Editorial

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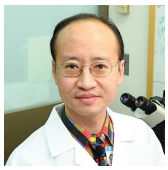

Management and treatment of inherited retinal dystrophies

Inherited retinal dystrophies (IRDs) are a rare group of hereditary diseases that lead to progressive degeneration of retinal cells.[1] While there are currently several ongoing clinical trials utilizing pharmacological agents and adeno-associated virus (AAV) vector-mediated gene augmentation therapeutics, only one Food and Drug Administration approved therapy currently exists that is merely capable of treating a small fraction of the population: those afflicted by mutations in the *RPE65* gene.[2-7] At this point in time, countless physicians and scientists are poised to address this unmet need for a treatment or cure for IRDs, however, given that most therapies are mutation specific, this task is both highly cost- and time-inefficient.[8] Moreover, we must overcome several crucial obstacles, including on- and off-targeting in genome editing techniques,[9] delivery of genes with a payload too large for that of an AAV vector delivery system,[10] the complexity of removing the gain-of-function allele to repair autosomal dominant genes, and a system of ensuring long-term efficacy of gene augmentation.[11]

Treatment options that circumvent the production of each therapy specified to the individual's genetic variant are promising solutions to this scientific and medical challenge.[12] Ryu *et al.* describe alternative pathways common to several IRDs that may hold the key to slowing retinal degeneration. Specifically, the authors' work highlights the damaging role that reactive oxygen species play in IRDs, leading to oxidative stress and subsequent cellular death. One pathway, the nuclear factor erythroid-2-related factor-Kelch-like ECH-associated protein 1 pathway presents a system whereby oxidative stress is neutralized. Similar work was reviewed by Nolan *et al*. in this series, addressing the role of metabolic coupling in healthy and atrophic retinal cells. Ultimately, investigations such as these have the potential to not only uncover the underlying pathology of each dystrophy but also identify points for therapeutic intervention capable of slowing progression, common to countless retinal degenerative processes. At present, metabolic reprogramming is making great strides in the field, buying time for genome surgery and stem cell transplantation techniques to excel and pave the way toward a long-term cure for IRDs.

Macula lesions often result in vision loss. Spooner *et al.* investigate the use of aflibercept, an antivascular endothelial growth factor agent, for patients with persistent macular edema due to retinal vein occlusion despite regular treatment with bevacizumab or ranibizumab. Here, the investigators identify that aflibercept significantly improved patient's visual functions, and as a result, quality of life. Abouhussein *et al.* also present data supporting the successful application of aflibercept in patients with bevacizumab-resistant diabetic macular edema. In addition, Chiu *et al.*'s study demonstrates the use of ranibizumab monotherapy versus concurrent ranibizumab with posterior subtenon triamcinolone acetonide. Their work revealed that patients with diabetic macular edema responded significantly better to the combined therapy option. Additional research has been directed toward surgical intervention

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for structural abnormalities. Macular holes are most commonly idiopathic, however, in rare cases, they are linked to genetic causes, schisis in highly myopic eyes, or age-related macular degeneration (AMD).[13] In this edition, Marlow *et al.* outline the various surgical strategies in autologous retinal transplants to address macular holes of various sizes. Taken together, these projects highlight how metabolome reprogramming and antioxidant therapies can be used in combination with conventional therapies for dry AMD and monogenic disorders (voretigene neparvovec).

It is imperative to treat secondary diagnoses – such as cystoid macular edema – as well as further investigate the underlying pathophysiology and metabolic processes leading to retinal degeneration. This special issue includes investigations that are critical to managing and ultimately treating these devastating and blinding dystrophies.

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Conflicts of interest

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