Journal of Stem Cell Research

Genesis-JSCR-6(1)-70
Volume 6 | Issue 1
Open Access
ISSN: 2582-8797

Treatment of Glaucoma with Progenitor/Precursor Stem Cells: Current Approaches and Future Prospects

Mike KS Chan[1*], Michelle BF Wong[2], Olha Nishkumai[3], Glen Alvin[4], Margarita Iemeliyanova[3] and Dmytro Klokol[3]

[1]European Wellness Biomedical Group (Malaysia)
[2]FCTI (Germany)
[3]European Wellness Biomedical Group and European Wellness Academy (Malaysia, Ukraine)
[4]EW Clinic (Malaysia)

***Corresponding author:** Chan MKS, European Wellness Biomedical Group (Malaysia).

Citation: Chan MKS, Wong MBF, Nishkumari O, Alvin G, Lemeliyanova M and Klokol D. Treatment of Glaucoma with Progenitor/Precursor Stem Cells: Current Approaches and Future Prospects. J Stem Cell Res. 6(1):1-6.

Received: February 17, 2025 | **Published**: March 10, 2025

Abstract

Glaucoma is a progressive optic neuropathy with multiple etiologies that involves the degeneration of retinal ganglion cells (RGCs) and their axons, leading to permanent vision loss. Elevated intraocular pressure (IOP) is a significant risk factor, yet glaucoma can also occur with IOP within the normal range. Despite current therapies—primarily aimed at IOP reduction—few treatments specifically address the cellular damage underlying the disease. The degeneration of the axons and retinal ganglion cells cannot be reversed, and the treatment becomes challenging when the disease is in its advanced stages. Therefore, new therapies with the potential to regenerate lost tissue and recover vision loss are urgently required.

Keywords

Glaucoma; Retinal ganglion cells; Ciliary epithelial cells; Lateral geniculate nucleus

DOI: https://doi.org/10.52793/JSCR.2025.6(1)-70

Introduction

Glaucoma is a progressive optic neuropathy with multiple etiologies that involves the degeneration of retinal ganglion cells (RGCs) and their axons, leading to permanent vision loss [1]. Elevated intraocular pressure (IOP) is a significant risk factor, yet glaucoma can also occur with IOP within the normal range. Despite current therapies—primarily aimed at IOP reduction—few treatments specifically address the cellular damage underlying the disease. The degeneration of the axons and retinal ganglion cells cannot be reversed, and the treatment becomes challenging when the disease is in its advanced stages. Therefore, new therapies with the potential to regenerate lost tissue and recover vision loss are urgently required [2,3].

Stem cell therapy has exhibited much potential for the treatment of glaucoma over the last few years. Stem cells, particularly progenitor and precursor stem cells, have shown potential for regenerating damaged tissues, offering hope for the restoration of vision in glaucoma patients. This review examines the role of progenitor/precursor stem cells in the treatment of glaucoma, their mechanisms of action, current clinical developments, and the challenges that need to be addressed before this approach becomes a standard therapeutic option [3,4].

Pathophysiology of glaucoma

Glaucoma encompasses a group of eye diseases, the most common of which is primary open-angle glaucoma (POAG). In POAG, damage to the optic nerve is progressive and irreversible [1]. This damage is primarily caused by the loss of retinal ganglion cells (RGCs) and their axons. Elevated IOP, resulting from an imbalance in the production and drainage of aqueous humor, is the most well-established risk factor for glaucoma. However, other factors such as genetic predisposition, vascular dysregulation, and excitotoxicity also play crucial roles in disease pathogenesis.

At the cellular level, glaucomatous damage begins when increased IOP compresses the optic nerve head, leading to impaired axonal transport and eventual RGC death. Once RGCs are lost, they cannot regenerate due to the limited regenerative capacity of the central nervous system (CNS). As RGC death progresses, patients experience visual field defects and, if left untreated, can go blind. The chronic nature of glaucoma requires long-term management, but current therapies primarily aim to control IOP and do not address the underlying loss of RGCs.

Stem Cell Therapy for Glaucoma

Stem cells, which have the potential to differentiate into a variety of cell types, offer a novel therapeutic strategy for treating glaucoma [5,6]. Progenitor and precursor stem cells, which are early-stage stem cells capable of differentiating into specific types of cells, have garnered significant attention for their regenerative potential in treating degenerative diseases like glaucoma. These cells could, in theory, replace lost RGCs, restore axonal connections, and improve the overall function of the retina [7].

Types of Stem Cells for Glaucoma Therapy:

1. **Retinal Progenitor Cells (RPCs):** RPCs are precursor cells derived from the retina itself. These cells have the ability to differentiate into retinal cells, including RGCs, and could potentially replace damaged cells within the retina. RPCs have shown promise in animal models of glaucoma [2,8].

2. **Ciliary Epithelial Cells (CECs):** CECs, located in the ciliary body, are considered a potential source of retinal progenitor cells. They have regenerative potential and are capable of transdifferentiating into RGCs, providing another avenue for stem cell-based therapies in glaucoma [9-10].

3. **The lateral geniculate nucleus:** (LGN) of the thalamus has recently gained attention as a potential source of progenitor cells for the treatment of glaucoma, due to its role in the processing and transmission of visual information from the retina to the brain. In animal models, research has shown that progenitor cells derived from the LGN can exhibit some regenerative potential, potentially supporting the repair of damaged optic nerve pathways in glaucoma. The idea is that these cells could be harnessed to promote axonal regeneration and restore the function of damaged retinal ganglion cells (RGCs) and their projections to the brain. While early studies are promising, suggesting that LGN progenitor cells may aid in the re-establishment of visual processing, their efficacy in clinical settings remains under investigation. Key challenges include ensuring the survival, proper differentiation, and integration of transplanted LGN progenitor cells into the visual pathway, as well as overcoming the complex nature of optic nerve damage caused by glaucoma. Nonetheless, this approach represents an exciting avenue for the future treatment of glaucoma, particularly in cases where axonal regeneration is critical [11,12].

4. **Progenitor cells derived from the optic nerve are an emerging area of interest for the treatment of glaucoma, primarily due to their potential to regenerate damaged retinal ganglion cells** (RGCs) and their axons [13]. The optic nerve, which transmits visual information from the retina to the brain, has a limited capacity for regeneration, making it a challenging target for restoring vision in glaucoma patients. However, recent research has demonstrated that progenitor cells isolated from the optic nerve have the ability to differentiate into retinal cells, including RGCs, and promote axonal growth in animal models. These progenitor cells may offer a way to repair the damaged optic nerve fibers and restore connections between the retina and the brain. In addition, they could potentially secrete neuroprotective factors that help preserve the survival of remaining RGCs, offering dual benefits of neuroprotection and regeneration. Although preclinical studies are promising, the efficacy of optic nerve progenitor cells in treating glaucoma in humans remains uncertain. Challenges such as ensuring proper differentiation, long-term survival of transplanted cells, and overcoming the complex environment of the glaucomatous optic nerve head need to be addressed before this approach can be translated into a viable clinical therapy [13,14].

Mechanisms of Action of Progenitor/Precursor Stem Cells in Glaucoma

The therapeutic potential of progenitor and precursor stem cells in glaucoma lies in their ability to regenerate lost retinal tissue and restore function to damaged optic nerves. Several mechanisms have been proposed through which stem cells can exert beneficial effects:

1. **Direct Differentiation into Retinal Ganglion Cells (RGCs):** Stem cells, particularly retinal progenitor cells, have the potential to directly differentiate into RGCs. This would enable the replacement of lost or damaged RGCs in the retina, restoring the transmission of visual signals to the brain [13,15].

2. **Neuroprotection and Rescue of Surviving RGCs:** Stem cells, particularly mesenchymal stem cells, can secrete a variety of neurotrophic factors, such as brain-derived neurotrophic factor (BDNF) and ciliary neurotrophic factor (CNTF). These factors can protect remaining RGCs from further damage and enhance cell survival, offering neuroprotection in glaucoma [14,15].

3. **Regeneration of Retinal Axons:** One of the most significant challenges in glaucoma therapy is the irreversible damage to the axons of RGCs. Stem cells may have the ability to stimulate axon regeneration, potentially restoring the damaged connections between the retina and the brain. This could involve the activation of intrinsic repair pathways or the promotion of axonal growth through the transplantation of stem cells that release growth factors [14].

4. **Retinal Remodeling and Repair:** Stem cells may also promote retinal remodeling and repair by secreting extracellular matrix components and cytokines that support retinal tissue regeneration. This could improve the structural integrity of the retina and optic nerve head, reducing the adverse effects of elevated IOP on tissue architecture [15,16].

Current Preclinical and Clinical Studies

Several preclinical and clinical studies have explored the potential of stem cell therapies for glaucoma. Animal models of glaucoma, particularly those that mimic the effects of increased IOP, have been used to assess the efficacy of stem cell transplantation. For instance, transplantation of retinal progenitor cells into glaucomatous rats has shown promising results, with improvements in RGC survival and retinal function [16].

In clinical studies, the use of stem cells in glaucoma treatment remains in the early stages. A few clinical trials have investigated the safety and efficacy of stem cell-based therapies, such as the transplantation of mesenchymal stem cells or retinal progenitor cells. Early-phase trials have demonstrated some safety, but significant challenges remain, including the long-term viability of transplanted cells, the risk of immune rejection, and the difficulty of ensuring that stem cells differentiate appropriately into RGCs.

While stem cell therapy holds great potential for the treatment of glaucoma, several challenges must be overcome before it becomes a mainstream therapeutic approach, in particular the cell survival and integration. Ensuring the long-term survival and integration of transplanted stem cells into the retina is a

DOI: *https://doi.org/10.52793/JSCR.2025.6(1)-70*

significant challenge. Many studies have shown that stem cells often fail to survive or integrate properly, limiting the effectiveness of the therapy [16].

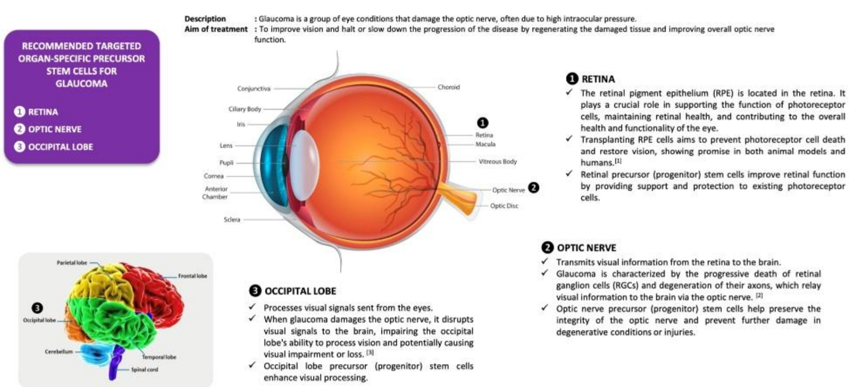
Future directions

Our research into stem cell therapies for glaucoma continues, and we are working on several strategies to improve the clinical application of progenitor/precursor stem cells. Advances in gene editing, biomaterials for stem cell delivery, and better understanding of the molecular mechanisms underlying glaucoma will contribute to the refinement of stem cell-based treatments [17-19].

Furthermore, the use of combination therapies, such as the integration of stem cells with neuroprotective peptides, exosomes and gene therapy, may enhance therapeutic outcomes. Ultimately, personalized medicine approaches, where treatment is tailored to individual patients based on their genetic profile, may allow for more effective stem cell therapies in glaucoma.

Conclusion

The treatment of glaucoma with progenitor and precursor stem cells represents an exciting and promising frontier in regenerative medicine. While significant progress has been made in understanding the potential mechanisms through which stem cells could restore vision and prevent further damage, there are still considerable challenges to overcome. With continued research and development, stem cell-based therapies may one day provide a viable solution to halt the progression of glaucoma and even restore lost vision. The future of glaucoma treatment lies in harnessing the regenerative potential of stem cells to repair the damaged retinal and optic nerve tissues, offering hope for millions of patients worldwide.



DOI: *https://doi.org/10.52793/JSCR.2025.6(1)-70*

References

1. Casson RJ and Chidlow G. (2008) The pathophysiology of glaucoma. Clinical & Experimental Ophthalmology, 36(3);206-213.
2. Johnson EC and Safran AB. (2006) Experimental models of glaucoma. Progress in Retinal and Eye Research, 25(4), 579-598.
3. Thanos S and Loussouarn G. (2011) Stem cell therapy in retinal diseases. Experimental Eye Research, 92(4), 265-273.
4. Yang Y and Lee H. (2020) Stem cell therapy for glaucoma: Current status and future directions. Stem Cells Int. Article ID 4130807.
5. Sapieha P and Chen M. (2015) Progenitor cells in the optic nerve: Sources and potential in glaucoma therapy. Ophthalmology. 122(4);805-812.
6. Cao S and Yang Z. (2017) Progenitor cells derived from the optic nerve in glaucoma: Mechanisms of regeneration. J Neurosci Res. 95(6);1249-1258.
7. Lamba DA and Reh TA. (2013) Retinal progenitor cells: Mechanisms and potential for retinal repair. Trends in Neuroscie. 36(8), 442-449.
8. Wang Y and Zhang L. (2014) Role of neuroprotection in the treatment of glaucoma. J Glauco. 23(9);681-87.
9. Liu C and Duh E. (2011) Ciliary epithelial cells as a source of retinal progenitors for glaucoma therapy. Ophthalmic Res. 45(6);309-315.
10. Gupta R and Shankar V. (2020) Ciliary body cells as potential retinal progenitors in glaucoma treatment. Cur Opin Ophthalmol. 31(5);353-358.
11. Cheng H and Pterocis T. (2016) "Potential role of progenitor cells of the thalamus in optic nerve regeneration." Neurosci. 313;140-153.
12. Tan Y and Liu Y. (2019) Thalamic progenitor cells and their application in visual pathway regeneration. J Neural Engi. 16(2);020305.
13. Vetter ML and Mattapallil MJ. (2010) Neuroprotective therapies in glaucoma: An update. Expert Opin Investigation Drugs. 19(3);439-453.
14. Calkins DJ. (2012) The pathophysiology of glaucoma: Insights into cell death and survival. Prog Brain Res. 195;115-141.
15. Schwartz SD and Regillo CD. (2019) Stem cells and gene therapy for glaucoma. J Clinical Investi. 129(10);3791-3797.
16. Mandel Y and Barak A. (2018) Challenges in clinical application of stem cells in ophthalmology. Ophthal Res. 59(5);237-245.
17. Zhang M and Li Y. (2020) Gene editing, biomaterials, and combination therapies in stem cell-based glaucoma treatment. Stem Cells Translat Med. 9(6);667-676.
18. Zhang H Lai J. (2022) Gene therapy combined with stem cells for glaucoma management. Frontie Neurol. 13;800-810.

DOI: *https://doi.org/10.52793/JSCR.2025.6(1)-70*