VISUAL IMPAIRMENT BY DESIGN

GENETIC DISORDERS

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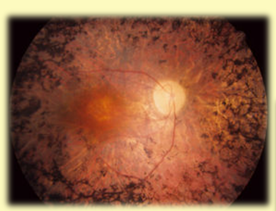
Introduction

- The following review of current gene therapy research of several genetic ocular diseases was outlined with the intention of improving patient care and stimulating interest in further research for the development of targeted therapies
- Eye-care providers must provide care beyond a diagnosis and prognostic data, such as access to rehabilitation or counseling, low-vision care or referral to a low-vision specialist, information for local or national foundations for the blind, referral to support groups, and referral for genetic counseling
- There is a current lack of curative or restorative therapy for many inherited ocular diseases, such as retinitis pigmentosa, Stargardt disease, and ocular albinism

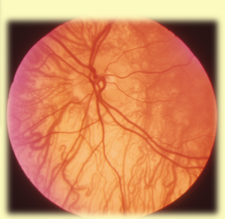
Methods

- The following literature review was executed via Ferris State University's FLITE library using the "SmartSearch" function
- Initial search phrases included "genetic disease", "ocular genetic disease", and "gene therapy"
- Further search phrases included "retinitis pigmentosa", Stargardt disease", "Stargardt disease treatment", "Stargardt disease gene therapy", "ocular albinism", and "ocular albinism gene therapy"



Retinitis pigmentosa

Stargardt disease



Ocular albinism

Results

- There have been over seventy-nine genes associated with retinitis pigmentosa. Patients experience nyctalopia, progressive visual field loss, and eventual central vision loss[1]
- A specific gene, ABCA4, which codes for a transport protein in the rod outer segment that removes excess lipofuscin, accounts for 95% of Stargardt cases. Patients experience blurred vision, subjective visual disturbances, central visual field loss, and photophobia[2]
- Ocular albinism is caused by changes in the G protein-coupled receptor 143 gene (GPR143), which controls the growth of melanosomes. Patients experience nystagmus, high refractive error, strabismus, decreased visual acuity, decreased stereopsis, and photophobia[1]

- Adenovirus vectors can be used to transduce retinal pigment epithelium, photoreceptors, trabecular meshwork cells, iris pigment epithelium, ganglion cells, and Muller cells[1]
- Retrovirus vectors, such as the lentivirus, can be used to transduce retinal pigment epithelium, corneal endothelium, trabecular meshwork cells, and retinal photoreceptors[1]

- A phase I clinical trial of six patients with retinitis pigmentosa, secondary to MERTK mutation, showed improvement in visual acuity after use of an adenovirus vector subretinal injection in three patients for less than two years without significant adverse effect. Visual function briefly improved, but the retinal degeneration was not reversed[3]

- Injection of human ABCA4 gene into Stargardt phenotypic mouse models using equine infectious anemia virus (EIAV)-based lentivirus vectors showed promise. Treated eyes showed reduced accumulation of ocular lipofuscin compared to control eyes by three to five times[4]

- A study of non-viral gene therapy using nanoparticles and an ABCA4 plasmid slowed disease progression for six months and showed a 35% reduction in lipofuscin accumulation in mice with phenotypic Stargardt disease[5]

- Adeno-associated viral vector mediated GPR143 gene was transferred to the retina via ocular albinism mouse-model, resulting in the recovery of retinal function of both rods and cones. The therapy also resulted in an increase in melanosomes within the mouse retinal pigment epithelium[6]

Conclusions

- Further investigations into ocular genetic disorders are warranted as genetic testing and targeted gene-therapies are developed and improved due to a general lack in current curative or restorative therapy
- The exact faulty or missing gene needs to be identified in each individual due to the numerous mutations that may result in disease phenotypes
- All eye-care providers should be comfortable making referrals and recommendations for community support services for those affected by genetic ocular disease
- Referrals need to be made for genetic testing upon every diagnosis with the intent of gathering data and a patient database in anticipation of imminent future gene therapies

References

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Photographs

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