The central function of p62 is involved in the degradation of misfolded proteins through UPS or the autophagy-lysosome pathway. These two pathways are the major self-regulating systems to degrade misfolded protein aggregation and maintain the cellular homeostasis in eukaryotic cells.

P62/SQSTM1, a multi-domain protein that regulates inflammation, apoptosis, and autophagy, has been linked to age-related pathologies. For example, previously we demonstrated that administration of p62/SQSTM1-encoding plasmid reduced chronic inflammation and alleviated osteoporosis and metabolic syndrome in animal models. Herein, we built upon these findings to investigate effect of the p62-encoding plasmid on an age-related macular degeneration (AMD), a progressive neurodegenerative ocular disease, using spontaneous retinopathy in senescence-accelerated OXYS rats as a model. Overall, the p62DNA decreased the incidence and severity of retinopathy. In retinal pigment epithelium (RPE), p62DNA administration slowed down development of the destructive alterations of RPE cells, including loss of regular hexagonal shape, hypertrophy, and multinucleation. In neuroretina, p62DNA prevented gliosis, retinal thinning, and significantly inhibited microglia/macrophages migration to the outer retina, prohibiting their subretinal accumulation. Taken together, our results suggest that the p62DNA has a strong retinoprotective effect in AMD [1)].

1)
Kolosova NG, Kozhevnikova OS, Telegina DV, Fursova AZ, Stefanova NA, Muraleva NA, Venanzi F, Sherman MY, Kolesnikov SI, Sufianov AA, Gabai VL, Shneider AM. p62 /SQSTM1 coding plasmid prevents age related macular degeneration in a rat model. Aging (Albany NY). 2018 Aug 28. doi: 10.18632/aging.101537. [Epub ahead of print] PubMed PMID: 30153656.