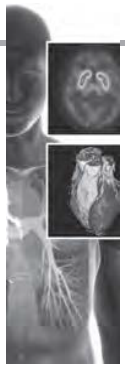

Sensorineural Hearing Loss by Aav-Mediated Gene Therapy

The number of people who suffer from hearing loss is increasing as a result of congenital defects, aging-related changes, and acquired injuries such viruses or drug-induced ototoxicity. Being deaf is a persistent and a crippling illness that significantly lowers quality of life Damage to the cochlear sensory epithelium cells, including hair cells and conch cells, in varied degrees characterises the pathophysiology of hearing loss in the inner ear. Supporting cells, spiral ganglion neurons, as well as basal, middle, and marginal cells from the stria vascularis. Treatment for sensorineural deafness involves regeneration or direct repair of the inner ear's damaged cells. Using a small molecule medication, it is presently feasible to rebuild hair cells to cure sensorineural hearing loss.

KEYWORDS: Hearing loss • Cochlea • Gene therapy • AAV • Auditory repair

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Introduction

With the advancement of genetic engineering technologies, gene therapy has brought potential method of treating several ailments that were previously incurable [1]. The use of gene therapy has been seen as Recombinant adenoassociated viral gene therapy has been extensively employed in basic research into hearing loss therapies, and it is a promising strategy in the treatment and rehabilitation of sensorineural hearing loss [2]. At currently, investigations into the safety and efficacy of gene therapy for hearing loss are moving from feasibility studies to its potential for healing. The principles, tactics, and uses of gene therapy are discussed in this article [3]. Mediated in the field of treating hearing loss via recombinant AAVs [4]. That there is a current hearing loss and that by 2025 there might be up to 700 million hearing-impaired persons worldwide. When the cochlea is damaged or ill, sensory hair cells (HCs) and primary auditory neurons are lost, which results in sensorineural hearing loss SNHL [5]. The causes of SNHL are both congenital and acquired, and the aetiology is complicated and multifaceted. Congenital deafness affects 1 in 500 babies [6]. Mutations are one of the primary causes of congenital deafness [7]. Genetic mutations account for around half of all congenital hearing loss, and the incidence is higher in wealthy nations [8]. Due to the critical role that hearing plays in a child's language development, information acquisition, and social integration, SNHL is particularly troublesome in young individuals [9]. Additionally, hearing loss gets worse Due to their limited communication skills, hearing loss in the elderly can cause loneliness, resentment, and social isolation. Clinically, SNHL is prevalent, but there are still no effective treatment options available. In order to restore hearing, electronic devices like hearing aids are typically utilised, however their efficiency is dependent on the existence of HCs [10]. Due to this, there is a huge need for innovative biological therapies for hearing restoration, and gene therapy has showed considerable promise in the treatment of hereditary deafness [11]. The recombinant adeno-associated virus has been around for 20 years. Has become a popular and generally secure therapeutic vector in genetic disease research at the clinical stage [12]. The use of AAV-mediated gene therapy allows the delivery of therapeutic genes or other molecular payloads to certain organs and tissues to influence the patient's recovery Studies on animals have demonstrated that AAV-mediated gene therapy Can at least partially reverse hereditary deafness brought on by gene deletions or mutations [13].

Discussion

Clinical research into therapies for deafness has strong possibilities for using rAAV since it is a therapeutically therapeutic "star vector [14]." In this review we will outline and analyse the scientific developments surrounding AAV-mediated gene therapy in the restoration of hearing. In the inner ear epithelium, auditory HCs serve as the primary functional organisers for hearing and accurately and sensitively convert mechanical vibration into electrical impulses (also called electro-mechanical transduction).

The auditory HCs in mammals are divided into two types: outer HCs and inner HCs, and they are found in the organ of Corti at the cochlear epithelium. And inner HCs, each of which has a unique structure and purpose [15]. For auditory sensitivity and fine discrimination, OHCs are primarily engaged in directly and positively modulating auditory signal transduction. Through the auditory nerves, the depolarized IHCs deliver electrical impulses that have been converted from sound vibrations to the auditory brainstem and cortex. The surrounding supporting cells, which play a part in the upkeep of the microenvironment and in the preservation of the HCs, keep OHCs and IHCs apart from their neighbours. Reduced cochlear sensitivity, decreased frequency selectivity, and suppression of electrical signal transduction are all effects of damaged auditory cells brought on by noise, medications, or hereditary factors. These effects eventually result in hearing loss or injury. After damage, non-mammalian organisms have the ability to repair healthy cells on their own. For Zebrafish's lateral wall may be induced to re-produce neuroblasts and to encourage the formation of new HCs and SCs following exposure to ototoxic chemicals; however, injured HCs in mammals' inner ears lose their ability to regenerate on their own. SNHL is hence perpetual in mammals. Currently, only assistive equipment, such as hearing aids, cochlear implants, and other auditory compensation devices, which are efficient treatment approaches, are used as intervention strategies for at least partial hearing restoration in the clinic. These, however, do not treat deafness biologically. Therefore, innovative and successful therapeutic techniques must be created, such as biotherapy for congenital deafness. Here, we will concentrate on the so-called AAV-mediated gene therapy method designed to replace or repair the damaged deafness gene. We list the methods for addressing monogenic problems. More than a billion people throughout the world are now affected by hearing loss, and at least 430 million of them need medical attention. The World Health Organization divides hearing loss into classes based on how severe it is compared to normal hearing. Genetic defects, age, and environmental variables including infections, chronic illnesses, noise, ototoxic drugs or chemicals, etc. all have an impact on the trajectory of hearing loss. Genetic reasons (50%), anatomical abnormalities of the temporal bones, and conductive SNHL combined are the most frequent causes of congenital SNHL. and cytomegalovirus in utero. Here, we focus primarily on the gene treatment using AAV for SNHL brought on by genetic alterations. Clinically speaking, SNHL's auditory abnormalities can either be solitary or non-syndromic. Morphologies or syndromic forms linked to extra-auricular symptoms. Therefore, there are two types of inherited deafness. The most prevalent kind of hearing loss, non-syndromic hearing loss, accounting for nearly half of all people with hereditary deafness. Each instance is monogenic, and mutations in over 120 genes have been confirmed to be causal. Monogenic NSHL shows Mendelian distributions with different forms of inheritance, including autosomal dominant non-syndromic hearing loss, autosomal recessive non-syndromic hearing loss, X-linked non syndromic hearing loss, Y-linked non-syndromic hearing loss, auditory neuropathy no syndromic hearing loss, and so on. About 30% of people with hereditary deafness fall into the second category of hearing loss, known as syndromic hearing loss, which is defined by hearing impairment and pathogenic alterations in other body systems. Organs like the kidney, skin, eyes, and so on. Since the discovery of the first deafness gene, a total of 128 non-syndromic deafness genes and more than 40 syndromic deafness genes have been discovered, thanks to advancements in molecular biology. Three genes associated with frequent deafness in the Chinese population include Gjb2, Slc26a4, and mitochondrial 12SrRNA. As the NSHL autosomal deafness susceptibility gene, Gjb2 was initially discovered in and is responsible for both Deafness that is autosomal recessive and dominant is known as DFNB1A and DFNA3. The gap-junction protein connexion 26 is encoded by the gene gjb2, which is genetically connected to chromosome 13q11–12.

Conclusions

More than half of all non-syndromic autosomal hearing loss cases, including congenital severe to profound deafness, are caused by mutations in the Gjb2 gene. Gene therapy has become a promising field. Technique of therapy for inherited deafness. The cochlea is regarded as an ideal target for gene therapy due to the following intrinsic benefits: the cochlea requires small therapeutic volumes due to its small size; the cochlea is relatively isolated from other parts of the body; and localised drug delivery, which reduces systemic risk, is made possible by the cochlea. In this article, we focus specifically on several gene therapy techniques in an effort to explain how treating congenital deafness involves replacing or repairing damaged genes. The exogenous gene delivery vector system for gene therapy now consists of two distinct forms.

The viral vector, which includes lentivirus, adenovirus, retrovirus, AAV, etc., is the first. The viral vectors are typically Recombined viruses that have been genetically altered to have little to no toxicity and a high level of transduction in target cells. The second is a nonverbal vector, such as liposomes, nano carriers, bare DNA, etc. Typically, carriers carrying target genes are injected directly into the inner ear in gene therapy treatments for deafness. Many viral vectors, including as Adv, AAV, lentivirus, herpes simplex virus, vaccinia virus, and Sendak virus, have been utilised to introduce genetic material into the cochlea. Additionally, non-viral delivery mechanisms, like as cationic liposomes, are used to transport genes to the cochlea.

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