

STEM CELL THERAPY FOR RETINITIS PIGMENTOSA : PROMISE, EVIDENCE, AND THE RISK OF PREMATURE CLINICAL CLAIMS

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Retinitis pigmentosa (RP) is an appealing target for regenerative medicine. Progressive photoreceptor degeneration provides an intuitive therapeutic rationale: if surviving photoreceptors could be protected, or those already lost could be replaced, vision might theoretically be preserved or restored. Advances involving mesenchymal stem cells (MSCs), retinal progenitor cells, induced pluripotent stem cells (iPSCs), and retinal organoids have consequently generated considerable enthusiasm.

However, enthusiasm should not be allowed to outpace evidence. Patients increasingly encounter claims that "stem cells can treat retinitis pigmentosa," sometimes accompanied by suggestions of retinal regeneration, restoration of vision, or high treatment success rates. Such terminology is problematic. Based on currently available evidence, including clinical data available through 2026, cell-based approaches for RP should still be regarded as investigational therapies rather than established treatments capable of reversing or curing the disease. The distinction is fundamental: biological plausibility is not equivalent to clinical efficacy.

The Genetic Basis Cannot Be Ignored

RP comprises a highly heterogeneous group of inherited retinal disorders caused by pathogenic variants affecting photoreceptor, retinal pigment epithelial, ciliary, phototransduction, RNA-processing, and other retinal pathways. Genes such as RHO, RPGR, USH2A, EYS, PDE6A, PDE6B, and PRPF31 represent only a fraction of the genes associated with RP. At its simplest, the disease process can be viewed as pathogenic variant → abnormal or deficient protein → photoreceptor dysfunction → progressive degeneration → visual loss.

This genetic basis is particularly relevant when evaluating nonspecific stem-cell interventions. Administration of MSCs does not correct a pathogenic RHO, RPGR, or PDE6B variant, nor does it restore the defective molecular pathway responsible for the disease. This does not mean that cell therapy is biologically irrelevant to a genetic disorder. It means that its proposed therapeutic action must be defined accurately.

Mesenchymal Stem Cells Are Not New Photoreceptors

The principal rationale for MSCs in retinal degeneration is neurotrophic and paracrine rather than true neuronal replacement. MSCs may release growth factors, modulate inflammation, influence apoptosis, and potentially support the survival of residual host photoreceptors. These mechanisms deserve scientific investigation, but they should not be equated with regeneration of a functional outer retina. A 2025 systematic review and meta-analysis of 11 studies involving 355 patients with RP found short-term signals of benefit in some visual outcomes, while also emphasizing heterogeneity among cell sources, delivery methods, and follow-up, and the need for larger randomized trials and long-term confirmation of sustained benefit.¹

A functional photoreceptor requires substantially more than the presence of a transplanted cell within or adjacent to the retina. A newly generated rod or cone must mature appropriately, form an outer segment, establish phototransduction machinery, interact continuously with the retinal pigment epithelium (RPE), generate a physiologically appropriate electrical response, and communicate synaptically with downstream retinal neurons. Thus, MSC administration is not synonymous with photoreceptor replacement.

True Photoreceptor Replacement Is a Different Concept

iPSC-derived photoreceptor or retinal-sheet transplantation represents a more direct regenerative strategy. Pluripotent cells can be differentiated toward retinal tissue or photoreceptor precursors and transplanted into the subretinal space. Importantly, the genetic nature of RP does not automatically prevent an allogeneic donor photoreceptor from functioning. A genetically normal donor rod transplanted into an eye affected by RHO-associated RP carries the donor genome and could theoretically express normal rhodopsin despite the pathogenic variant present in the patient's native cells.

Autologous iPSC therapy presents a different problem. Patient-derived iPSCs retain the patient's disease-causing variant; consequently, photoreceptors derived from uncorrected autologous iPSCs would retain the same genetic defect. Gene correction before differentiation and transplantation may therefore be required. Proof-of-concept genetic repair of an RP-associated mutation in patient-derived stem cells has already been demonstrated experimentally.²

Graft Survival Is Not the Same as Visual Restoration

Yet overcoming the genetic defect addresses only one component of the problem. A landmark clinical study by Hirami and colleagues transplanted allogeneic iPSC-derived retinal organoid sheets into two patients with advanced RP. The grafts survived in a stable condition for two years without serious graft-associated adverse events, representing an important milestone in human retinal regenerative medicine. However, the primary endpoint concerned graft survival and safety; the study did not establish restoration of a normal retinal circuit or reproducible recovery of vision.³

The current development pathway confirms this limitation. DSP-3077, an allogeneic iPSC-derived retinal sheet containing abundant photoreceptor precursors, is being evaluated in a Phase 1/2 study in adults with RP, with safety and tolerability as central early-phase objectives.⁴

Similarly, OpCT-001 consists of iPSC-derived photoreceptor precursor cells administered subretinally and is being investigated in a first-in-human Phase 1/2a study of primary photoreceptor diseases, including RP. Phase 1 emphasizes safety and dose escalation, while later evaluation includes visual-function and anatomical outcomes.⁵

If photoreceptor replacement were already an established treatment for RP, current trials would not still be centered on fundamental questions of safety, engraftment, dose, tolerability, and preliminary efficacy.

The Retina Is More Than a Collection of Photoreceptors

The challenge becomes even greater in advanced RP. Long-standing photoreceptor loss triggers secondary retinal remodeling, including Müller-cell gliosis, alterations of bipolar and horizontal cells, changes in extracellular architecture, disruption of RPE-photoreceptor relationships, metabolic abnormalities, and remodeling of inner-retinal circuitry. Therefore, producing a cell that expresses recoverin, rhodopsin, or cone opsin is not equivalent to restoring vision.

For meaningful visual restoration, a transplanted photoreceptor must survive; establish appropriate polarity; form and continuously renew outer segments; interact physiologically with the RPE; perform phototransduction; form functional ribbon synapses; connect appropriately with bipolar and horizontal cells; and transmit usable information through retinal ganglion cells and the visual pathway. The central question is consequently no longer simply, "Can we generate a photoreceptor?" It is, "Can a transplanted photoreceptor become a durable, physiologically integrated component of a chronically remodeled human retinal neural circuit?" Current human evidence has not yet answered this question.

Lessons From Earlier Photoreceptor Transplantation

The history of photoreceptor transplantation provides an important cautionary lesson. Earlier transplantation experiments appeared to demonstrate extensive integration of donor photoreceptors into the host outer nuclear layer. Subsequent studies showed that a substantial proportion of apparent donor-cell integration could instead result from cytoplasmic material transfer between donor and host photoreceptors.^{6,7}

This finding did not invalidate retinal cell transplantation. Rather, it illustrated how apparently convincing biological observations may require reinterpretation as experimental methods improve. The same caution should apply when translating graft survival, marker expression, anatomical changes, or modest functional signals into therapeutic claims.

The Most Recent Human Evidence Remains Early-Phase

Recent clinical evidence remains encouraging but preliminary. A Phase I/IIa study of intravitreal human retinal progenitor cells in 28 adults with nonsyndromic RP reported acceptable safety and tolerability, with exploratory visual-acuity signals at some dose levels. However, the trial was designed primarily as a safety study, and the findings require confirmation in appropriately controlled efficacy trials.⁸

More recently, previously unpublished Phase 1/2a data presented at the International Society for Stem Cell Research meeting in July 2026 showed that subretinally transplanted human neural progenitor cells remained detectable for at least one year in 13 patients with RP. Visual acuity was generally stable, and OCT demonstrated persistent graft presence. Cell-related adverse events included three epiretinal membranes and one persistent subretinal bleb. Importantly, whether such long-term engraftment can slow visual deterioration remains unanswered.⁹

These observations reinforce several distinctions that should remain explicit: cell survival is not equivalent to functional integration; functional integration is not equivalent to clinically meaningful restoration of vision; and short-term functional change is not equivalent to durable modification of a lifelong degenerative disease.

Premature Clinical Claims Carry Consequences

Precision of language is particularly important in RP because patients face progressive visual loss and, for most genotypes, limited disease-modifying options. Statements such as "stem cells regenerate the retina," "stem cells restore vision in RP," or percentage-based treatment success rates require much stronger evidence than uncontrolled observations or short-term changes in visual acuity. Clinical efficacy should be supported by appropriately controlled studies with clearly defined eligibility criteria, molecular diagnosis where relevant, prespecified endpoints, standardized functional testing, adequate sample size, appropriate comparators, and sufficiently long follow-up.

Safety must also remain central. Severe visual complications have been reported following inadequately validated intravitreal "stem-cell" procedures, including retinal detachment, vitreous hemorrhage, ocular hypertension, and proliferative vitreoretinopathy-like responses.¹⁰

Cell identity, differentiation status, genomic stability, purity, tumorigenicity, immunogenicity, route of administration, surgical technique, and long-term behavior cannot be treated as secondary considerations. Promising biology does not eliminate the requirement for rigorous clinical development.

Where Should We Draw the Line?

Cell-based therapy for RP should therefore neither be dismissed nor prematurely promoted. MSCs may eventually provide mutation-independent neuroprotective effects. Retinal or neural progenitor cells may prolong survival of remaining host photoreceptors. iPSC-derived retinal sheets and photoreceptor precursors offer a scientifically compelling route toward genuine cell replacement in advanced disease. These are important and legitimate fields of research.

Nevertheless, the evidence available in 2026 does not establish that stem cells or iPSC-derived retinal cells cure RP, reliably restore vision, or provide proven long-term disease modification. The scientifically appropriate description remains investigational cell-based therapy for retinitis pigmentosa.

Maintaining this distinction is not therapeutic pessimism. It protects patients from premature claims while preserving the scientific credibility of a field that may ultimately transform the management of inherited retinal degeneration. The promise of regenerative medicine is substantial; the responsibility of retinal specialists is to ensure that the language used to describe that promise never advances faster than the evidence supporting it.

Conflict of Interest

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