Review > Mol Aspects Med. 2026 Apr:108:101462. doi: 10.1016/j.mam.2026.101462. Epub 2026 Feb 16.

CRISPR as a therapeutic tool for inherited retinal degenerations: Advances, challenges, and future directions

Egle Galdikaite-Braziene [1], Raulas Krušnauskas [2], Emiline Henderson [2], Kinga M Bujakowska [2]

Affiliations + expand

PMID: 41702027
DOI: 10.1016/j.mam.2026.101462

Abstract

Inherited retinal diseases (IRDs) are a genetically diverse group of disorders characterized by progressive photoreceptor degeneration, leading to vision loss and blindness. With over 320 associated genes and significant phenotypic variability, effective treatment remains challenging. Recent advances in genome editing, particularly CRISPR/Cas-based technologies, have revolutionized therapeutic approaches by enabling precise and customizable DNA and RNA editing. This review explores the application of various CRISPR strategies-such as gene knockout via non-homologous end joining (NHEJ), exon skipping using dual-sgRNAs, homology-directed repair (HDR), base editing (BE), prime editing (PE), RNA editing with Cas13, and epigenetic modulation through CRISPRa/i-in preclinical models of IRDs. Emphasis is placed on allele-specific targeting, gene-agnostic approaches, and mutation-independent strategies to address dominant and recessive forms of disease. We also highlight recent clinical milestones, including the first human trial using CRISPR gene editing for CEP290-associated Leber congenital amaurosis. Finally, we discuss critical challenges, including delivery constraints, immune responses, and off-target effects, along with emerging solutions such as engineered Cas variants, split-intein systems, and advanced off-target detection methods. Together, these

advances underscore the transformative potential of CRISPR technologies in treating IRDs and lay the foundation for future clinical translation.

Keywords: Base editing; CRISPR/Cas9; Gene editing; Inherited retinal degenerations; Ophthalmic genetics; Prime editing; Retinal therapy.

Conflict of interest statement

Declaration of interest statement The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Similar articles

Genome-Editing Strategies for Treating Human Retinal Degenerations.
Quinn J, et al.Hum Gene Ther. 2021.PMID: 32993386Free PMC article.Review.

Using CRISPR-Cas9 to Generate Gene-Corrected Autologous iPSCs for the Treatment of Inherited Retinal Degeneration.
Burnight ER, et al.Mol Ther. 2017.PMID: 28619647Free PMC article.

CRISPR-Based Genome Editing as a New Therapeutic Tool in Retinal Diseases.
Rasoulinejad SA, et al.Mol Biotechnol. 2021.PMID: 34057656Review.

From bench to bedside: Developing CRISPR/Cas-based therapy for ocular diseases.
Zhao Q, et al.Pharmacol Res. 2025.PMID: 39889868Review.

CRISPR-cas9 genome editing delivery systems for targeted cancer therapy.
Ghaemi A, et al.Life Sci. 2021.PMID: 33385410Review.

See all similar articles

Publication types

- Review

MeSH terms

- Animals
- CRISPR-Cas Systems*
- Clustered Regularly Interspaced Short Palindromic Repeats*
- Gene Editing* / methods
- Genetic Therapy* / methods
- Humans
- Retinal Degeneration* / genetics
- Retinal Degeneration* / therapy

Related information

GEO Profiles

LinkOut - more resources

Full Text Sources

Elsevier Science

Medical

MedlinePlus Health Information

National Library of Medicine
8600 Rockville Pike
Bethesda, MD 20894