Editorial

Taiwan J Ophthalmol 2021;11: 329-330

Access this article online

Quick Response Code:

Website:
www.e-tjo.org

DOI:
10.4103/tjo.tjo_50_21

Innovations in retinitis pigmentosa – Metabolic rescue of cones, gene therapy, retinal transplantation

The December issue of the *Taiwan Journal of Ophthalmology* expands on the theme introduced in September – management and treatment of inherited retinal dystrophies. Retinitis pigmentosa (RP) is a group of inherited retinal diseases with variable clinical presentations from mild nyctalopia to total blindness. The gene mutations responsible for RP occur overwhelmingly in rod photoreceptors. Although the visual disability from rod dysfunction is significant, it is the subsequent loss of central vision in later life due to cone degeneration that is catastrophic. Until recently, the reason for cone dysfunction in RP was unknown. However, it is now recognized that cones degenerate losing outer segment (OS) synthesis and inner segment disassembly because of glucose starvation.[1,2] Rod OS phagocytosis by the apical microvilli of retinal pigment epithelium (RPE) is necessary for the transport of glucose from the choriocapillaris to the subretinal space. Although cones lose OS with the onset of rod degeneration in RP, regardless of the gene mutation in rods, cone nuclei remain viable for years (i.e., enter cone dormancy) so that therapies aimed at reversing glucose starvation can prevent and/or recover cone function and central vision.[3] The *Metabolic Rescue of Cone Photoreceptors in RP* by Kaplan *et al*. explores these events in more detail.

Rhodopsin (RHO)-mediated autosomal-dominant RP is the most common type of hereditary retinal degeneration in North America with a Pro23His (P232H) mutation in RHO the most frequent cause.[4] Multiple approaches are being pursued to correct this genetic defect either involving replacement or editing the mutant gene in rod photoreceptors. In gene therapy for RP by Piri *et al*., antisense oligonucleotide-based therapy, short hairpin RNA-based therapy, gene editing (CRISPR-Cas, meganuclease), and optogenetics are discussed. Recently, there have been advances in gene therapy for the treatment of Leber congenital amaurosis type 2 (NCT00999609), which is the result of a null mutation or biallelic loss of function in the *RPE65* gene. Treatment involves replacement of the null mutation in the RPE through subretinal injection of an adeno-associated virus vector carrying a human RPE65 gene. This resulted in the first and only Food and Drug Administration-approved gene therapy for retinal degeneration to date in the United States (voretigene neparvovec-rzyl: Luxturna).[5]

An alternative to metabolic or gene therapy to maintain vision in RP is retinal transplantation. Restoring damaged retinal circuitry by transplanting photoreceptors is an appealing idea. Recent developments in stem cell technology, retinal imaging techniques, tissue engineering, and transplantation techniques have brought us closer to this goal. The recent availability of human embryonic stem cells, induced pluripotent stem cells, and retinal organoids

How to cite this article: Kaplan HJ. Innovations in retinitis pigmentosa – Metabolic rescue of cones, gene therapy, retinal transplantation. Taiwan J Ophthalmol 2021;11:329-30.

Submission: 24-10-2021
Accepted: 24-10-2021
Published: 09-12-2021

have advanced this field. However, integration of transplanted photoreceptor cells to reconstitute the neural network or sustaining transplanted paracrine secreting donor cells still has many major obstacles to overcome, including immunologic rejection of allogeneic cells. In retinal cell transplantation in RP by Tezel and Ruff, these issues and other up-to-date advances in the field are eloquently discussed in a comprehensive fashion.

This issue of the Journal has three original articles in retina including a 48-week prospective study of the successful response of refractory macular edema following retinal vein occlusion after switching to aflibercept by Spooner *et al*.; the beneficial effect of hemodialysis on macular thickness in end-stage retinal disease by Suryakanth *et al*.; the maternal risk factor of vaginal delivery in retinopathy of prematurity in Saudi Arabia by Badeeb *et al*.; the concern for ophthalmologists because of the prevalence of SARS-CoV-2 in tears of hospitalized patients with COVID-19 by Sehgal *et al.*

There are also four interesting case reports, including multimodal imaging in Susac syndrome by Rahhal-Ortuno *et al*.; nodular posterior scleritis, as a great masquerader by Babu *et al*.; iris metastasis from small-cell lung cancer by Huang; and different therapeutic responses to lipemia retinalis by Lai and Chang.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors declare that there are no conflicts of interest of this paper.

Henry J. Kaplan*

Department of Ophthalmology, Saint Louis University School of Medicine, Saint Louis, Missouri, USA

***Address for correspondence:**

Dr. Henry J. Kaplan,
44 Kingsbury Place, Saint Louis 63112, Missouri, USA.
E-mail: henry.kaplan@health.slu.edu

References

1. Wang W, Lee SJ, Scott PA, Lu X, Emery D, Liu Y, *et al.* Two-step reactivation of dormant cones in retinitis pigmentosa. Cell Rep 2016;15:372-85.
2. Wang W, Kini A, Wang Y, Liu T, Chen Y, Vukmanic E, *et al.* Metabolic deregulation of the blood-outer retinal barrier in retinitis pigmentosa. Cell Rep 2019;28:1323-34.e4.
3. Kaplan HJ, Wang W, Dean DC. Restoration of cone photoreceptor function in retinitis pigmentosa. Transl Vis Sci Technol 2017;6:5.
4. Jacobson SG, Kemp CM, Sung CH, Nathans J. Retinal function and rhodopsin levels in autosomal dominant retinitis pigmentosa with rhodopsin mutations. Am J Ophthalmol 1991;112:256-71.
5. Maguire AM, Russell S, Wellman JA, Chung DC, Yu ZF, Tillman A, *et al.* Efficacy, safety, and durability of voretigene neparvovec-rzyl in RPE65 mutation-associated inherited retinal dystrophy: Results of phase 1 and 3 trials. Ophthalmology 2019;126:1273-85.