1. ADENO-ASSOCIATED VIRUS (AAV) - BASED GENE THERAPIES FOR RETINAL DISEASES

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Introduction. Retinal degeneration and macular dystrophies are the leading causes of visual acuity loss and blindness in middle-aged people worldwide. Existing treatment, although considered effective, often does not lead to a complete recovery of the patient, which leads to the need to find new alternatives. It has been proven that genetic factors play an important role in the development of retinal degeneration. Consequently, gene therapy has always been of great interest to scientists as a very promising field of study.

Aim of study. The adeno-associated virus has become the vector of choice for retinal diseases. This virus is very compact, has a high tropism to the retina and a relatively low immune response. The increased interest of the scientific community in this area led to the fact that in 2017 the FDA approved a gene therapy for Leber congenital amaurosis caused by the RPE65 mutation.

Methods and materials. Hu ML, Edwards TL, O'Hare F, Hickey DG, Wang JH, Liu Z, Ayton LN. Gene therapy for inherited retinal diseases: progress and possibilities. Clin Exp Optom. 2021 May;104(4):444-454. doi: 10.1080/08164622.2021.1880863. Epub 2021 Mar 2. PMID: 33689657. Bucher K, Rodríguez-Bocanegra E, Dauletbekov D, Fischer MD. Immune responses to retinal gene therapy using adeno-associated viral vectors - Implications for treatment success and safety. Prog Retin Eye Res. 2021 Jul;83:100915. doi: 10.1016/j.preteyeres.2020.100915. Epub 2020 Oct 15. PMID: 33069860. Botto C, Rucli M, Tekinsoy MD, Pulman J, Sahel JA, Dalkara D. Early and late stage gene therapy interventions for inherited retinal degenerations. Prog Retin Eye Res. 2022 Jan;86:100975. doi: 10.1016/j.preteyeres.2021.100975. Epub 2021 May 29. PMID: 34058340. Ku CA, Pennesi ME. The new landscape of retinal gene therapy. Am J Med Genet C Semin Med Genet. 2020 Sep;184(3):846-859. doi: 10.1002/ajmg.c.31842. Epub 2020 Sep 5. PMID: 32888388. Ail D, Malki H, Zin EA, Dalkara D. Adeno-Associated Virus (AAV) - Based Gene Therapies for Retinal Diseases: Where are We? Appl Clin Genet. 2023 May 30;16:111-130. doi: 10.2147/TACG.S383453. PMID: 37274131; PMCID: PMC10239239. Castro BFM, Steel JC, Layton CJ. AAV-Based Strategies for Treatment of Retinal and Choroidal Vascular Diseases: Advances in Age-Related Macular Degeneration and Diabetic Retinopathy Therapies. BioDrugs. 2023 Oct 25. doi: 10.1007/s40259-023-00629-y. Epub ahead of print. PMID: 37878215.

Results. Despite all the advantages, there are still many obstacles to the effective use of AAV for a wider range of retinal diseases. For example, the small size of AAV particles is also a disadvantage, since the viral capsid has a limited capacity. In addition, although the immune response is considered relatively low, various complications often occur that prevent the full delivery of AAV to the target organ.

Conclusion. Gene editing and gene replacement techniques have become a real breakthrough in the treatment of inherited retinal diseases. However, this treatment is effective if it is applied at an early stage of the disease, before the degeneration of photoreceptors. In addition, taking into account the fact that the use of AAV still causes an immune response, it is important to distinguish between an acceptable immune response and a destructive one, which exacerbates the course of the disease and prevents effective treatment.