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The retinal pigment epithelium: the silent guardian and mother of photoreceptors

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ABSTRACT

The retinal pigment epithelium (RPE) is a highly specialized, polarized monolayer that sustains photoreceptor survival through metabolic coupling, chromophore regeneration, phagocytosis, ion and fluid transport, immune regulation, and trophic factor secretion. Although historically viewed as a structural support layer, modern molecular, imaging, and therapeutic evidence positions the RPE as the central regulator of outer retinal homeostasis. This review synthesizes structural biology, developmental polarity, cellular stress responses, retinal degenerative diseases, imaging biomarkers, and emerging therapies through a unifying maternal paradigm. We propose that the RPE functions biologically as the "mother" of photoreceptors-nourishing, cleansing, protecting, and responding dynamically to injury. Clinical and experimental data from age-related macular degeneration (AMD), retinitis pigmentosa (RP), Stargardt disease, and RPE-targeted gene therapy support the conceptual re-centering of retinal disease around RPE dysfunction.

Keywords: Phagocytosis, photoreceptor support, retinal pigment epithelium, visual cycle, vitamin A metabolism

INTRODUCTION

The vertebrate retina is frequently described as a neuronal tissue optimized for phototransduction. However, photoreceptors exist in a uniquely dependent relationship with the retinal pigment epithelium. Strauss1 described the retinal pigment epithelium (RPE) as indispensable for visual function, emphasizing that photoreceptors cannot sustain phototransduction without RPE-mediated support. Bok[2] earlier characterized the RPE as a "versatile partner in vision," highlighting its multifaceted responsibilities.

Unlike neurons supplied by direct vasculature, photoreceptors lack an intrinsic blood supply and rely entirely on the RPE for nutrient delivery, waste removal, chromophore recycling, and environmental regulation.[1,3] Each RPE cell supports dozens of photoreceptors, establishing a marked asymmetry of dependence.[3]

This structural and metabolic interdependence supports a maternal conceptualization: the RPE sustains photoreceptor survival through continuous caregiving functions. Disease states frequently reveal that RPE dysfunction precedes and amplifies neuronal degeneration.

STRUCTURAL ARCHITECTURE

Outer Blood-Retina Barrier

The RPE forms the outer blood-retina barrier (oBRB) via apicolateral tight junctions composed of claudins, occludin, and zonula occludens (ZO-1).[3,4] This barrier establishes immune privilege and regulates molecular exchange between the choroidal circulation and neural retina.[1,4] Barrier breakdown is an early feature of age-related macular degeneration (AMD) and inflammatory retinal disease.[1-4] Disruption of ZO-1 and cytoskeletal reorganization compromises selective permeability and promotes edema.

Apical Microvilli and Photoreceptor Coupling

The apical RPE surface extends elongated microvilli that ensheath photoreceptor outer segments, expanding surface area approximately threefold.[3,5] These structures facilitate retinoid exchange, ion regulation, and phagocytosis.

A distinctive feature of RPE polarity is the apical localization of Na^+/K^+-ATPase, reversed relative to classical epithelia.[3] This polarity adaptation optimizes ion transport within the subretinal space.

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Basal Infoldings and Bruch's Membrane Interface

Basal infoldings form a labyrinthine interface with Bruch's membrane and the choriocapillaris, increasing membrane surface area for nutrient transport.[1,3] Glucose, retinoids, and water traverse this interface via glucose transporters (GLUT) transporters, aquaporins, and ion channels.[1,6]

Kirchhof and Ryan[7] demonstrated differential permeance between retina and RPE, establishing hydrostatic forces that contribute to retinal adhesion. Age-related thickening of Bruch's membrane impairs exchange and predisposes to AMD.[8,9] These structural specializations and their functional and pathological correlates are summarized in Table 1.

Table 1. Structural specializations of the RPE and functional significance

Structural domain	Key components	Functional role	Disease relevance
Tight junctions	Claudins, ZO-1	Outer blood-retina barrier	AMD barrier failure
Apical microvilli	Na^+/K^+-ATPase, CRALBP	Visual cycle, ion balance	RP, AMD
Basal infoldings	GLUT-1, aquaporins	Nutrient & water exchange	Bruch's thickening
Melanosomes	Melanin	Light absorption	Aging depigmentation

AMD: Age-related macular degeneration, RP: Retinitis Pigmentosa

FUNCTIONAL BIOLOGY: THE MATERNAL TASKS

Visual Cycle and Vitamin A Metabolism

Phototransduction requires continuous regeneration of 11-cis-retinal. The RPE mediates this process through RPE65-dependent isomerization.[1,6] Mutations in RPE65 result in Leber congenital amaurosis and autosomal recessive retinitis pigmentosa (RP).[6]

The success of RPE65 gene therapy confirms that restoration of RPE metabolism partially rescues photoreceptor function, even after significant degeneration.[6]

Phagocytosis of Outer Segments

Photoreceptors shed distal outer segment discs daily. The RPE recognizes these membranes via αvβ5 integrin and activates Mer Tyrosine Kinase (MerTK) to initiate engulfment.[3,5] Failure of this pathway leads to accumulation of debris and secondary degeneration, as seen in the Royal College of Surgeons (RCS) rat model.[3] Lysosomal degradation intersects with autophagy. Impairment promotes lipofuscin accumulation and oxidative injury.[4,6]

Ion, Fluid, and Metabolic Coupling

The RPE maintains ionic homeostasis through Na^+/K^+-ATPase, Kir7.1 channels, chloride transporters, and aquaporins.[1,6] It delivers glucose to photoreceptors and removes lactate via monocarboxylate transporters.[1] Disruption results in subretinal fluid accumulation and detachment.[7]

Immune Modulation and Growth Factor Secretion

The RPE secretes vascular endothelial growth factor (VEGF) basally to support the choriocapillaris and pigment epithelium-derived factor (PEDF) apically to protect neurons.[4] It expresses complement regulators and inflammasome components such as NLR family pyrin domain containing 3 (NLRP3).[4] Chronic complement activation and inflammasome signaling contribute to AMD progression.[4,9] These interdependent maternal functions of the RPE-spanning retinoid cycling, phagocytosis, metabolic transport, and immune regulation-are schematically integrated in Figure 1.

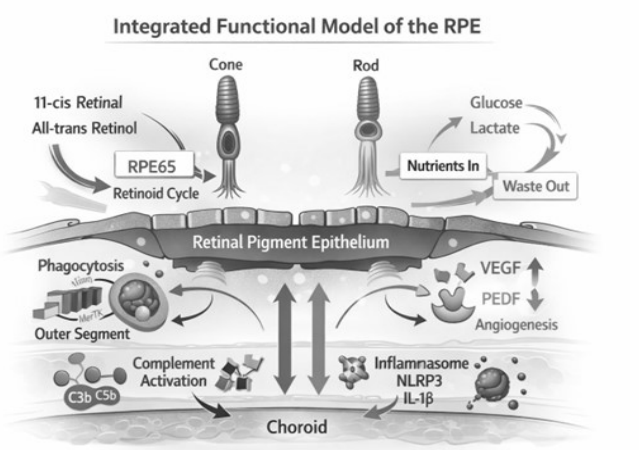

Figure 1. Integrated functional model of the RPE

Molecular Heterogeneity Revealed by Single-Cell Transcriptomics

Recent advances in single-cell RNA sequencing (scRNA-seq) and spatial transcriptomic technologies have revealed that the RPE is not a completely uniform epithelial layer but exhibits regional and functional heterogeneity. Transcriptomic analyses demonstrate differences in metabolic gene expression, oxidative stress responses, and visual cycle components across macular and peripheral RPE populations. Spatial mapping within intact retinal tissue further shows gradients of metabolic, inflammatory, and transport-related gene expression across the RPE layer. Notably, macular RPE displays distinct transcriptional signatures associated with lipid metabolism, mitochondrial function, oxidative stress resistance, and complement regulation. These regional molecular differences may contribute to the selective vulnerability of the macula in AMD and reinforce the concept that the RPE functions as a dynamic regulatory interface rather than a passive support layer.[10]

Aging: Maternal Exhaustion and Progressive Functional Decline of the RPE

The RPE operates under intense oxidative stress due to high oxygen consumption and light exposure.[1,9] With aging, mitochondrial Deoxyribonucleic acid (DNA) damage accumulates, reducing Adenosine triphosphate (ATP) production and increasing reactive oxygen species.[6]

Lipofuscin accumulation-particularly N-retinyl-N-retinylidene ethanolamine (A2E)-impairs lysosomal acidification and proteolysis.[6,9] Boulton and Dayhaw-Barker9 described age-related decline in RPE pigmentation and topographic vulnerability.

Recent metabolomic studies further highlight the metabolic specialization of the RPE. The RPE functions as a metabolic hub that coordinates glucose transport, lipid recycling, and mitochondrial oxidative phosphorylation. Mitochondrial

biogenesis and quality control mechanisms are critical for sustaining ATP production required for phagocytosis and ion transport. Disruption of mitochondrial homeostasis has been increasingly implicated in early AMD pathogenesis, linking metabolic insufficiency with oxidative injury and impaired autophagy.[11]

Complement dysregulation further promotes sublethal injury.[4] Together, oxidative stress, lysosomal dysfunction, and immune activation erode RPE polarity and function. These converging mechanisms of oxidative, lysosomal, and immune-mediated injury and their structural consequences are summarized in Table 2.

Table 2. Mechanisms of age-related RPE degeneration

Mechanism	Molecular drivers	Structural consequence	Clinical outcome
Oxidative stress	ROS, mtDNA damage	Mitochondrial loss	Early AMD
Lipofuscin	A2E	Lysosomal dysfunction	Geographic atrophy
Complement activation	CFH variants	Membrane injury	Drusen
Inflammasome activation	NLRP3	Pyroptosis	RPE atrophy

DNA: Deoxyribonucleic acid, AMD: Age-related macular degeneration, A2E: N-retinylidene-N-retinylethanolamine, CFH: Complement factor H

Retinitis Pigmentosa: Migration as Maternal Response

In most forms of RP, photoreceptor degeneration precedes RPE pathology.[1] Histopathologic studies demonstrate that bone-spicule pigmentation results from RPE migration into the neural retina following photoreceptor loss.[1] Loss of photoreceptor-derived trophic signaling destabilizes RPE polarity and adhesion.[1-3] Detached RPE cells transdifferentiate and deposit melanin along retinal vessels. Within the maternal framework, this migration represents a reactive and maladaptive attempt to engage dying photoreceptors.[1-4] This sequential process of photoreceptor apoptosis, RPE polarity loss, intraretinal migration, and bone-spicule pigmentation is schematically illustrated in Figure 2.

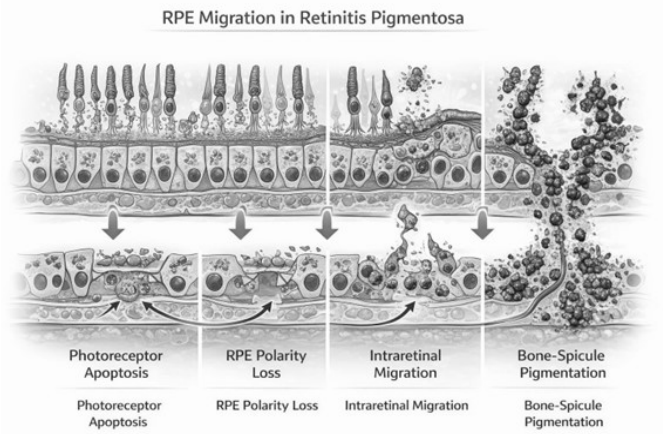

Figure 2. RPE migration in retinitis pigmentosa

RPE DYSFUNCTION IN DEGENERATIVE AND PROLIFERATIVE RETINAL DISEASES: MATERNAL FAILURE ACROSS PATHOLOGIES

If RP illustrates reactive maternal migration following photoreceptor death, age-related macular degeneration, pathologic myopia, and proliferative disorders illustrate progressive maternal exhaustion, mechanical stress, and maladaptive remodeling. Across these distinct clinical entities, a unifying principle emerges: RPE dysfunction destabilizes the outer retinal ecosystem.

Age-Related Macular Degeneration: Progressive Maternal Exhaustion

AMD represents the most extensively studied example of RPE-driven retinal degeneration. Although photoreceptor loss defines advanced disease, substantial evidence indicates that RPE dysfunction precedes and drives neuronal degeneration.[1,4,9] Aging RPE cells accumulate lipofuscin, particularly A2E, derived from incompletely degraded outer segment material.[6,9] Lipofuscin impairs lysosomal acidification, inhibits proteolytic enzymes, and generates reactive oxygen species under light exposure.[6] Concurrent mitochondrial DNA damage reduces ATP production and amplifies oxidative stress.[4,6] These changes compromise phagocytosis, visual cycle efficiency, and barrier integrity.

At the level of Bruch's membrane, age-related thickening and accumulation of basal deposits impair metabolic exchange between choriocapillaris and RPE.[9] Reduced permeability limits glucose delivery and waste removal, leading to chronic metabolic insufficiency. Complement dysregulation further accelerates RPE injury. The RPE expresses complement components and regulators; genetic variants affecting complement control predispose to sublethal RPE damage and drusen formation.[4] Chronic activation of the NLRP3 inflammasome promotes IL-1β release and pyroptotic cell death.[4]

In neovascular AMD, loss of RPE polarity disrupts directional secretion of VEGF and PEDF.[4] Normally, VEGF is secreted basally to support the choriocapillaris, while PEDF is secreted apically to maintain neuroprotection.[4] Polarity failure shifts this equilibrium toward pathologic angiogenesis.

Thus, AMD may be conceptualized not primarily as photoreceptor disease but as progressive maternal exhaustion culminating in secondary photoreceptor degeneration.

Pathologic Myopia: Mechanical Stretch and Maternal Thinning

Pathologic myopia introduces a distinct but equally revealing model of RPE vulnerability. Progressive axial elongation imposes chronic mechanical stretch on the RPE-Bruch's membrane-choroid complex.

Mechanical thinning of the RPE compromises barrier integrity and reduces metabolic buffering capacity. Bruch's membrane attenuation impairs nutrient transport and predisposes to focal atrophy. Loss of RPE melanin with age further reduces photoprotective capacity.[12]

Stretch-induced stress may alter RPE polarity and VEGF secretion patterns, increasing susceptibility to myopic choroidal neovascularization. In this context, maternal failure is not primarily metabolic but biomechanical: structural deformation disrupts the caregiving interface.

Proliferative Disorders: Loss of Maternal Identity

In proliferative vitreoretinopathy (PVR), RPE cells detach from Bruch's membrane, lose epithelial polarity, and undergo epithelial-mesenchymal transition (EMT).[3,4] Tight junction proteins such as ZO-1 are downregulated, cytoskeletal architecture reorganizes, and cells acquire migratory and contractile phenotypes.[3,4]

This represents not simply dysfunction but identity transformation. The RPE ceases to function as a polarized caregiver and becomes a fibrogenic participant in membrane formation. Such transdifferentiation illustrates the fragility of epithelial identity when polarity and environmental cues are lost.

Similarly, in diabetic retinopathy, inflammatory cytokines and hyperglycemic stress disrupt tight junctions and impair autophagy.[4,6] Although classically vascular, diabetic retinal disease includes significant RPE barrier compromise, contributing to edema.

Across AMD, pathologic myopia, and proliferative disease, a shared principle emerges: disruption of RPE polarity, metabolic competence, or structural integrity destabilizes photoreceptor survival. The shared and disease-specific mechanisms of RPE dysfunction across these conditions are comparatively summarized in Table 3.

Table 3. RPE-centered pathophysiology across retinal diseases

Disease	Primary stressor	RPE dysfunction	Downstream consequence
AMD	Aging, complement dysregulation	Oxidative stress, lipofuscin, polarity loss	Geographic atrophy, CNV
Pathologic Myopia	Mechanical stretch	RPE thinning, VEGF imbalance	Atrophy, CNV
PVR	Inflammation, trauma	EMT, polarity loss	Fibrotic membranes
Diabetic Retinopathy	Hyperglycemia	Barrier breakdown, autophagy decline	Edema

AMD: Age-related macular degeneration, CNV: Choroidal neovascularization, PVR: Proliferative vitreoretinopathy, EMT: eEpithelial-mesenchymal transition

IMAGING THE RPE INTERFACE: VISUALIZING MATERNAL STRESS IN VIVO

Advances in multimodal retinal imaging have transformed the study of the RPE from a largely histologic discipline into a dynamic, in vivo science. Modern imaging techniques allow direct visualization of RPE morphology, polarity integrity, pigment distribution, and metabolic stress. Importantly, these technologies often detect RPE dysfunction before irreversible photoreceptor loss becomes clinically apparent.

Optical Coherence Tomography (OCT): Structural Integrity of the RPE Band

Spectral-domain and swept-source optical coherence tomography (OCT) provide high-resolution cross-sectional imaging of the outer retina and RPE–Bruch's membrane complex.[13,14] On OCT, the RPE appears as a hyperreflective band beneath the photoreceptor outer segments. Disruption, attenuation, or irregularity of this band is strongly associated with outer retinal degeneration.[14]

In AMD, OCT demonstrates several hallmark manifestations of RPE dysfunction, including: Pigment epithelial detachment (PED), Subretinal hyperreflective material, Focal RPE elevation, Geographic atrophy with complete RPE loss, Outer retinal tubulations secondary to chronic degeneration.[14]

Pigment epithelial detachment reflects altered hydrostatic and osmotic balance across the RPE-Bruch's membrane interface.[1,4] When metabolic exchange is impaired, fluid accumulates beneath the RPE, separating it from Bruch's membrane. This mechanical separation compromises polarity and disrupts directional secretion of trophic factors.

In advanced geographic atrophy, OCT reveals complete absence of the RPE band with increased choroidal signal transmission due to loss of melanin-containing cells.[4,9] These structural changes precede and predict overlying photoreceptor collapse. Thus, OCT provides a direct window into maternal structural integrity.

Fundus Autofluorescence (FAF): Mapping Metabolic Load

Fundus autofluorescence (FAF) exploits the intrinsic fluorescence of lipofuscin within RPE lysosomes.[6,15] Because lipofuscin accumulates as a byproduct of incomplete phagocytosis of photoreceptor outer segments, FAF serves as a metabolic map of RPE stress. Increased autofluorescence corresponds to lipofuscin overload and lysosomal dysfunction.[6,15] In contrast, decreased autofluorescence indicates RPE atrophy and cell loss. In Stargardt disease and AMD, patterned hyperautofluorescence frequently surrounds areas of geographic atrophy, suggesting zones of heightened metabolic strain preceding cell death.[6] These findings support the concept that lysosomal exhaustion is an early marker of maternal failure. FAF therefore visualizes not simply structure, but metabolic burden.

Multi-Contrast OCT and Melanin Mapping

Beyond conventional reflectivity imaging, multi-contrast OCT (MC-OCT) allows three-dimensional quantification of melanin within the RPE.[13,16] Miura et al[13] demonstrated that serous PED in AMD is associated with regional increases in RPE melanin thickness (≥70 μm), termed "RPE70".

This thickening likely reflects hypertrophic or activated RPE responding to mechanical and metabolic stress. In slope regions of PED, melanin redistribution may represent early remodeling before irreversible atrophy. Because melanin plays a critical role in light absorption and oxidative buffering, quantitative melanin mapping offers a functional biomarker of photoprotective capacity. MC-OCT thus extends structural imaging into pigment physiology.[12,16]

Adaptive Optics and Cellular-Level Visualization

Adaptive optics scanning laser ophthalmoscopy (AO-SLO) permits visualization of individual RPE cells in vivo.[4,18] In the healthy retina, RPE cells exhibit a regular hexagonal mosaic. Aging and degeneration are associated with: loss of hexagonal geometry, cell enlargement (compensatory hypertrophy),

patchy mosaic disruption. These microstructural alterations reflect polarity destabilization and epithelial stress. AO imaging therefore captures early architectural breakdown of the maternal interface.[4,18]

Functional Testing: Visual Cycle Assessment

Structural imaging is complemented by functional testing of RPE-dependent processes. Dark adaptation kinetics provide a sensitive measure of visual cycle efficiency.[1] Because regeneration of 11-cis-retinal depends on RPE65-mediated enzymatic activity, delayed dark adaptation represents impaired maternal metabolic function. Electrooculography (EOG), which measures the Arden ratio, reflects RPE ion transport and barrier activity.[1] Reduced Arden ratios are characteristic of diffuse RPE dysfunction. Functional impairment often precedes overt structural collapse, reinforcing the importance of early RPE-directed assessment. The principal structural, metabolic, and functional imaging biomarkers of RPE dysfunction are summarized in Table 4.

Table 4. Imaging and functional biomarkers of RPE dysfunction

Modality	Biomarker	Biological process assessed	Disease relevance
OCT	RPE band disruption	Barrier integrity	AMD, RP
OCT	PED	Fluid transport failure	Neovascular AMD
FAF	Hyperautofluorescence	Lipofuscin overload	Stargardt, AMD
MC-OCT	RPE70 thickening	Melanin remodeling	Serous PED
AO-SLO	Mosaic irregularity	Cellular polarity loss	Aging, atrophy
Dark adaptation	Delayed recovery	Visual cycle dysfunction	Early AMD
EOG	Reduced Arden ratio	Ion transport defect	Diffuse RPE disease

OCT: Optical coherence tomography, RPE: Retinal pigment epithelium, AMD: Age-related macular degeneration, RP: Retinitis pigmentosa, PED: Pigment epithelium-derived, MC-OCT: Multi-contrast optical coherence tomography, AO-SLO: Adaptive optics scanning laser ophthalmoscopy, EOG: Electrooculography

Modern imaging has fundamentally altered the understanding of retinal degeneration. Rather than detecting only late-stage photoreceptor loss, contemporary modalities visualize RPE stress, metabolic overload, polarity disruption, and pigment remodeling at early stages. These findings reinforce the central thesis of this review: degeneration of the outer retina is frequently initiated at the level of the RPE. Imaging now allows clinicians to observe maternal distress before neuronal orphaning occurs. In doing so, it shifts both diagnosis and therapeutic strategy toward preservation of the caregiver.

EMERGING RPE-DIRECTED THERAPIES: RECONSTRUCTING THE MATERNAL INTERFACE

The increasing recognition of RPE centrality has reshaped therapeutic strategy. Rather than exclusively targeting neurons, modern interventions aim to restore or replace RPE function.

Gene Therapy: Restoring Metabolic Competence

RPE65 gene replacement therapy provides proof-of-concept that correcting RPE metabolic deficiency restores photoreceptor function.[6,19] Adeno-associated viral delivery of functional RPE65 reestablishes 11-cis-retinal production, improves rod-mediated vision, and demonstrates durable benefit. Beyond RPE65, investigational gene therapies target complements modulation, VEGF regulation, and intracellular trafficking pathways implicated in polarity maintenance.[4,6,19] The success of these strategies confirms a fundamental principle: rescuing the caregiver can stabilize dependent neurons.

Stem Cell-Derived RPE Transplantation

Because native RPE has minimal proliferative capacity, cell replacement has emerged as a rational approach. Human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs) can differentiate into polarized, pigmented RPE expressing RPE65 and capable of phagocytosis.[8,20] Clinical studies of stem cell-derived RPE transplantation in AMD and Stargardt disease demonstrate graft survival, pigmentation, and partial functional stabilization.[8,20] Scaffolds that restore epithelial polarity and Bruch's membrane contact improve integration. This approach does not merely replace cells-it seeks to reconstruct the maternal architecture of the outer retina.

Modulating Oxidative Stress and Mitochondrial Health

Given the central role of oxidative injury, therapeutic strategies aim to enhance NRF2 signaling, improve mitochondrial resilience, and restore autophagic flux.[4,6,21] Interventions targeting lysosomal acidification and lipofuscin reduction may preserve phagocytic competence.

Complement and Inflammasome Inhibition

Complement inhibition is now a major therapeutic frontier in AMD.[4,21,22] Recent therapeutic advances have translated complement biology into clinical practice. Complement inhibitors targeting C3 and C5 pathways have demonstrated the ability to slow geographic atrophy progression in AMD. These therapies highlight the importance of immune regulation at the level of the RPE-Bruch's membrane interface and further support the concept that protecting RPE integrity is central to preventing photoreceptor degeneration.[23] Targeting complement components or regulators seeks to prevent chronic RPE injury. Similarly, NLRP3 inflammasome inhibitors aim to suppress IL-1β-mediated pyroptosis and preserve RPE viability.[4,21,22]

Bioengineering and Precision Editing

Emerging strategies combine gene-corrected iPSC-derived RPE, biodegradable scaffolds, and controlled growth factor delivery systems.[8,19] CRISPR-based gene correction offers the potential to restore defective trafficking or polarity proteins in inherited RPE disorders. These approaches reflect a paradigm shift: rebuilding the maternal interface rather than merely treating downstream neuronal loss.[8,19,24] These complementary strategies for restoring metabolic competence, replacing damaged RPE, modulating immune injury, and enhancing mitochondrial resilience are conceptually integrated in Figure 3.

Across degenerative, mechanical, and proliferative retinal diseases, a recurring theme emerges: RPE dysfunction destabilizes the photoreceptor ecosystem. Whether through

oxidative exhaustion (AMD), structural thinning (myopia), EMT transformation (PVR), or reactive migration (RP), the breakdown of maternal function precedes or amplifies neuronal degeneration. Modern imaging visualizes RPE stress before irreversible photoreceptor death.[1,13,25] Contemporary therapies increasingly target RPE metabolism, immune signaling, and structural integrity. The future of retinal therapeutics lies not solely in saving neurons but in preserving-or reconstructing-the caregiver that sustains them. Protecting the RPE means protecting vision.

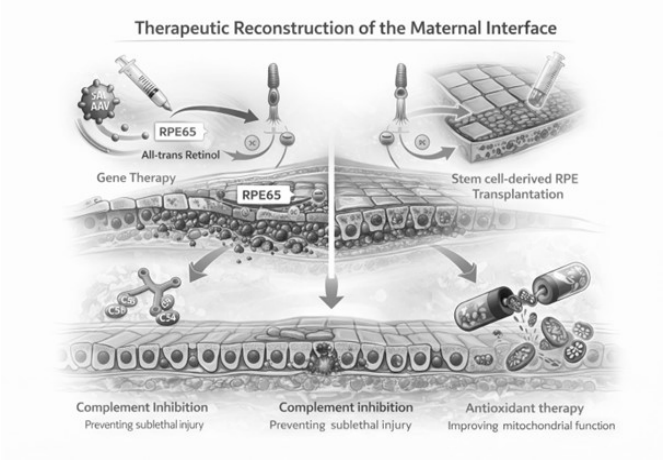

Figure 3. Therapeutic reconstruction of the maternal interface

RPE Organoids and Disease Modeling

Advances in stem-cell biology have enabled the generation of three-dimensional retinal organoids containing functional RPE layers. These organoid systems recapitulate many aspects of RPE polarity, pigmentation, and phagocytic activity. Importantly, organoid models allow investigation of disease mechanisms in inherited retinal degeneration and provide platforms for drug screening and gene-editing strategies. RPE organoids therefore represent a powerful bridge between basic molecular research and translational therapeutic development.[26,27]

CONCLUSION

The RPE is not a passive anatomical boundary but the central regulator of photoreceptor survival. It regenerates chromophore, clears debris, regulates ion balance, maintains immune privilege, and stabilizes retinal adhesion. Aging and disease represent progressive erosion of these maternal functions. Imaging now detects RPE stress before photoreceptor loss, and modern therapies increasingly target the RPE directly. Re-centering retinal biology around the RPE provides a unifying framework for understanding degeneration and guiding future intervention. Protecting the RPE means protecting vision.

ETHICAL DECLARATIONS

Peer Review Process

This review was externally peer-reviewed.

Conflict of Interest

The author declare no conflicts of interest.

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Author Contributions

The author is solely responsible for the conception, data collection, analysis, and writing of this manuscript.

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