation of molecular and cellular therapeutics for inherited retinal disease. Int J Mol Sci. 2021 Nov 1;22(21).
Fuller-Carter PI, Basiri H, Harvey AR, Carvalho LS. Focused Update on AAV-Based Gene Therapy Clinical Trials for Inherited Retinal Degeneration. BioDrugs. 2020 Dec 1;34(6):763–81.
Ziccardi L, Cordeddu V, Gaddini L, Matteucci A, Parravano M, Malchiodi-Albedi F, et al. Gene therapy in retinal dystrophies. Int J Mol Sci. 2019 Nov 2;20(22).
Amato A, Arrigo A, Aragona E, Manitto MP, Saladino A, Bandello F, et al. Gene Therapy in Inherited Retinal Diseases: An Update on

Current State of the Art. Front Med. 2021 Oct 15;8.
87. N. Sahni J, Angi M, Irigoyen C, Angi M, Semeraro F, R. Romano M, et al. Therapeutic Challenges to Retinitis Pigmentosa: From Neuroprotection to Gene Therapy. Curr Genomics. 2011 May 30;12(4):276–84.
88. Scholl HPN, Strauss RW, Singh MS, Dalkara D, Roska B, Picaud S, et al. Emerging therapies for inherited retinal degeneration. Sci Transl Med. 2016 Dec 7;8(368).
89. Daruich A, Robert MP, Bremond-Gignac D. Gene therapies in pediatric ophthalmology. Front Ophthalmol. 2023;3.
90. Carvalho C, Lemos L, Antas P, Seabra MC. Gene therapy for inherited retinal diseases: exploiting new tools in genome editing and nanotechnology. Front Ophthalmol. 2023;3.
91. Brar AS, Parameswarappa DC, Takkar B, Narayanan R, Jalali S, Mandal S, et al. Gene Therapy for Inherited Retinal Diseases: From Laboratory Bench to Patient Bedside and Beyond. Ophthalmol Ther. 2024 Jan 1;13(1):21–50.
92. Sarzi E, Seveno M, Piro-Mégy C, Elzière L, Quilès M, Péquignot M, et al. OPA1 gene therapy prevents retinal ganglion cell loss in a Dominant Optic Atrophy mouse model. Sci Rep. 2018 Dec 1;8(1).
93. Antas P, Carvalho C, Cabral-Teixeira J, de Lemos L, Seabra MC. Toward low-cost gene therapy: mRNA-based therapeutics for treatment of inherited retinal diseases. Trends Mol Med. 2024 Feb 1;30(2):136–46.
94. McClements ME, Staurenghi F, MacLaren RE, Cehajic-Kapetanovic J. Optogenetic Gene Therapy for the Degenerate Retina: Recent Advances. Front Neurosci. 2020 Nov 11;14.
95. Charbel P, Febo I, Maclaren RE, Frcophth D. Non-viral retinal gene therapy: A review. Clin Exp Ophthalmol [Internet]. 2012 Feb [cited 2025 May 13];40(1):39–47. Available from: https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1442-9071.2011.02649.x
96. Nuzbrokh Y, Ragi SD, Tsang SH. Gene therapy for inherited retinal diseases. Ann Transl Med. 2021 Aug;9(15):1278–1278.
Zhang X, Reilly J. Reflection on the Efficacy of Gene Therapy in the Treatment of Inherited Retinal Degeneration. Cloning Transgenes. 2015;05(01).
Strauß O. mRNA-Technologien im Einsatz gegen Augenerkrankungen. Kompass Ophthalmol [Internet]. 2024 Oct 25 [cited 2025 May 13];10(4):135–6. Available from: https://karger.com/article/doi/10.1159/000542139
Khaparde A, Mathias GP, Poornachandra B, Thirumalesh MB, Shetty R, Ghosh A. Gene therapy for retinal diseases: From genetics to treatment. Indian J Ophthalmol. 2024 Aug 1;72(8):1091–101.
Thompson DA, Ali RR, Banin E, Branham KE, Flannery JG, Gamm DM, et al. Advancing therapeutic strategies for inherited retinal degeneration: Recommendations from the monaciano symposium. Investig Ophthalmol Vis Sci. 2015;56(2):918–31.
Arbabi A, Liu A, Ameri H. Gene Therapy for Inherited Retinal Degeneration. J Ocul Pharmacol Ther. 2019 Mar 1;35(2):79–97.
Bansal M, Acharya S, Sharma S, Phutela R, Rauthan R, Maiti S, et al. CRISPR Cas9 based genome editing in inherited retinal dystrophies. Ophthalmic Genet. 2021;42(4):365–74.
Bansal M. Advances in retina genetics: Progress, potential, and challenges. Indian J Ophthalmol. 2025 Jan 1;73:S31–6.
Farrar GJ, Millington-Ward S, Chadderton N, Mansergh FC, Palfi A. Gene therapies for inherited retinal disorders. Vis Neurosci. 2014 May 22;31:289–307.
Trapani I, Banfi S, Simonelli F, Surace EM, Auricchio A. Gene therapy of inherited retinal degenerations: Prospects and challenges. Hum Gene Ther. 2015 Apr 1;26(4):193–200.
John MC, Quinn J, Hu ML, Cehajic-Kapetanovic J, Xue K. Gene-agnostic therapeutic approaches for inherited retinal degenerations. Front Mol Neurosci. 2023 Jan 9;15.

107. LUO X, LIU Y, WANG F, SUN X. Opportunities and challenges of gene therapy for retinitis pigmentosa. Sci Sin Vitae. 2022 Jul 1;52(7):1015–22.
108. Sergouniotis PI. Inherited Retinal Disorders: Using Evidence as a Driver for Implementation. Ophthalmologica. 2019 Oct 1;242(4):187–94.