



## Cellular responses following retinal injuries and therapeutic approaches for neurodegenerative diseases



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### ABSTRACT

Retinal neurodegenerative diseases like age-related macular degeneration, glaucoma, diabetic retinopathy and retinitis pigmentosa each have a different etiology and pathogenesis. However, at the cellular and molecular level, the response to retinal injury is similar in all of them, and results in morphological and functional impairment of retinal cells. This retinal degeneration may be triggered by gene defects, increased intraocular pressure, high levels of blood glucose, other types of stress or aging, but they all frequently induce a set of cell signals that lead to well-established and similar morphological and functional changes, including controlled cell death and retinal remodeling. Interestingly, an inflammatory response, oxidative stress and activation of apoptotic pathways are common features in all these diseases. Furthermore, it is important to note the relevant role of glial cells, including astrocytes, Müller cells and microglia, because their response to injury is decisive for maintaining the health of the retina or its degeneration. Several therapeutic approaches have been developed to preserve retinal function or restore eyesight in pathological conditions. In this context, neuroprotective compounds, gene therapy, cell transplantation or artificial devices should be applied at the appropriate stage of retinal degeneration to obtain successful results. This review provides an overview of the common and distinctive features of retinal neurodegenerative diseases, including the molecular, anatomical and functional changes caused by the cellular response to damage, in order to establish appropriate treatments for these pathologies.

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*List of abbreviations:* AAV, Adeno-associated virus; AGEs, Advanced glycation end products; AMD, Age-related macular degeneration; Apaf-1, Apoptotic protease-activating factor-1; BDNF, Brain-derived neurotrophic factor; bFGF, Basic fibroblast growth factor; BRB, Blood retinal barrier; CNS, Central nervous system; CNTF, Ciliary-derived neurotrophic factor; CNV, Choroidal neovascularization; DR, Diabetic retinopathy; EGCG, Epigallocatechin gallate; ERG, Electroretinogram; ESC, Embryonic stem cells; FGF, Fibroblast growth factor; GCL, Ganglion cell layer; GDNF, Glial-derived neurotrophic factor; GFAP, Glial fibrillary acidic protein; hESC, Human embryonic stem cells; hiPSC, Human induced pluripotent stem cells; IL, Interleukin; INL, Inner nuclear layer; IPL, Inner plexiform layer; iPSC, Induced pluripotent stem cells; LIRD, Light-induced retinal degeneration; mGluR6, Metabotropic glutamate receptor; MOMP, Mitochondrial outer membrane pores; MPTP, 1-methyl-4-phenyl-1,2,3,6-tetra-hydropyridine; NAC, N-acetylcysteine; NMDA, N-methyl-D-aspartate; NO, Nitric oxide; NF- $\kappa$ B, Nuclear factor, B; Nrf2, Nuclear factor erythroid 2-related factor 2; ONL, Outer nuclear layer; OPL, Outer plexiform layer; PEDF, Pigment epithelium derived factor; PVR, Proliferative vitreoretinopathy; RCS, Royal College Surgeon rats; RGC, Retinal ganglion cells; ROS, Reactive oxygen species; RP, Retinitis pigmentosa; RPE, Retinal pigment epithelium; TGF- $\beta$ , Transforming growth factor- $\beta$ ; TLR, Toll-like receptor; TNF, Tumor necrosis factor; TUDCA, Tauroursodeoxycholic acid; UPS, Ubiquitin-proteasome system; VEGF, Vascular endothelial growth factor; VEPs, Visual evoked potentials.

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