EDITORIAL

Oman Medical Journal [2015], Vol. 30, No. 3: 149–150

Insight into Ocular Genetic Research: Trends in Oman

Rayhanah Al-Mjeni

Department of Genetics, Sultan Qaboos University, Muscat, Oman

ARTICLE INFO

Article history:

Received: 31 March 2015

Accepted: 7 April 2015

DOI 10.5001/omj.2015.33

Ocular genetic abnormalities occur due to alterations in DNA. Such changes might affect various cellular structures and functions of the eye contributing to an array of ocular disorders, which may or may not be reversible. These genomic changes could be spontaneously occurring or inherited as a result of a pre-existing mutation.

In 2010, a global estimate showed that 285 million people were visually impaired, of which 39 million were blind and 246 million had low vision. Those visually impaired (about 35%) ranged from infancy to 49 years of age and the major causative factors were of a non-communicable and undetermined nature.[1]

Non-communicable diseases (NCD) are increasing,[2] and ocular related disorders are not exempt from this group. The rise in ocular diseases requiries attention considering the negative impact it will have on the global economy, especially in developing nations.

In Oman, the causes of visual impairment are changing from communicable treatable diseases to incurable chronic ones with lifelong consequences.[3] Although improved health services and initiatives have assisted in lowering some of the visual impairment cases, further intervention is needed as the transition to NCD continues.

Environmental factors (e.g. ultraviolet radiation) play a role in ocular disease manifestation, but there are genetic components associated with NCD. This becomes an issue of personal, societal, and governmental concern when disease-causing alleles are at high frequencies in the populations. Cultural preferences, such as consanguineous marriages (56.4% of all unions in Oman[4]), endogamous unions, and bearing of many children, might increase allele frequencies in a population. As these practices are common in Middle Eastern countries the chances of individuals inheriting a recessive disease trait and possibly several ancestral disease alleles is elevated.[4] Homozygosity or autozygosity mapping is a suitable method for disease gene detection in most cases. It can be used for the identification of known or novel variations in autosomal recessive conditions, even if a singleton sample pool is available. An example of this is the detection of a new variant in the *FAM161A* gene of a Palestinian family causing retinitis pigmentosa.[5] Homozygosity mapping in combination with exome sequencing is also an option. Although exome sequencing has limitations, such as the difficulty in distinguishing disease from non-disease causing variants, it compensates for limitations associated with homozygosity mapping, where dominant, X-linked and compound heterozygous mutations cannot be detected.[6] Both approaches have been used to identifiy a novel autosomal recessive retinitis pigmentosa variant with late-onset hearing loss in a Middle Eastern family.[7]

Considering the cultural practices, genetic research as well as epidemiological investigations becomes of immense importance for Oman. The results obtained would enhance the understanding of the underlying disease pathophysiology and would facilitate drug-design and the development of treatments and therapeutic strategies. So, where does Oman stand with regard to ocular genetic research?

Approximately 313 publications relating to ophthalmology have been associated with Oman. These were found in the PubMed database using ophthalmology and Oman as keywords. Publications retrieval was set from the year 1980, before the construction of the first university in Oman, to the present date. Only two articles on the genetics of ocular diseases existed.[8,9] Without a doubt all research fields are important, but the

*Corresponding author: ✉rayhanah@squ.edu.om

low number of publications from Oman on ocular genetic research is of concern. The acquisition of such information is essential in determining the role of these genes in the population. Additionally, the initiation of translational research or targeted gene therapy requires basic knowledge of the genetic disease, such as gene location, altering mutations, and functional effect. Furthermore, the concept of private mutations, globally encountered, probably occurs in the Omani population too. However, with limited ocular genetic research, the identification of mutation profile of ocular genetic variants in Oman and their implications is limited.

Ocular genetic disorders have been the center of gene therapy success stories, such as the restoration of sight in adults and children with retinoblastoma. Patients received injections of an adenoviral vector containing a herpes simplex thymidine kinase gene with no systemic immune response.[10] In patients with Leber congenital amaurosis administration of a recombinant adeno-associated virus transporting the retinal pigment epithelium-specific protein 65kDa gene resulted in improved retinal and visual function measurements.[11] Surprisingly, sometimes gene therapy may be self-mediated. An example is the spontaneous chromothriptic cure of an individual with a rare congenital immunodeficiency disorder known as warts, hypogammaglobulinemia, infections, and myelokathexis syndrome (WHIM), which is caused by mutations in the chemokine receptor *CXCR4* gene.[12] However, cellular events in which chromosomes undergo massive deletion and rearrangement resulted in the splicing out of the mutated gene in a hematopoietic stem cell. This cell then repopulated and restored the immune function.

Ocular genetic research is fascinating not only in terms of therapeutic outcome, but also the extraordinary cases of vision perception. An example of enhanced vision is the ability to perceive color spectrums unnoticed by the ordinary person (behavioral tetrachromacy),[13] and to see under water with clarity reaching that experienced on land without the use of visual aids.[14] Although, such instances are infrequently encountered, they are moments of inspiration, reflection, and immense curiosity, which will assist in a better understanding of ocular biology. However, such knowledge will only be possible if there is more enthusiasm locally to perform studies on ocular genetics. Additionally, research continuity is required to make meaningful scientific and medical contributions. That is, treatment applications and an insight into the biological processes will not be attainable by gene hunting and mutation detection alone. Information on how gene products operate and altered protein function is essential. This will allow for greater comprehension of the pathophysiology associated with ocular disorders to improve patient care.

REFERENCES

1. Global data on visual impairment. In: World Health Organization. 2010. WHO/NMH/PBD/12.01.
2. Miranda JJ, Kinra S, Casas JP, Davey Smith G, Ebrahim S. Non-communicable diseases in low- and middle-income countries: context, determinants and health policy. Trop Med Int Health 2008 Oct;13(10):1225-1234.
3. Khandekar R, Mohammed AJ, Raisi AA. Prevalence and causes of blindness & low vision; before and five years after 'VISION 2020' initiatives in Oman: a review. Ophthalmic Epidemiol 2007 Jan-Feb;14(1):9-15.
4. Rajab A, Al Rashdi I, Al Salmi Q. Genetic services and testing in the Sultanate of Oman. Sultanate of Oman steps into modern genetics. J Community Genet 2013 Jul;4(3):391-397.
5. Zobor D, Balousha G, Baumann B, Wissinger B. Homozygosity mapping reveals new nonsense mutation in the FAM161A gene causing autosomal recessive retinitis pigmentosa in a Palestinian family. Mol Vis 2014;20(20):178-182.
6. Khan AO. Ocular genetic disease in the Middle East. Curr Opin Ophthalmol 2013 Sep;24(5):369-378.
7. Khateb S, Zelinger L, Ben-Yosef T, Merin S, Crystal-Shalit O, Gross M, et al. Exome sequencing identifies a founder frameshift mutation in an alternative exon of USH1C as the cause of autosomal recessive retinitis pigmentosa with late-onset hearing loss. PLoS One 2012;7(12):e51566.
8. Manayath GJ, Namburi P, Periasamy S, Kale JA, Narendran V, Ganesh A. A novel mutation in the NR2E3 gene associated with Goldmann-Favre syndrome and vasoproliferative tumor of the retina. Mol Vis 2014;20:724-731.
9. El-Gayar S, Ganesh A, Chavarria-Soley G, Al-Zuhaibi S, Al-Mjeni R, Raeburn S, et al. Molecular analysis of CYP1B1 in Omani patients with primary congenital glaucoma: a pilot study. Mol Vis 2009;15:1325-1331.
10. Chévez-Barrios P, Chintagumpala M, Mieler W, Paysse E, Boniuk M, Kozinetz C, et al. Response of retinoblastoma with vitreous tumor seeding to adenovirus-mediated delivery of thymidine kinase followed by ganciclovir. J Clin Oncol 2005 Nov;23(31):7927-7935.
11. Maguire AM, High KA, Auricchio A, Wright JF, Pierce EA, Testa F, et al. Age-dependent effects of RPE65 gene therapy for Leber's congenital amaurosis: a phase 1 dose-escalation trial. Lancet 2009 Nov;374(9701):1597-1605.
12. McDermott DH, Gao JL, Liu Q, Siwicki M, Martens C, Jacobs P, et al. Chromothriptic cure of WHIM syndrome. Cell 2015 Feb;160(4):686-699.
13. Jordan G, Deeb SS, Bosten JM, Mollon JD. The dimensionality of color vision in carriers of anomalous trichromacy. J Vis 2010;10(8):12.
14. Sea Gypsies of Asia Boast. "Incredible" Underwater Vision. Available at www.news.nationalgeographic.com/news/2004/05/0514_040514_seagypsies.html. Accessed February 2015.