Gene Therapy for Neurological Disorders-A Review

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ABSTRACT
This review article is based on improving knowledge on gene therapy which treats many neurological disorders. 150 articles were obtained, and 36 articles were filtered. Gene therapy is one of the most important treatments in the future as well as in the present. It has high chances of reducing many disorders in future. Many neurological disorders have been cured, but still many more researches are being done to express the potential of gene therapy to its maximum. Gene therapy improves the motor system in mouse models. Few neurological disorders that can be treated are Alzheimer’s disease and Parkinson’s disease. This review is an attempt to update recent advances in gene therapy.

INTRODUCTION
Genetic diseases can be wiped out by gene therapy before they can begin and eliminate suffering for future generations. The devastating effects of the diseases of the nervous system are prevalent in the elders, which is caused by inherited genetic mutations that lead to neurological problems. This therapy for such diseases has been made progress in understanding the underlying disease mechanisms in those involving sensory neurons is also by the improvement of gene vector design, therapeutic gene selection and methods of delivery (Simonato et al., 2013). Adeno associated viral vectors are the treatment of neurological diseases which is a rapidly emerging therapy platform. In preclinical studies, transgenes encoding therapeutic proteins, MicroRNAs, Antibodies which are gene-editing machinery which has been successfully delivered (Deverman et al., 2018).

Severe combined immune deficiency such as Adenosine deaminase deficiency, hereditary blindness, hemophilia, blood diseases, fat metabolism disorders, cancer and more can be cured by gene therapy. The different target cell population of different vectors and both in vivo and ex Vivo approaches help in treating a variety of disorders (Philippidis, 2020). Researchers testing several approaches to gene therapy by replacing mutated gene with a healthy copy of gene, inactivating or knocking down (out) mutated gene and if the healthy gene is not functioning properly, the introduction of a new gene into the body to fight the disease is done (JGMGT, 2020).

Background information on experimental details of gene therapy tools for the neurological disorder was provided. Emerging new technologies such as CRISPR/Cas9 genome was introduced to cure
Supports long-term transgene expression, which vectors are one of the techniques that immunize basic neurological problems. Adeno-virus derived current application of gene therapy helps address currently available gene therapy techniques strong, moderate and weak (Table 1). The level of evidence of the reviewed articles was categorized as per the criteria of Centre for Evidence-Based Medicine, Oxford, UK. (Blihm, 2011) and graded as strong, moderate and weak (Table 1).

Currently available Gene Therapy techniques

Current application of gene therapy helps address basic neurological problems. Adeno virus-derived vectors are one of the techniques which immunize humans from natural infections (Lownenstein et al., 2003) Recombinant Adeno Associated Virus (rAAV) supports long term transgene expression which is derived from small human parvovirus (Mandel, 2006). Gene replacement therapy is a cell-based therapy for treating transplantation of neural stem and progenitor cells (Goldman et al., 2006). Adeno associated virus, from 1982 is used to find virology and biology of viruses and improvement of AAV is also done (Coursa and Nardi, 2007).

Partial problems derived from Gene Therapy strategies

Mesenchymal stem cells are used for myocardial infarction which has migratory properties of MSCs for any brain injury, and tumors (Picinich et al., 2007). Scientific obstacles, vehicles used to deliver normal genes and immune response of vector becomes devastating are few problems (Ali, 1998) neurological disorders treated by the recent development of gene therapy. This therapy approaches such as addition, knockdown and alteration of genes and correction are used. Gene therapy, in combination with stem cell therapy, is useful for future (Kay et al., 1997) Histone deacetylases, HDAC inhibitors provide autoimmunity. Preclinical models have been tested for finding such results (Falkenberg and Johnstone, 2014).

Alzheimer’s disease

To prevent AD, proteins in specific brain regions containing degenerating neurons must be achieved in adequate concentrations which will prevent non-targeted regions from getting infected (Tuszyński et al., 2007). Stem cell therapy and gene replacement therapy are helpful in treating AD. Prolonged protection of central cholinergic system is the cure which has been done experimentally to prove (Meccacci et al., 2007). Alzheimer’s disease leads to dementia, memory loss and more. Alpha-beta aggregation causes AD-HN derived lentiviral vector to heat. AAV is the most frequently used vector to heat AD (Nilsson et al., 2010). Gene modified cells are the promising therapeutic approach for AD-potential clinical application. Cholesterol metabolism is connected to AD-AAV gene therapy reduces the amyloid plaque with cholesterol 24 hydroxylase. It was tested in a mouse having amyloid plaque of AD (Hudry et al., 2010) Acriltransferase1 (ACAT1) which knockdowns Gene therapy and amyloid-beta in a mouse model of AD is reduced (Murphy et al., 2013; Pratha and Thenmozhi, 2016).

Parkinson’s disease

Early-stage of PD patients is significant of nigrostriatal dopamine innovation which is the efficacy of GDFLs Symptoms of PD caused by nigrostriatal degeneration, innovative gene delivery disease pathology (Coune et al., 2012). PD has many gene therapy cures, some are successful by design
<table>
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<tr>
<th>S No</th>
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<tr>
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<td>review</td>
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but failure by efficacy. Oral dopaminergic molecules control PD’s symptoms (Bartus et al., 2014). AAV2-GAD in the subthalamic nucleus with sham surgery in patients is delivered bilaterally and is done for patients with advanced PD (Hallett and Paine, 2011). Gene therapy is safe, tolerable and efficient. Local and continuous dopamine production is restored by lentiviral vector-based therapy (Pali, 2014). GABA-non disease modify treatment whereas neurotrophic factors are disease-modifying treatment (Axelsen and Woldbye, 2018).

Potential of Gene Therapy
Applying ChRs for treatment is a molecular modification, targeting methods with sophisticated electrical devices are also done in gene therapy (Ji et al., 2013). Gene therapy is used for multiple diseases. GT is also a new option for treatment of various cancers (Mugilan et al., 2017). Regulatory path complex helps in translation process which ensures Long term effects that is best to intervene (Hodgson et al., 2017) promising finding from preclinical animal studies to involve deliver of genes to the spinal cord which is an ongoing research treatment for rare diseases, unique challenges and more effective larger genes and multiple small genes are delivered by promoters. They remain active for a long time.

RESULTS AND DISCUSSION
Potential candidates for gene therapy but are minimally responsive to existing treatments. It involves an outlook of a replacement allele or cells or silencing dominant mutant alleles that is pathological. Neurological Disorders such as PD, AD clinical trials using these approaches are likely to be implemented soon. (AAV) or vector with an excellent safety profile derived from small human parvovirus. Supporting Long term transgene expression in the nervous system and acting as efficient transducers are few qualities of this vector. Therefore, neurological disorders can be treated using this vector due to such properties. rAAV is being used currently for various neurological disorders in five early stages of a clinical trial (Mandel, 2006). Channelrhodopsins (Chrs) can be targeted to specific neurons for neural circuits using genetic methods, which is also used to manipulate neuronal activities. To advance the potential in treating neurological disorders and its application. The spectral and kinetic properties of Chrs by generating variants of ChRs or exploring new rhodopsins from other species must be optimised according to the application. One of the potential of GT, ChRs through gene expression system union cell or tissue-specific promot-

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