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**Surita Majumder**
Assistant Professor, Department of AGB, Institute of Veterinary Science and Animal Husbandry, SOA, Odisha, India

**Namrita Sharma**
PG Scholars, Department of AGB, Institute of Veterinary Science and Animal Husbandry, SOA, Odisha, India

**Suraj Das**
PG Scholars, Department of AGB, Institute of Veterinary Science and Animal Husbandry, SOA, Odisha, India

**Corresponding Author:**
**Surita Majumder**
Assistant Professor, Department of AGB, Institute of Veterinary Science and Animal Husbandry, SOA, Odisha, India

# Gene therapy technology: Recent advances and applications: A review

**Surita Majumder, Namrita Sharma and Suraj Das**

**Abstract**
The transfer of genetic material to treat a disease or at the very least to improve a patient's clinical condition is commonly referred to as gene therapy. Transforming viruses into genetic shuttles that convey the desired gene to the target cells is one of the fundamental ideas behind gene therapy. Many viral and non-viral vectors have been developed as safe techniques for accomplishing this. *Ex vivo* and *in vivo* alteration are the two main strategies that have been developed. Gene transfer protocols have been approved for human use in inherited diseases, cancers and acquired disorders. This review highlights various application, methods of gene therapy.

**Keywords:** *Ex vivo*, gene therapy, *in vivo*, viral vectors

## 1. Introduction
Gene therapy normally entails inserting a functional gene into cells to treat a cellular defect or to provide a new cellular function (Culver K., 1994) [6]. For instance, the existence of faulty genes causes conditions including cystic fibrosis, combined immunodeficiency syndromes, muscular dystrophy, haemophilia, and numerous malignancies. Gene therapy can be used to replace or repair the offending genes. Combination immunodeficiency syndromes have responded exceptionally well to gene therapy, which has demonstrated long-lasting and exceptional therapeutic benefit (Cavazzana *et al*., 2000-2007) [3-5].
A genetic target of interest may be collected and altered outside of the organism before being returned to the host in order to transfer genetic material *in vivo* by local or systemic inoculation. Transfection or transduction are two ways to transfer synthesised DNA. Direct DNA injection into the target cells is one such form of transfer, as is the use of techniques to promote membrane penetration, receptor-mediated uptake, or endocytosis. Recombinant viruses are used in transduction as a vehicle for gene transfer. Cell-surface receptors facilitate the entry of these vectors.
Somatic gene therapy and germline gene therapy are two approaches for gene therapy.

**Table 1:** Human gene therapy trials (Dube *et al.*, 1995) [7]

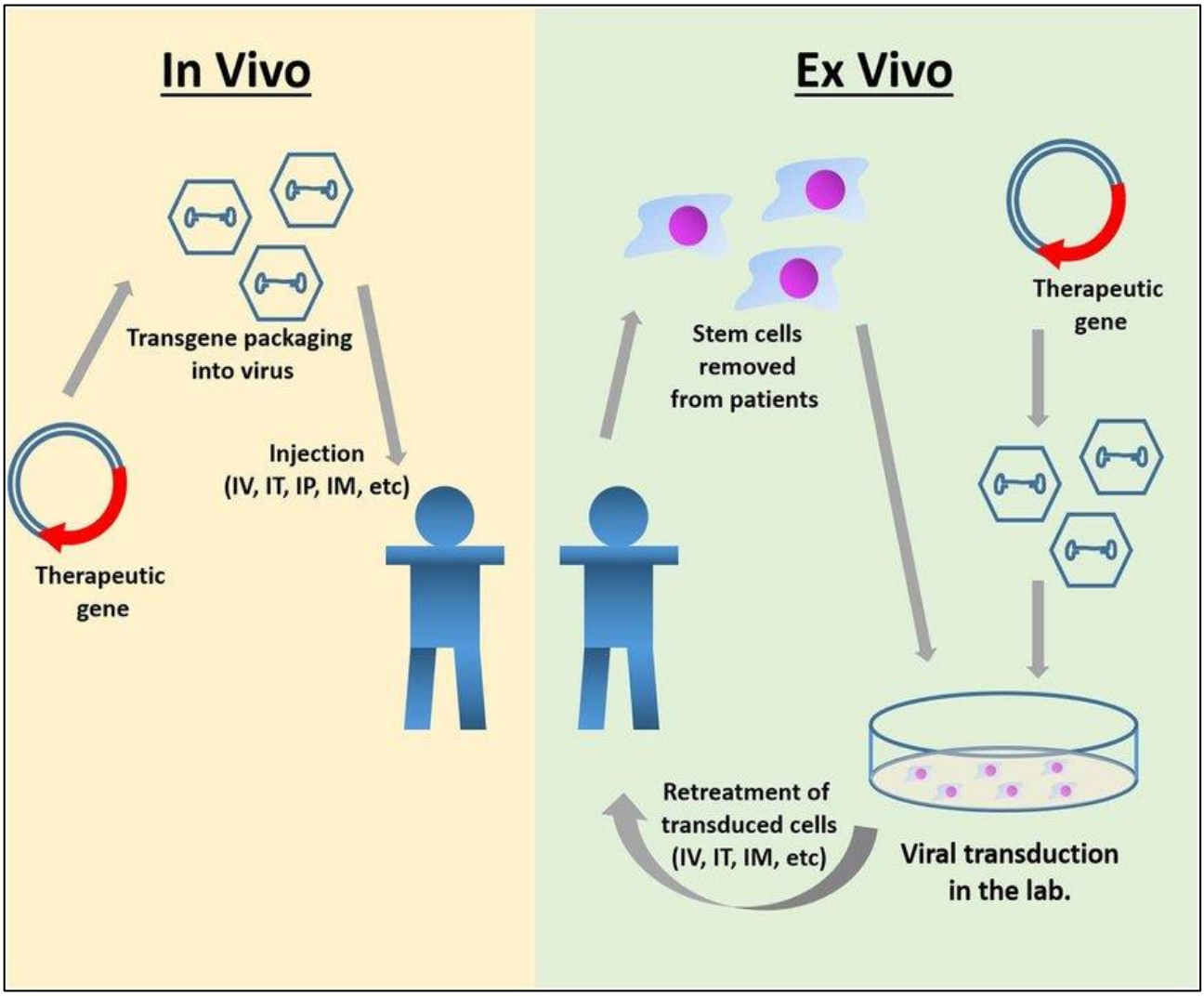
| | |
|---|---|
| Thalassemia | Alpha or beta globin |
| Sickle-cell anemia | Beta-globin |
| Fanconi anemia | Complement group C gene delivery |
| Melanoma | Tumour necrosis factor (TNF) |
| Diabetes mellitus | Glucose transporter-2 (GLUT-2) |

## 2. Gene Therapy History
The results of the initial clinical gene transfer study were published (Rosenberg *et al.*, 1990) [11]. Using a retroviral vector, Rosenberg and his colleagues inserted the neomycin resistance marker gene into tumor-infiltrating cells isolated from five patients with metastatic melanoma. These lymphocytes were subsequently multiplied *in vitro* and then reinfused back into the corresponding patients. This initial work demonstrated the feasibility and safety of retroviral gene transfer, which prompted numerous further experiments. Almost 900 clinical trials have been approved globally since 1989, in fact (Edelstein *et al.*, 2004) [8]. Between 1963 and 1990, recombinant DNA technology was developed, making gene therapy a reality. On September 14, 1990, at the National Institutes of Health, under the supervision of professor William French Anderson, the first effective gene therapy trial was carried out on a 4-year-old girl named Ashanti Desilva who had a rare genetic immune system disorder called severe

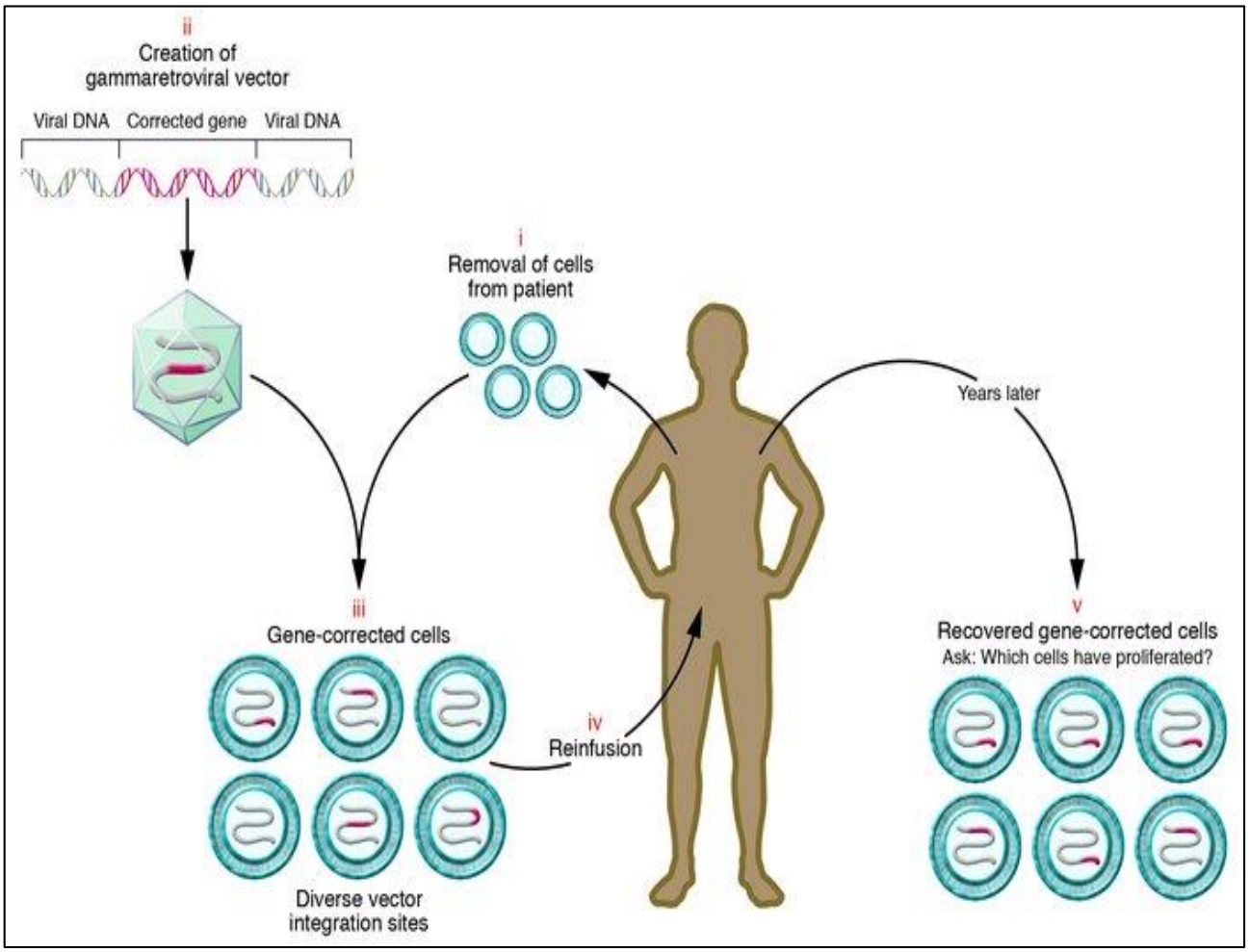
combined immune deficiency (SCID) (25). Claudio Bordignon of Italy carried out the initial gene therapy surgery in 1992, employing hematopoietic stem cells as carriers to treat a genetic illness. (26) China approved the first gene therapy medications in November 2005 and in 2003 for the treatment of specific malignant cancers. Researchers at the University of Oxford reported remarkable improvement in the vision of six persons with choroideremia, an inherited genetic eye condition, in January 2014. These patients had received treatment using a genetically modified AAV that carried a copy of the REP1 gene (MacLaren *et al.*, 2014) [10]. 12 HIV patients had received treatment since 2009 in a trial using a genetically modified virus with a rare mutation known to be protective against HIV, according to a report published in March 2014 by researchers at the University of Pennsylvania (CCR5 deficiency). (Tebas *et al.*, 2014) [13].

**3. Types**

Mainly two types. *Ex vivo* and *in vivo* gene therapy. *Ex vivo* is genetically altering cells outside of the body to produce therapeutic components and then re-injecting them into patients. Many cell types can be genetically modified. *In vivo* gene therapy refers to the process of delivering a therapeutic gene directly to the target cells of a certain tissue. The potential prospects for this method include many tissues. They include the liver, muscles, skin, spleen, lungs, brain, and blood cells, among others. The following factors have a major role in *in vivo* gene therapy's effectiveness: The effectiveness of target cells utilising the therapeutic gene, the gene's ability to express itself and the gene's intracellular breakdown and nuclear uptake;




*In-vivo* and *ex-vivo* methods




Retrovirus as a vector

**4. Vectors**

Vehicles with the terse name of "vectors" facilitate the passage of genetic information into a cell. Retrovirus, Adenovirus, baculovirus, herpes simplex virus, adeno-associated virus are the viral vectors. Non-viral vectors have a number of benefits over virus-derived ones, including the safety of delivery without immunogenicity, almost limitless transgene size, and the potential for recurrent administration. (Gardlik *et al.*, 2005) [9].

Non-viral systems comprise all the physical and chemical systems except viral systems.

**4.1 Physical Techniques for Improving Delivery**

Naked DNA, electroporation, gene gun, sonoporation, magnetofection are the types of physical methods which applied for *in-vivo* and *in-vitro* gene delivery.

**4.2 Chemical Methods to enhance gene Delivery**

Oligonucleotides, lipoplexes and polyplexes, dendrimers, hybrid methods, human artificial chromosome are mainly used for this method. This are more common than physical methods.

**4.3 Oral squamous cell carcinoma**

Chemotherapy, radiation therapy, and surgery are currently used in the management of oral squamous cell carcinoma (OSCC). But it has some toxic effects. According to a number of investigations, radiation and gene therapies work together to limit the growth of a variety of cancer cells, including ovarian, colorectal, nasopharyngeal, and head and neck cancer cells. (Schwartz *et al.*, 2000) [12].

There is little evidence, therefore, to suggest that a successful gene-transfer strategy for the treatment of Cystic Fibrosis lung disease is about to emerge, despite the amazing amount of research in this field. A variety of infectious disorders that are resistant to conventional therapeutic management are being treated as alternatives using gene therapy. Other than these this is also useful for diabetic neuropathy, arthritis, Periodontics and parkinson's disease.

**5. Conclusion**

The majority of experts concur that gene therapy has the potential to be the most intriguing use of DNA research to date. The ease of the process will determine how widely this therapy is used. Scientists predict that, in 20 years, gene therapy will be the only method left for treating all hereditary diseases. A simple i/v injection of a gene transfer agent may one day be used to administer genes as medicine. And now that a preliminary map of the human genome has been created, study is concentrating on how each gene works and how defective genes contribute to disease.

**6. References**

1. Abott A. Gene therapy. Italians first to use stem cells. Nature. 1992;356:465-99.
2. Blaese RM. Development of gene therapy for immunodeficiency: adenosine deaminase deficiency. Pediatr Res. 1993;33(suppl):S49S55.
3. Cavazzana-Calvo M, Fischer A. Gene therapy for severe combined munodeficiency: are we there yet? J Clin

Invest. 2007;117:1456-65.
4. Cavazzana-Calvo M, Hacein-Bey S, de Saint Basile G, Gross F, Yvon E, Nusbaum P, *et al*. Gene therapy of human severe combined immunodeficiency (SCID)-X1 disease. 2000;288:669-672.
5. Cavazzana-Calvo M, Hacein-Bey S, Yates F, de Villartay JP, Le Deist F, Fischer A. Gene therapy of severe combined immunodeficiencies. J Gene Med. 2001;3:201-206.
6. Culver K. Gene Therapy—A Handbook for Physicians. Mary Ann Liebert, Inc., New York; c1994. p. 78-86.
7. Dube ID, Cournoyer D. Gene therapy: here to stay. Can Med Assoc J. 1995;152:1605-1613.
8. Edelstein ML, Abedi MR, Wixon J, Edelstein RM. Gene therapy clinical trials worldwide 1989-2004: An overview. J Gene Med. 2004;6:597-602.
9. Gardlik R, Palffy R, Hodosy J, Lukacs J, Turna J, Celec P. Vectors and delivery systems in gene therapy. Med. Sci. Monit. 2005;11(4):110-121.
10. MacLaren RE, Groppe M, Barnard AR, Cottriall CL, Tolmachova T, Seymour L, *et al*. Retinal gene therapy in patients with choroideremia: initial findings from a phase 1/2 clinical trial. Lancet. 2014;383(9923):1129-1137. doi:10.1016/S0140-6736(13)62117-0. PMID 24439297.
11. Rosenberg SA, Aebersold P, Cornetta K, Kasid A, Morgan RA, Moen R, *et al*. Gene transfer into humans—immunotherapy of patients with advanced melanoma, using tumor-infiltrating lymphocytes modified by retroviral gene transduction. N Engl J Med. 1990;323:570-78.
12. Schwartz GJ, Mehta RH, Wenig BL, Shaligram C, Portugal LG. Salvage treatment for recurrent squamous cell carcinoma of the oral cavity. Head Neck. 2000;22:34-41.
13. Tebas P, Stein D, Tang WW, Frank I, Wang SQ, Lee G, *et al*. Gene Editing of CCR5in Autologous CD4 T Cells of Persons Infected with HIV. New England Journal of Medicine. 2014;370(10):901. Doi:10.1056/NEJMoa1300662. PMID 24597865.