STATE-OF-THE-ART OF GENE THERAPY FOR INHERITED RETINAL DYSTROPHIES

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INTRODUCTION

Inherited retinal dystrophies (IRDs) constitute a large group of genetically and phenotypically heterogeneous diseases that are characterized by progressive loss of photoreceptor cells leading loss of vision. Many of the genes causing IRDs have now been identified, and could ultimately be amenable to treatment by gene-replacement therapies. There is also a robust proof of concept for gene transfer in animal models of retinal dystrophy. Furthermore, three independent clinical trials have shown the vision improvement in patients with an early-onset autosomal recessive retinal dystrophy. In addition, substantial progress has also been made in the development of treatment strategies for autosomal dominant diseases: a promising approach is the gene silencing using RNA-interference (RNAi).

GENE THERAPY FOR INHERITED RETINAL DYSTROPHIES

Gene-based therapy is defined as the introduction, using a vector, of nucleic acids into cells with the intention of altering gene expression to prevent, cease or reverse a pathological process.

In the following figure show the location of proteins whose genes are candidates for gene-based therapy. Most of the candidate genes have protein products that are located in the outer segments (OS) of the photoreceptor cells or in the retinal pigment epithelium (RPE). Five of these genes are examined in deeper detail. Abbreviations: ONL, outer nuclear layer; AR, autosomal recessive; AD, autosomal dominant; EIAV, Equine Infectious Anemia Virus.

CONCLUSIONS

The retina is one of the most promising target tissues for gene therapy.

Gene therapy will soon become a realistic treatment choice for many more retinal dystrophies.

The main challenge over the next years is to rescue the vision of more IRDs mouse models, to translate more of the bench findings into clinical studies for more IRDs and to optimize treatments in patients already available.