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A Review on Gene Therapy

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ABSTRACT
Gene therapy is an emerging concept that gives hope to people with highly fatal conditions. It's almost three decades since the emergence of the idea of gene therapy. Since then, hundreds of medical trials have been conducted worldwide from which we not only have gained enough knowledge but have experienced the need for it in society. Even though the concept of gene therapy has experienced setbacks, success stories are increasing exponentially, proof of which are recommendations and approvals of gene therapy from various medical associations worldwide. Our knowledge has grown over the years, and during this period, we have come across various safety datahelp help us develop better gene therapy approaches. The chief concept of this procedure is to revamp the vehicles for delivery which typically are nanostructures, plasmids, and viruses. The USA and Europe have been pioneers in gene therapy for a very long period; various reports have come from Asian countries, including India, in recent times. Our knowledge of the concept of gene therapy is increasing day by day. New information and data are being analyzed regularly to help provide gene therapies for different diseases. New research has led to various new drug applications for approval at the FDA. In this review, various points, from the history of gene therapy and its requirement in today's society to the most recent advances in gene therapy, have been discussed. It also covers the works and advances of gene therapy in India.

KEY WORDS; Gene therapy, Vectors, Genetic diseases, Molecular therapy.

I. INTRODUCTION

Gene, cell, and RNA therapies, collectively called cell and gene therapies (CGTs) in this review, represent the cutting edge of drug discovery . Owing to their precise nature, targeted against the genetic and molecular drivers of disease, these therapeutic approaches are the embodiment of precision medicine.[1]. CGTs may provide pa tients with a given disease, in which the causation is well known and characterized, a therapy specifically designed to correct the root genetic cause.[2]. Identifying a need to accurately report on the state of clinical and preclinical development of these therapies, the American Society of Gene and Cell Therapy (ASGCT) initiated a partnership with Citeline in 2021. The purpose of the partnership is for Citeline and ASGCTtojointly acquire, develop, and maintain relevant indus try corporate, financial, and clinical data that can be used to report regularly on the performance of the gene, cell, RNA, and regenerative medicine sectors. CGTs may provide patients with certain diseases, in which the root genetic causation is well known and characterized, a therapy specifically designed to correct such causes, by delivering genetic material that modifies the expression of the target gene.[3]. Recent advances for the treatment of spinal muscular atrophy (SMA), an autosomal recessive disease, have yielded two examples of new advanced genetic therapies. It is an antisense oligonucleotide (ASO), a single-stranded nucleic acid matched to a specific sequence in intron 7 of SMN2 pre-mRNA. This mechanism causes splicing correction and production of full-length functional SMN protein, with accompanying clinical benefit for SMA patients of all ages.1 Pe 3376 diatric patients younger than 2 years now also have the gene therapy onasemnogeneabeparvovec as a one-time, potentially curative treatment option. Onasemnogeneabeparvovec is an adeno-associated virus (AAV) vector-based gene therapy that delivers a functional copy of the SMN1 gene encoding SMN protein to motor neuron cells.2 This restores SMN levels and reverses skeletal muscle atrophy, with clinical benefits demonstrated for upto 7.5 years thus far.

HISTORY OF GENE THERAPY

During mid 1960s, researchers estimated that DNA groupings could be embedded into patients' cells to treat hereditary diseases. [4].It was Martin Cline that initially endeavored to adjust

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human DNA in 1980, anyway the first fruitful result of atomic quality was seen after a long stretch finally in May 1989 . The main helpful use and furthermore the initial direct addition of human DNA into atomic genome was accomplished in September 1990 by French Anderson. In the year 1990, 4-year-old Ashanthi de Silva turned into the principal quality treatment example of overcoming adversity. She was brought into the world with an extreme joined immunodeficiency (SCID) because of the absence of protein adenosine deaminase (ADA). In absence of ADA, her T cells died off, making her inadequate to battle contaminations. Infusions of an engineered ADA compound aided, however just immediately. Specialists chose to convey a relatively solid ADA quality into her platelets, by the utilization of an impaired infection that can't spread in the body.

Starting at spark therapeutics Luxturna in 2017(for visual deficiency prompted by RPE65 Mutation) and Novartis' Kymriah (antigen T cell treatment of chimeric receptor) are principal quality treatments to enter the market endorsed by the FDA .[5].[Since that time, medications like Alnylam'sPatisiran and Novartis' Zolgensma have likewise gotten the backing of the FDA, notwithstanding other organizations' quality treatment drugs. The vast majority of these techniques use Adeno Associated Virus (AAVs) and lentivirus for executing quality inclusions, ex-vivo and in-vivo individually.

TYPES OF GENE THERAPY

It becomes essential to understand some of the terminologies and the types of gene therapy. Alternative, Deoxyribonucleic Acid (DNA) based therapy and molecular therapy are often used by laymen and biologists. Gene therapy is one of the genetic engineering tools used to alleviate suffering from hereditary diseases [6]. However, in broader terms, gic engineering not only aims to alter genes to correct genetic defects but may also be involved in modifying the genes to enhance the organism's abilities beyond what is expected. The latter is a dangerous proposition of genetic engineering. A. Gene therapy can be classified into the somatic cell and germ cell types, depending upon the type of cells that are modified by the therapeutic genes [7,8]. All the gene therapies to date are directed towards somatic cells only.

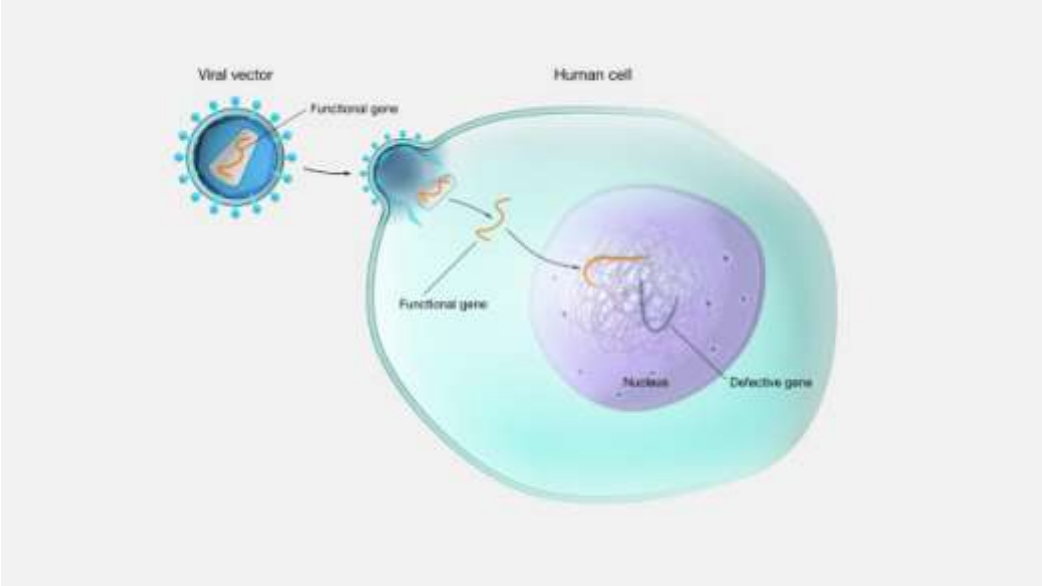

FIG.1.Concept of gene therapy

1.SOMATIC CELL GENE THERAPY

In this type, genetic changes are directed towards somatic cells. As these cells are non- The reproductive effect is not passed into future generations, making it safer. The disadvantage is the short duration of the effects of somatic cell therapy, as most tissues will be replaced by new tissues.[9].

2.GERM CELL GENE THERAPY

This is the type of gene therapy where germ cells, i.e., either sperm or ova, are introduced with therapeutic gene, leading to inheritable

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changes, i.e., changes in the gene may affect future generations. B. Based upon the technique of delivery of vectors to the target cell, gene therapy can be further classified into ex-vivo and in-vivo therapy.

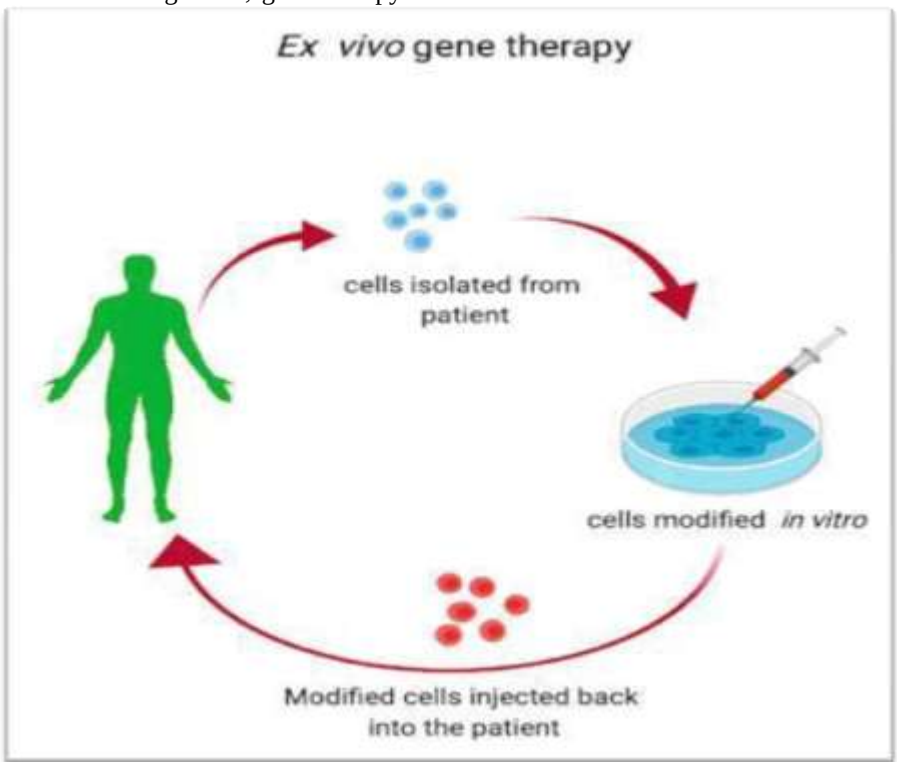

FIG 2.TYPES OF GENE THERAPY BASED ON TECHNIQUE OF THERAPY

3.EX-VIVO GENE THERAPY

Ex -vivo gene therapy is where the defective cells are extracted from the body and targeted with a therapeutic gene. Once successfully modified, they are cultured ex-vivo and transferred back to the host, where now the corrected gene replicates.

4.IN-VIVO GENE THERAPY

In this modality, a vector capable of carrying the therapeutic gene injects host cells with a normal genes. C. The type of change in the faulty gene classifies gene therapy as either gene replacement or gene addition.

5.GENE REPLACEMENT

Gene replacement means the replacement of defective gene with a corrected one.

6.GENE ADDICTION THERAPY

Gene addition means restoring the normal function of cell by adding normal or functional copy of gene into genome. This concept is primarily used in various gene therapy related research on cancer. It is important to understand some terms that are commonly associated with gene therapy, because laymen and biologists often use terms such as genetic engineering, molecular therapy or DNA-based therapy. Many genetic engineering tools that can help alleviate genetic diseases are available, Gene therapy is one of them. A. It can be classified on the basis of modification of cells by therapeutic genes into gene therapy of somatic cell and gene therapy of germ cell.

7.GENE THERAPY OF SOMATIC CELL

Genetic changes in somatic cells are targeted in this type. It is comparatively safer as somatic cells are non reproductive, so the effect will not be passed on to the offsprings.

8.GENE THERAPY OF GERM CELL

Genetic changes in germ cells are targeted in this type. In this type of gene therapy, genetic changes are heritable because the germ cells (either egg or sperm) are introduced into the therapeutic gene. This type can affect future generations. B. It can be classified on the basis of delivery technique of vectors into target cells as In vivo or Ex-vivo .

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9.GENE THERAPY OF EX-VIVO TYPE

In this method defective cells are taken out from the body and are targeted with gene of therapeutic activity. Once the cells are altered successfully, they are cultivated in ex-vivo conditions and are transported back to the host from where replication of modified gene takes place.[10].

10.GENE THERAPY OF IN-VIVO TYPE

In this type of gene therapy a vector is injected into the host which carries the healing gene to the host cells. C. It can be classified based on the type of changes that are brought in the defective gene into gene replacement and gene addition therapy .

11.GENE REPLACEMENT

In this method, the faulty gene is replaced with a modified one.

12.GENE ADDICTION THERAPY

3.12 Gene Addiction Therapy In this method, regular function of the cell is restored by the addition of a functional or standard copy of the gene into the genome. Above mentioned type is principally used in research related to gene therapy

PREREQUISITES FOR GENE THERAPY

Fundamentals for gene therapy consist of choosing the most suited delivery system for the gene (usually a virus, often called a viral vector), indicating that the transported gene can be expressed in the host cell, also defining that used technology is harmless.[11]. Very few human gene therapy clinical trials can pass all of these conditions, generally due to the delivery system not reaching the cell or because the cell does not express the gene. Nanotechnology is being used to develop better-quality gene therapy systems. One hopeful application of this research involves targeting cancer cells by packaging genes into nanoparticles, thereby precisely killing cells causing cancer and protecting healthy cells from damage.

VECTORS FOR GENE THERAPY

A cell-carrying substance called a vector can be used for delivering cells to DNA by various methods. The two main categories are non viral and viral vectors.

VIRAL VECTOR

During the replication process, the virus introduces into the host cell its genetic material, enticing the cellular apparatus of the host to use it as a blueprint for viral proteins.

The retrovirus takes it a step further, in which the genetic material is copied into the host cell genome. The advantage of this is taken by scientists by placing healing DNA in place of the genetic material of the virus. (Some viruses have RNA as genetic material, so gene therapy can also use RNA.) Numerous viruses are being utilized in human gene therapy, including adenoviruses, herpes simplex virus, retrovirus, and adeno associated and vaccinia viruses. [12].Like the hereditary substance (DNA or RNA) of a virus, remedial DNA can be used simply as a transitory outline, either naturally degraded or (in theory at least) entering the host's genome, turning into an everlasting part of the DNA of the host in the infected cells .

NON VIRAL VECTORS

Big-scale manufacture and lower host immunogenicity are advantages of non-viral vectors over viral vectors. However, the non viral methods first produce minor gene expression and transfection stages and therefore have lesser therapeutic effects. After the onset of subcellular transport control and cell-specific targeting, new technologies can solve these nonoperation, problems. naked Gene gun, DNA injection, magnetotransfection, oligonucleotides, electroporation, lipoplexes, inorganic nanoparticles, and dendrimers are methods of non-viral gene therapy.

Newer methods, such as those implemented by companies such as Ligandal, provide opportunities to produce targeting technologies that are cell-specific for various gene therapy methods, including some gene excision tools such as RNA, DNA, and CRISPR. Some other companies, such as Arcturus Therapeutics and Arbutus Biopharma, provide non-targeted and non-viral methods that mainly incluthe de liver nutrtheition. Recently, startups like GenEdit, Spotlight Therapeutics and Sixfold Bio have commenced to resolve the problem of non viral gene delivery. Benefit of non viral methods is that it provides opportunities for repeated administration and greater adaptability of gene payloads, which will replace virus-based delivery systems in the future. Companies including Intellia Therapeutics, Editas Medicine, CRISPR Therapy, Cellectis, Casebia, Precision Biosciences, Sangamo and bluebird bio have invented non-viral gene editing technologies; though, they usually even now use viruses after being guided by nucleases for

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genome cleavage to carry the gene insertion material.

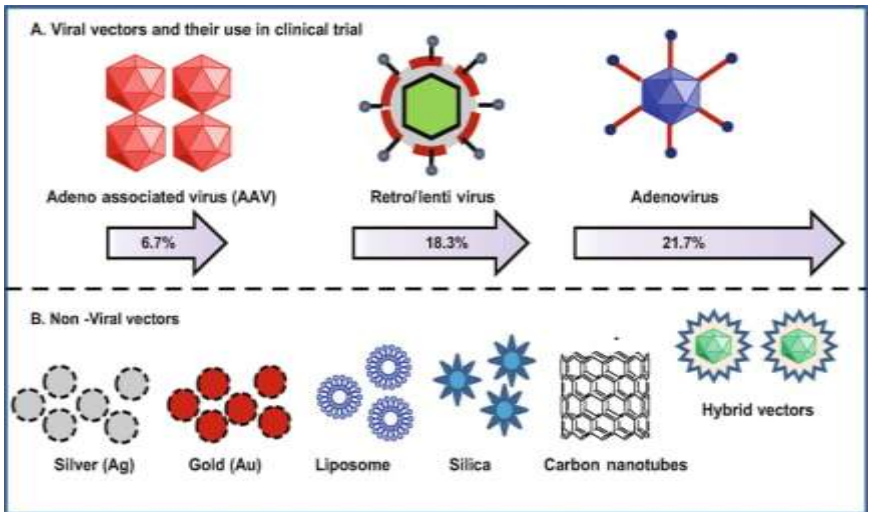

FIG.3.TYPES OF VECTORS IN GENE THERAPY

APPLICATIONS OF GENE THERAPY

CANCER

Gene therapy-related research and its clinical application have been mostly utilized in the field of malignancy. By the end of 2009, nearly two third of gene therapy-related research was concentrated on cancers. Oncolytic viruses are used to introduce genes into malignant cells, thereby causing death of Gene Therapy in India- Current Status malignant cells. Another approach is to deliver p53 gene (tumor suppressor gene) and thereby induce oncolysis. Gendicine that was first approved anticancer drug which was based on this gene therapy principle. Suicide gene therapy is another attempt to treat tumor by delivering of gene coding for enzyme that metabolizes prodrugs into locally active chemotherapeutic drug moiety. Research related to gene therapy and its clinical presentation have been generally applied in the concept of malignancy. Cancer amounts to nearly two-third of all gene therapy-related research being conducted. Oncolytic viruses are being used to administer genes into the malignant cells, thus producing death of the involved malignant cell. A different strategy is to administer p53 gene (tumor suppressor gene) inducing oncolysis. [13].The first permitted anticancer drug which was created on this principle of gene therapy was Gendicine . Suicide gene therapy is one more effort to cure cancer by delivering of gene coding for enzyme that metabolizes prodrugs into locally active chemotherapeutic drug moiety.

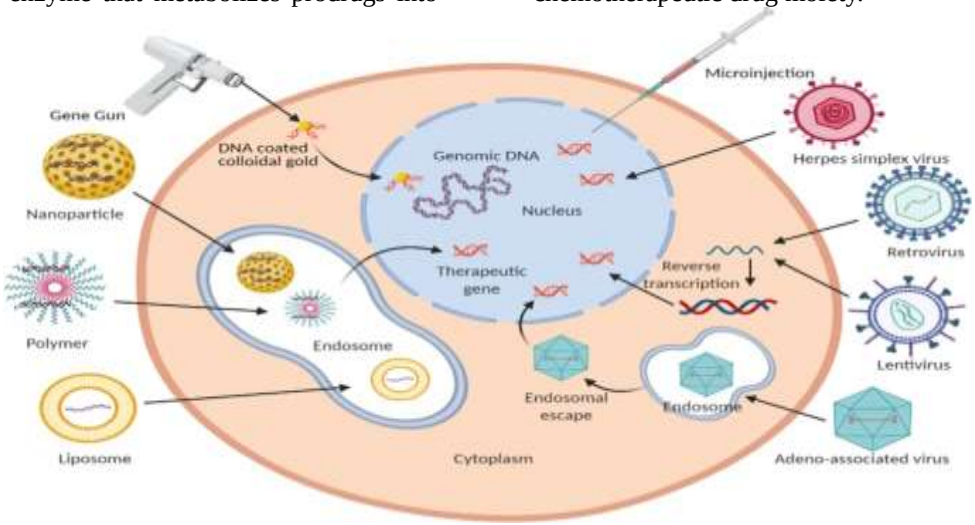

FIG.4.CANCER DISEASES IN GENE THERAPY

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SINGLE GENE DISORDER

There are numerous single gene disorders namely alpha-1-antitrypsin deficiency, cystic fibrosis, muscular dystrophies, lysosomal storage disease, chronic granulomatous disease, Huntington's disease, junctional epidermolysis bullosa, haemophilia , ornithine transcarbamylase deficiency, in which an important role is played by gene therapy for their treatment.

IMMUNO DEFICIENCY

It has been years since the improvement of gene therapy started but the first remarkable development seen ever since the first trial was in early 90s. During the preliminary set back where two patients had died after being treated for X linked severe combined immunodeficiency (X SCID) using retroviral vectors due to leukemia, even though there were clinical trials that showed strong therapeutic benefits of gene therapy in management of both X-SCID and SCID caused by the deficiency of adenosine deaminase (ADA). Secondary immunodeficiency states like Human Immunodeficiency Virus (HIV) in addition to primary immunodeficiency infection has likewise grew as a probable contestant for gene therapy. For specific defence against HIV infection to these cells, Transgenes can be transported into haematopoietic stem cells or into T-cells. They make the milieu unsuitable for HIV 1replication or disable the HIV-1 protein.

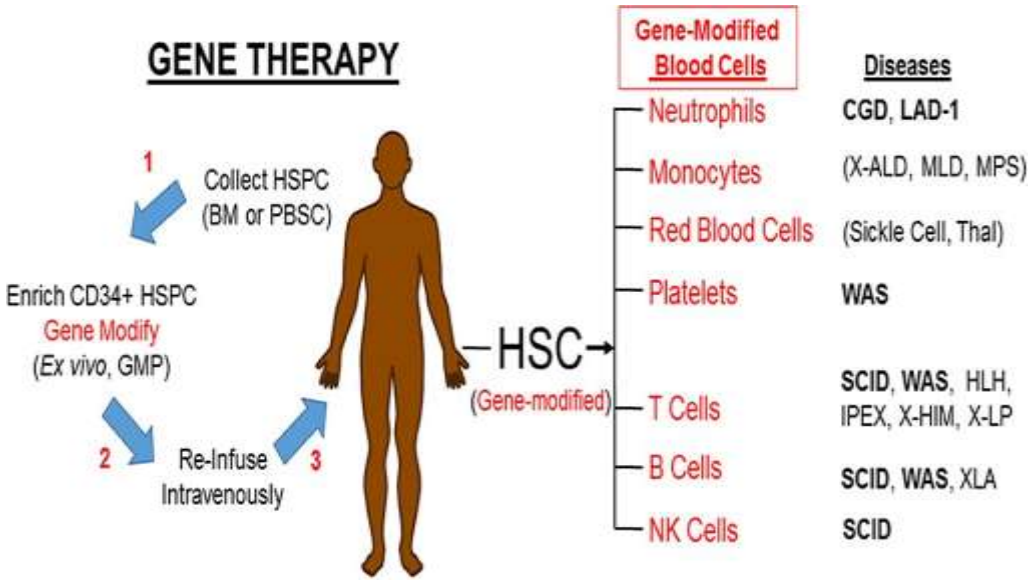

FIG.5.IMMUNO DEFICIENCY IN GENE THERAPY

EYE DISEASES

After the preliminary set back seen in SCID the regeneration of trust in gene therapy occurred due to Leber's congenital amaurosis. Eye is a small organ, hence there is possibility of transfecting a great amount of ocular cells. Leber's hereditary optic neuropathy, glaucoma, macular degeneration and red-green colour blindness are clinical ophthalmologic conditions for gene therapy. A phase I study is going on to treat age-related macular degeneration which shows effects of antiangiogenic cytokine Pigment Epithelium-derived Factor (PEDF).[14]. By injecting subretinal injections of adeno-associated virus containing a L-opsin gene, significant improvement is seen in red-green colour blind monkeys.

CARDIAC DISEASES

Cardiac diseases are difficult to treat as they are multigenic in origin. Trials are being conducted in which scientists have developed methods to transport genes for different growth factors like Fibroblast Growth Factors (FGF), Vascular Endothelial Growth Factors (VEGF) to encourage vascular angiogenesis. However their outcomes did not display remarkable enhancement in stress-induced myocardial perfusion but enhanced regional wall motion indicated a favourable anti-ischemic effect inspiring more research in this field.

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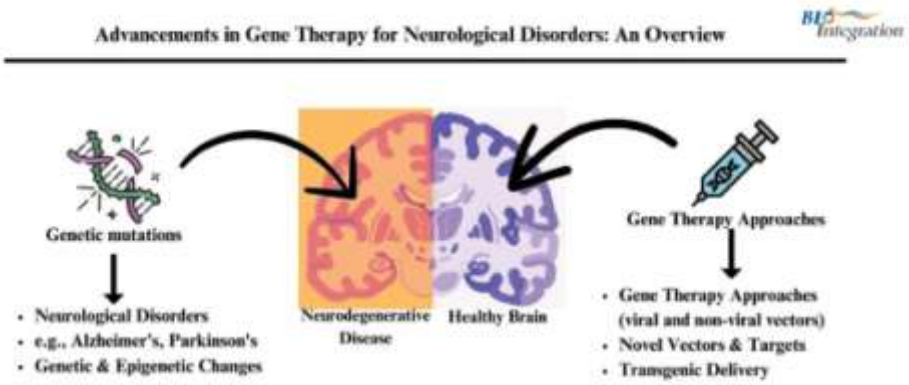
CENTRAL NERVOUS SYSTEM [CNS] DISORDERS

Gene therapy has revealed hopeful results in neurological disorders to cure Alzheimer's and Parkinsonism disease unlike cardiac diseases. Several trials are being conducted on gene therapy in Parkinsonism which are now either in phase 1 and phase 2 but are screening gene therapy to be potential , harmless and tolerable for in-vivo studies. Numerous methods used are, delivery of the gene in putamen cell bodies for neurturin or transmitting the gene into the subthalamic nucleus for glutamic acid decarboxylase. Similarly in Alzheimer's disease delivery of nerve growth factor into the CNS is being attempted using gene therapy .



Gene Therapy for Neurodegenerative Diseases: Challenges and Advancements

GENE THERAPY IN INDIA

Monetary assistance given by different government agencies has helped the nation to achieve speedy development in research associated to gene therapy. In the context of gene therapy laboratories, India ranks third among Asian countries. The main goal should be to invent new research institutions for gene therapy, while solidifying currently present institutions with better experience in molecular genetics to reduce the load of genetic diseases in India. The Advanced Cancer Treatment, Research and Education Center (ACTREC) is a pioneer in gene therapy-related research in our country. The center is using synthetic vectors to conduct research on head and neck cancer. It should be pointed out that Indian scientists are working hard day after day to contribute to the development of gene therapy in India.

FUTURE OF GENE THERAPY

Dr. Michael Gottesman (NIH) is working on the growth of a dominant selectable marker which is to be used in gene therapy. An international combined work to produce high quality genetic maps of the human genome and also the wide ranging DNA sequence is known as The Human Genome Project. Main intention behind this is to recognize and arrange all of the genes that have an important function in human disease and human health. In future it is expected to be more cost effective. There has been significant progress in the production of maps of the genome. Due to increasing accuracy of map information, isolating the genes responsible for human genetic diseases upto 4000, which are inherited in a Mendelian style by using a positional cloning technique is made possible. The technology involves mapping disease genes by linking disease occurrence in the family with identified DNA markers, and then separating the gene from DNA clones that span the region of interest . The genes secluded in this way include those used for Huntington's disease, Duchenne muscular dystrophy and CF. It has been predicted that hundreds of these disease causing genes would be isolated in the next few years, so that gene therapy can cure or be expected to treat these diseases.[15].

In different diseases that incline to be inherited in the family, such as diabetes, cancer or heart disease, the inheritance is even more complicated. The reason for seems to be the affected susceptibility by various environmental factors and genes. In this case, the plotting tools of the Human Genome Project might be used to identify susceptible genes. This information will help predict the possibility of disease development and targeted interventions (including somatic gene

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therapy) to decrease the severity or likelihood of the disease. Laboratory of Dr.Gottesman's focuses on the problem of missing expression of transferred genes, which do not have any selective advantage over target cells. One way to solve this problem is to associate the gene of interest with the gene encoding the selectable marker which is dominant. One of those genes, MDR1, encodes a 1280 amino acid protein that acts as an energy-based pump conferring resistance to many cytotoxic capsules utilized in most cancers treatment. It does this via way of means of binding capsules to the mobileular membrane (or cytoplasm) and expelling them from the mobileular. dr. Gottesman and his colleagues have correctly added MDR1 into bone marrow cells and feature proven that it's miles drug resistant and does now no longer look like poisonous to goal cells. In different experiments, his lab connected the MDR1 gene to genes that reason sickness in people and proved the expression of those genes. Using MDR1 as a choice marker has numerous advantages. It is probably relevant to somatic cells and hematopoietic stem cells, consisting of muscle, pores and skin or liver cells, and may be utilized in vivo and in vitro. Because the MDR1 gene product is expressed at the cellular surface, monoclonal antibodies may be used to pick out and classify cells that explicit it. Since the pump can apprehend masses of reagents, it's miles feasible to pick a reagent to choose transfected cells with out trendy systemic toxicity. In addition, the advent of factor mutations withinside the MDR1 gene might also additionally lessen pump specificity and enhance the ability to choose agents with useful properties. We are keen to switch this approach from the lab to the clinic .

SAFETY AND ETHICAL ISSUE

From the time since first gene therapy clinical trial was accepted in 1988 and launched in 1989, more than 3,000 patients have received gene therapy. Most of the early security concerns raised in early trials still exist till date. Some of them can be broadly classified as related to the expression of transfer vehicles or transferred genes. Viruses are used to transfer the expression of genetic material into cells in most of the clinical trials. Inflammation or active infection can be caused by administration of viruses. In a study by University of Pennsylvania, personally experienced the risk of excessive inflammation caused by administration of viruses. It caused death of a participant who was 18 years old. Second, infections with unrestrained activity can occur by multiple recombination events (since currently the design is unlikely) or contaminate stocks of viruses that do not replicate through helper viruses. There are no known cases of transmission of infected viruses to patients.

Obviously, testing the materials used in clinical trials is extremely important and very regular. Third, the administration of retroviruses haphazardly incorporated into the genome can lead to insertional mutations and malignant alteration . As stated above, autologous stem cell transplantation infested with a retrovirus stating the defective gene is used to treat severe combined immunodeficiency, resulting in a reduction in patients' symptoms. However, 2 out of 11 patients aquired T-cell leukemia due to the virus integrated downstream of the oncogene, causing it to be up-regulated. The expression of several healing genes makes patients prone to adverse reactions. As stated above, the use of growth factors to treat neurodegenerative diseases or the usage of proangiogenic molecules to treat CAD can encourage tumor development. Similarly, the appearance of pro inflammatory cytokines used to treat malignant tumors can lead to abnormal inflammatory problems. Though with the insertion of any therapeutic agent, side effects are associated the total incapability to withdraw drugs delivered through gene therapy is predominantly problematic. Lastly, theoretically there is danger of accidentally disrupting germ line cells.[16].

II. CONCLUSION

In deduction, gene therapy remains to offer great hope for the treatment of diseases for which there are ineffective forms or no cure present. The simple model of gene delivery has remained the same in vivo and in vitro. However, the techniques for delivering genetic material in these models are highly flexible, and new and revealing technologies continue to emerge. Currently, clinical trials based on gene therapy are ongoing in many important disease procedures and rare inherited diseases, which are generally well defined. With the continued advancement of basic science in the pitch of gene therapy, more efficient clinical trials will be launched one after another, and will at the end efficaciously cure and even treat patients. When this happens, all the clinicians would adapt with these gene therapies to treat their patients. So, we can say that gene therapy has a great future ahead.

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REFERENCES

[1]. Rogers K, Harris J, Stanton C, Griffiths AJF. gene therapy. In: Encyclopedia Britannica;2021.
[2]. Zimmer C. DNA Double Take. The New York times .
[3]. Carty NC, Nash K, Lee D, Mercer M, Gottschall PE, Meyers C, et al. Adeno associated viral (AAV) serotype 5 vector mediated gene delivery of endothelin converting enzyme reduces Abeta deposits in APP + PS1 transgenic mice. MolTher. 2008;16(9):1580–6.
[4]. Monteys AM, Hundley AA, Ranum PT, Tecedor L, Muehlmatt A, Lim E, et al. Regulated control of gene therapies by drug-induced splicing. 2021;596(7871):291–5.
[5]. 5. Nature. Ortolano S, Spuch C, Navarro C. Present and future of adeno associated virus based gene therapy approaches. Recent Pat EndocrMetab Immune Drug Discov. 2012;6(1):47–66.
[6]. 6. 7. 8. 9. Hasan SA, Almutairi SN, Alhemaid LA, Al Ghazwi AH, Alkhathaami BS, Alrumaihi TS, Altarooti NA, Fallatah AS, Moamina O. S, Alkhayri YA, Almutairi MA. "Joint preservation using orthobiologic therapies in osteoarthritis". Journal of Pharmaceutical Research International. 2021;33(50B):161-167. DOI: 10.9734/jpri/2021/v33i50B33439.
[7]. Patil PM, Chaudhari PD, Sahu M, Duragkar NJ. Review article on gene therapy. Res j pharmacolpharmacodyn. 2012;4(2):77–83.
[8]. Tang X, Zhang S, Fu R, Zhang L, Huang K, Peng H, et al. Therapeutic prospects of mRNA-based gene therapy glioblastoma. Front Oncol. 2019;9:1208.
[9]. for Rogers K, Stanton C, Griffiths AJF, Harris J. gene therapy. In: Encyclopedia Britannica. 2021.
[10]. Nayerossadat N, Maedeh T, Ali PA. Viral and nonviral delivery systems for gene delivery. Adv Biomed Res. 2012;1(1):27.
[11]. Bertrand N, Grenier P, Mahmoudi M, Lima EM, Appel EA, Dormont F, et al. Mechanistic understanding of in vivo protein corona formation on polymeric nanoparticles and impact on 644 Nilay and Damke; JPRI, 33(60B): 635-645, 2021; Article no.JPRI.79825 Nat pharmacokinetics. 2017;8(1):777.
[12]. Immunocore.(2022).Immunocoreannounces FDAapprovalofKIMMTRAK (tebentafusp-tebn) for the treatment of unresectable or metastatic uveal melanoma. https://ir. immunocore.com/news-releases/news-release-details/immunocore-announces-fda approval-kimmtrakr-tebentafusp-tebn.
[13]. Gaissmaier, L., Elshiaty, M., and Christopoulos, P. (2020). Breaking Bottlenecks for the TCR Therapy of Cancer. Cells 9, 2095.
[14]. (2019). Natural killer cells for cancer immunotherapy: a new CAR is catching up. EBioMedicine 39,1–2.
[15]. Bajan, S., and Hutvagner, G. (2020). RNA-Based Therapeutics: From Antisense Oligonucleotides to miRNAs. Cells 9, 137.
[16]. (2023). Trialtrove (Citeline)