Homozygous Nonsense Mutations in $RBP3$ Gene Cause Early-Onset Retinal Dystrophies Associated With High Myopia

Marc M. Abitbol
Necker-Enfants Malades University Hospital, Department of Ophthalmology, Université Paris-Descartes, Paris, France; marc.abitbol@parisdescartes.fr

The very detailed report by Arno et al.\(^1\) of early-onset autosomal recessive dystrophies associated with high myopia occurring in young children carrying homozygous nonsense mutations of the $RBP3$ gene highlights the power of the combination of meticulous phenotyping and whole-exome sequencing analysis in the field of inherited retinal dystrophies. A homozygous missense mutation of the $RBP3$ gene was previously associated with autosomal recessive retinitis pigmentosa (RP) and high myopia in adult patients.\(^2\) The recent findings emphasize the importance of longitudinal phenotypic studies based on the addition of the most modern methods of investigation, such as fundus autofluorescence imaging and spectral-domain optical coherence tomography (OCT), to the classical methods used for the diagnosis of retinal dystrophies. The authors not only have discovered novel phenotypes of retinal dystrophies caused by different mutations in the same gene $RBP3$, but also show unequivocally that the loss of the inner segment ellipsoid band over peripheral macular areas is a key marker of the novel dystrophies found. Whether these novel phenotypes will evolve toward RP remains to be demonstrated by rigorous follow-up studies of each affected patient. This report illustrates the necessity of increasing our knowledge on the unknown and probably diverse functions of the interphotoreceptor retinoid binding protein (IRBP).\(^3\) The roles of IRBP in the normal development of human eye and retina are far from being fully understood.

The exploration of the role of IRBP in the pathophysiology of nonsyndromic myopia requires the urgent implementation of cleverly designed innovative experiments. Finally, this important study points toward the possibility of a window of opportunity for gene therapy or pharmacological therapies in some patients affected by $RBP3$ homozygous mutations.

References