



## Autophagy in the eye: Development, degeneration, and aging



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### ABSTRACT

Autophagy is a catabolic pathway that promotes the degradation and recycling of cellular components. Proteins, lipids, and even whole organelles are engulfed in autophagosomes and delivered to the lysosome for elimination. In response to stress, autophagy mediates the degradation of cell components, which are recycled to generate the nutrients and building blocks required to sustain cellular homeostasis. Moreover, it plays an important role in cellular quality control, particularly in neurons, in which the total burden of altered proteins and damaged organelles cannot be reduced by redistribution to daughter cells through cell division. Research has only begun to examine the role of autophagy in the visual system. The retina, a light-sensitive tissue, detects and transmits electrical impulses through the optic nerve to the visual cortex in the brain. Both the retina and the eye are exposed to a variety of environmental insults and stressors, including genetic mutations and age-associated alterations that impair their function. Here, we review the main studies that have sought to explain autophagy's importance in visual function. We describe the role of autophagy in retinal development and cell differentiation, and discuss the implications of autophagy dysregulation both in physiological aging and in important diseases such as age-associated macular degeneration and glaucoma. We also address the putative role of autophagy in promoting photoreceptor survival and discuss how selective autophagy could provide alternative means of protecting retinal cells. The findings reviewed here underscore the important role of autophagy in

**Abbreviations:** 3-MA, 3-methyl adenine; 8-OH DPAT, 8-hydroxy-2-(di-n-propylamino)-tetralin; AAV, adeno-associated vector; ADOA, autosomal dominant optic atrophy; AGEs, age-related glycation end products; AMD, age-related macular degeneration; ASM, acid sphingomyelinase; BDNF, brain-derived neurotrophic factor; BMP, bis(monoacylglycerol)phosphate; BRB, brain-retina barrier; CMA, chaperone-mediated autophagy; CNS, central nervous system; EGCG, epigallocatechin gallate; ER, endoplasmic reticulum; ERG, electroretinogram; E, embryonic day; GCD2, granular corneal dystrophy type 2; GCL, ganglion cell layer; HMA, 5-(N,N-hexamethylene)amiloride; Hsc70, heat shock cognate of the Hsp70 family; HSP70, heat shock protein 70; IPL, inner plexiform layer; INL, inner nuclear layer; IOP, intraocular pressure; LAP, LC3-associated phagocytosis; LCD, lysosomal cell death; LDL, low density lipoprotein; LIR, LC3-interacting domain; LMP, lysosomal membrane permeabilization; LPS, lipopolysaccharide; LSD, lysosomal storage disorder; MCT, monosaccharide transporter; MPT, mitochondrial permeability transition; MNU, N-methyl-N-nitrosourea; Nmnat3, nicotinamide mononucleotide adenylyltransferase 3; NTG, normal tension glaucoma; ONH, optic nerve head; ONL, outer nuclear layer; ONT, optic nerve transection; PI, protease inhibitors; PI3P, phosphatidylinositol 3-phosphate; POS, photoreceptor outer segment; PR, photoreceptor; ROCK, Rho-associated protein kinase; ROS, reactive oxygen species; RPE, retinal pigment epithelium; RGC, retinal ganglion cell; RP, retinitis pigmentosa; SIPS, stress-induced premature senescence; TAK-1, transforming growth factor  $\beta$ -activating kinase 1; TGF $\beta$ 1p, transforming growth factor  $\beta$ -induced protein; TLK, tousel-like kinase; TM, trabecular meshwork; TRAIL, tumour necrosis factor-related apoptosis-inducing ligand; TXNIP, thioredoxin-interacting protein; UBD, ubiquitin binding domain; UPR, unfolded protein response; VEGF, vascular endothelial growth factor.

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