www.ijarp.com ISSN 2456-9992 Page: 01-11

International Journal Advanced Research Publications

Review Article

Volume: 02
Issue: 04

AN OVERVIEW OF GENE THERAPY USED IN CANCER TREATMENT

Noor Rahi*[1], Madhukar Prabash[2], Tanya Sharma[3], Kamalesh Mistry[4], Noorul Huda[5], Tusar Ranjan pati[6]

[1]Research Scholar, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[2]Assistant Professor, Department of Pharmacy, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[3]Assistant Professor, Department of Pharmacy, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[4]Associate Professor, Department of Pharmacy, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[5]Assistant Professor, Department of Pharmacy, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[6]Assistant professor, Dept. Of pharmaceutical Analysis, Nityananda college of pharmacy Balasore Odisha India – 756060.

Article Received: 04 March 2026, Article Revised: 24 March 2026, Published on: 14 April 2026

***Corresponding Author: Noor Rahi**

Research Scholar, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

DOI: https://doi-doi.org/101555/ijarp.6388

ABSTRACT

By addressing the genetic foundation of malignancies, gene therapy has emerged as a novel and extremely promising method to cancer treatment, providing targeted and customised therapeutic techniques. In order to prevent tumour growth, trigger apoptosis, or strengthen the body's defences against cancer, this method entails introducing, altering, or silencing particular genes within cancer cells or surrounding tissues. Numerous approaches, including suicide gene therapy, gene replacement therapy, RNA interference-based gene silencing, and immune cell modification (such as CAR-T cell therapy), have shown great promise in preclinical and clinical contexts. Effective gene delivery mechanisms, such as viral vectors

like adenoviruses and retroviruses as well as non-viral techniques like liposomes and nanoparticles, are crucial to the success of gene therapy.

Compared to traditional treatments like chemotherapy and radiation, gene therapy has demonstrated enhanced specificity and less systemic toxicity in the treatment of a variety of cancers, including solid tumours and haematological malignancies. However, obstacles like immunological reactions, ineffective administration, expensive expenses, and safety issues still prevent it from being widely used in clinical settings. The accuracy and efficacy of gene-based treatments have been substantially improved by recent developments in gene-editing technologies, especially CRISPR-Cas9. All things considered, gene therapy is a revolutionary development in oncology that has the potential to greatly enhance patient outcomes and completely change the way that cancer is treated in the future.

KEYWORDS: Gene therapy; Cancer treatment; Targeted therapy; Personalized medicine; Gene therapy; Tumor suppression; Apoptosis; Gene replacement; Gene silencing; RNA interference (RNAi); CAR-T cell therapy; Immunotherapy; Viral and non-viral vectors; Nanoparticles; Gene delivery systems; Hematological malignancies; Solid tumors; Reduced toxicity; CRISPR-Cas9; Gene editing; Precision medicine; Drug resistance; Molecular therapy; Cancer immunotherapy; Advanced therapeutics.

INTRODUCTION

One of the most promising and quickly developing methods in contemporary cancer is gene therapy. In order to treat or prevent illness, genetic material within a patient's cells is altered or manipulated. Gene therapy is used in cancer treatment to either directly kill cancerous cells, improve immune responses, or fix faulty genes. Gene therapy provides a more tailored and targeted approach than traditional treatments like chemotherapy and radiation, reducing harm to healthy tissues while enhancing therapeutic results. Gene therapy has moved from experimental research to clinical use thanks to developments in molecular biology and biotechnology, giving patients with previously incurable cancers fresh hope. [1]

Despite tremendous advancements in detection and treatment, cancer continues to be one of the world's top causes of morbidity and mortality, posing a large global health burden. Uncontrolled cell proliferation, apoptosis evasion, persistent angiogenesis, tissue invasion, and metastasis are the hallmarks of this complicated group of illnesses. At the molecular level, genetic and epigenetic changes that interfere with regular cellular regulatory processes are the main cause of cancer. Oncogene mutations, tumour suppressor gene inactivation,

flaws in DNA repair pathways, and dysregulation of cell signalling networks are a few examples of these changes. Surgery, chemotherapy, and radiation therapy are examples of conventional cancer treatments that have greatly increased patient survival. Nevertheless, these methods frequently lack specificity, harm healthy tissues, and are linked to serious side effects and the emergence of drug resistance. [2]

In the second half of the 20th century, the idea of gene therapy first emerged, with the goal of treating inherited genetic diseases. Its use to complicated diseases like cancer has grown over time due to developments in molecular biology, genetic engineering, and biotechnology. The Human Genome Project's completion and the quick advancement of gene-editing technologies have sped up this field's advancement. Gene therapy is now seen as a crucial part of precision medicine, which customises treatments based on the genetic makeup of each patient and their tumours. [3]

Based on how it works, gene therapy in cancer treatment can be roughly divided into a number of approaches. Gene replacement therapy is a crucial strategy that replaces mutant or inactivated genes with functional copies of tumour suppressor genes. For example, it has been demonstrated that p53 tumour suppressor gene restoration induces apoptosis and inhibits tumour growth in a variety of malignancies. Another tactic is gene silencing, which suppresses the production of oncogenes that cause unchecked cell division by using methods like RNA interference (RNAi). Suicide gene therapy also entails inserting genes that create enzymes that can selectively destroy cancer cells by transforming non-toxic prodrugs into toxic chemicals.[4]

Cancer immunotherapy, which uses genetic modification to improve the immune system's capacity to identify and eliminate cancer cells, is a particularly promising field of gene therapy. Chimeric antigen receptor T-cell (CAR-T) treatment, in which a patient's T-cells are genetically modified to express receptors that specifically target tumour-associated antigens, is one of the most prominent instances. Leukaemia and lymphoma are two examples of haematological cancers that this strategy has shown exceptional success in treating. Additionally, cytokines and other immune-modulating molecules that boost antitumor immune responses can be produced using gene therapy. [5]

Anti-angiogenic therapy, which attempts to prevent the development of new blood vessels that provide nourishment and oxygen to tumours, is another significant use of gene therapy. Gene therapy can effectively starve tumours and restrict their development and spread by preventing angiogenesis. Gene therapy can also be used in conjunction with traditional therapies like radiation and chemotherapy to increase their effectiveness and lessen side

effects. By improving tumour susceptibility to therapy and overcoming resistance mechanisms, this combined method has demonstrated synergistic results. [6]

Delivering therapeutic genes into target cells is a key component of gene therapy. Vectors, which serve as carriers for genetic material, are used to do this. Adenoviruses, retroviruses, and lentiviruses are examples of viral vectors that are frequently employed because of their high gene transfer efficiency. These vectors have undergone genetic modification to remove their pathogenicity without compromising their capacity to transfer genes into host cells. Although they typically show lower transfection effectiveness than viral systems, non-viral vectors such liposomes, nanoparticles, and bare DNA have also drawn attention because of their better safety profile and decreased immunogenicity. Because vector selection affects gene delivery efficiency, it is a critical factor in determining the effectiveness of gene therapy. [6]

Basic Principles of Gene Therapy

Delivering genetic material (DNA or RNA) into cells to alter their function is the foundation of gene therapy. Usually, vectors carriers made to deliver therapeutic genes into target cells—are used to do this. These vectors can be non-viral (like liposomes and nanoparticles) or viral (like adenoviruses and retroviruses). Once inside the cell, the inserted gene can either produce proteins that cause cancer cell death, mute the expression of dangerous genes, or replace a faulty gene. Effective gene delivery, consistent gene expression, and a low immune response are necessary for gene therapy to be successful. [7]

The idea behind gene therapy is to alter a patient's cells' genetic makeup in order to treat or prevent illness. This strategy focuses on fixing or modifying the molecular flaws that cause malignant transformation and development in the setting of cancer. Gene therapy targets these genetic abnormalities rather than just treating symptoms because cancer is essentially a genetic illness caused by mutations, deletions, or aberrant expression of genes. Fundamentally, gene therapy is introducing external genetic material into target cells, either RNA or DNA. This genetic material is intended to carry out particular tasks, such creating a therapeutic protein, replacing a faulty gene, or deactivating a dangerous gene. [8]

Gene delivery is a key component of gene therapy and impacts the treatment's overall effectiveness. To guarantee that the therapeutic gene reaches the target cells in adequate amounts without being broken down, effective delivery methods are needed. Vectors, which serve as carriers of genetic material, are used to do this. Both viral and non-viral vectors can be generically categorised. Adenoviruses, retroviruses, and lentiviruses are examples of viral

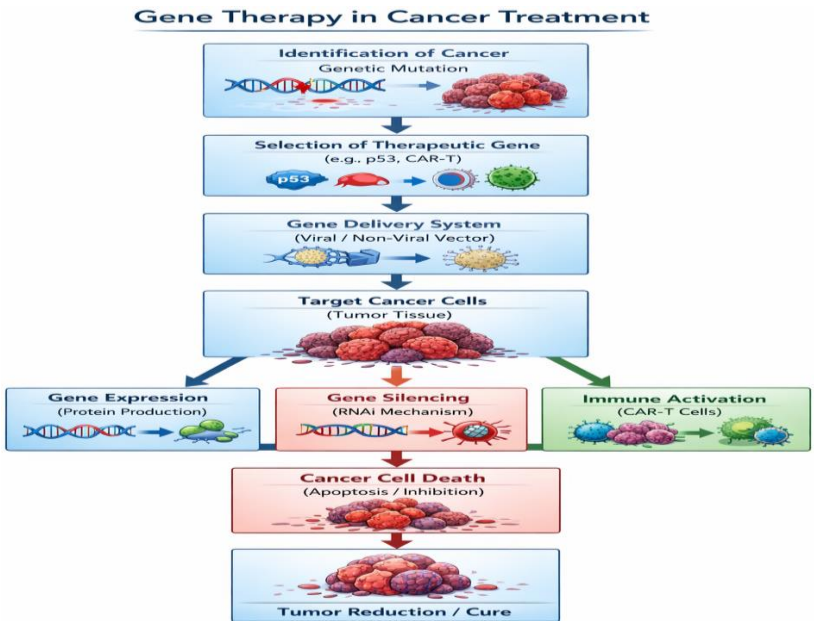
vectors that are frequently employed because of their innate capacity to penetrate cells and efficiently transfer genetic information. These viruses have been genetically modified to eliminate their harmful elements while maintaining their ability to spread. However, non-viral vectors, such as liposomes, nanoparticles, and bare DNA, have benefits including reduced immunogenicity and increased safety. [9]

In gene therapy, gene expression and regulation are also very important. To achieve the intended therapeutic effect, the therapeutic gene must be correctly expressed after it is introduced into the cell. This entails the inserted gene being transcribed into messenger RNA (mRNA) and then translated into a useful protein. To guarantee efficacy without producing harm, the amount and duration of gene expression must be carefully regulated. To regulate expression patterns, regulatory elements including enhancers, terminators, and promoters are added to the gene construct.

Depending on the targeted therapeutic result, gene therapy can operate through a variety of ways. Gene replacement, which replaces a damaged or altered gene with a functional copy, is a crucial mechanism. Gene silencing is another. [10]

Types of Gene Therapy in Cancer Treatment

Based on the target cells and the therapeutic strategy employed, gene therapy in cancer treatment can be broadly categorised. These divisions aid in comprehending the use of gene therapy in both experimental and clinical oncology. Somatic gene therapy and germline gene therapy are the two main categories; other functional classes are determined by the therapeutic action mechanism. [11]



1.Somati Gene Therapy

The most popular and clinically approved type of gene therapy for the treatment of cancer is somatic gene therapy. It entails inserting therapeutic genes into the patient's somatic (non-reproductive) cells. This method's genetic alterations are limited to the person receiving treatment and are not inherited by subsequent generations. [12]

Somatic gene therapy is used in cancer treatment to target tumour cells or surrounding tissues in order to suppress tumour development, trigger apoptosis, or boost immune responses. This can be accomplished by either directly injecting genetic material into tumours (in vivo technique) or by altering cells outside the body and then reintroducing them (ex vivo approach). For instance, it is possible to remove immune cells like T-lymphocytes, genetically modify them to identify cancer cells, and then reintroduce them into the patient. Certain forms of lymphoma and leukaemia have responded very well to this treatment. [13]

Because somatic gene therapy is safer than germline techniques and has less ethical issues, it is preferred. The majority of modern gene therapy-based cancer treatments are built upon it.

2. Germline Gene Therapy

In germline gene therapy, genes in early embryos or reproductive cells (ovum or sperm) are altered to produce heritable genetic alterations that can be passed on to subsequent generations. Due to serious ethical, legal, and safety issues, this method is not used in the treatment of human cancer, despite the possibility that it could eradicate genetic predispositions to the disease.

Unintentional genetic changes, erratic long-term consequences, and moral dilemmas pertaining to genetic inheritance and human modification are among the possible hazards. Germline gene therapy is therefore not allowed in clinical oncology practice and is still limited to experimental research in specific model organisms. [14]

3. In Vivo Gene Therapy

Direct introduction of therapeutic genes into a patient's body, usually targeting tumour tissues, is known as "in vivo gene therapy." This strategy uses injection, infusion, or localised delivery techniques to deliver vectors containing the therapeutic gene. [15]

When treating solid tumours when direct access to the tumour site is feasible, this approach is especially helpful. Although it enables targeted gene delivery, it may encounter obstacles such immunological reactions, restricted gene uptake, and trouble regulating gene expression. In vivo gene therapy is still being investigated in clinical trials for a variety of tumours in spite of these obstacles. [16]

4. Ex Vivo Gene Therapy

Ex vivo gene therapy is taking the patient's cells, genetically altering them in a lab setting, and then returning them into the patient's body. Before reinfusion, this technique enables the selection of successfully altered cells and offers more control over gene transfer. Modifying immune cells to improve their capacity to identify and combat cancer cells is a well-known example of ex vivo gene therapy. Advanced immunotherapies, such as engineered T-cell treatments, have been developed as a result of this strategy. Ex vivo techniques can be complicated and expensive, but they can improve treatment precision and lower the possibility of side effects. [17]

Types of Gene Therapy Approaches in Cancer

Approach Type	Examples	Advantages	Limitations
Gene Replacement Therapy	p53 gene therapy	Restores normal gene function	Limited delivery efficiency
Gene Silencing	siRNA, shRNA	Targets specific oncogenes	Short-lived effects, delivery challenges
Suicide Gene Therapy	HSV-TK system	Selective killing of cancer cells	Requires prodrug administration
Immunogene Therapy	Cytokine genes (IL-2, IFN-γ)	Enhances immune response	Risk of systemic toxicity
Gene Editing	CRISPR-Cas9	Precise genetic modification	Off-target effects, ethical concerns
Oncolytic Gene Therapy	Oncolytic viruses (e.g., modified HSV)	Selective tumor destruction	Immune clearance, safety concerns

Strategies of Gene Therapy in Cancer

1. Gene Replacement Therapy

Since non-reproductive cells are the objective of somatic gene therapy, the genetic alterations are not inherited. In the treatment of cancer, this is the most widely utilised type. In order to stop tumour growth or trigger apoptosis, therapeutic genes are directly inserted into tumour cells or adjacent tissues. [18]

2. Gene Silencing Therapy

RNA interference (RNAi) is one strategy used in gene silencing to prevent the expression of oncogenes that cause tumour growth.

3. Gene therapy for suicide

This method involves genetically modifying cancer cells to create enzymes that selectively destroy tumour cells by converting non-toxic prodrugs into toxic chemicals.

4. Gene transfer immunotherapy

This entails altering immune cells to better identify and combat cancer cells. CAR-T cell therapy, in which T-cells are modified to target particular cancer antigens, is a prominent example.

5. Gene therapy that is anti-angiogenic

This strategy seeks to limit tumour growth by preventing angiogenesis, the development of new blood vessels that deliver nutrition to tumours.

Advantages of Gene Therapy in Cancer Treatment

Leukaemia, lymphoma, melanoma, and solid tumours including breast and lung cancer have all been treated by gene therapy. CAR-T cell therapy, in which genetically altered T-cells target and eliminate cancer cells, is one of the most effective treatments for haematological malignancies. Gene therapy is also being investigated for use in conjunction with radiation and chemotherapy to improve its efficacy and lessen negative effects. [19]

High specificity, decreased systemic toxicity, and the possibility of long-term therapeutic effects are only a few benefits of gene therapy. By focusing on the genetic cause of cancer, it makes personalised medicine possible and can be applied when conventional treatments don't work. Additionally, gene therapy can boost the immune system's ability to identify and eradicate cancer cells. [20]

CHALLENGES AND LIMITATIONS

Despite its potential, gene therapy faces several challenges. These include difficulties in gene delivery, immune system reactions, high cost, and limited long-term safety data. There is also a risk of insertional mutagenesis, where the introduced gene disrupts normal cellular function. Ethical concerns and regulatory issues further complicate its widespread adoption. [21]

Prospects for the Future

With continued research concentrating on better gene targeting, improving vector design, and reducing side effects, gene therapy has a very bright future in the treatment of cancer. The field is undergoing a change thanks to technological advancements like CRISPR-Cas9 gene editing, which allows for precise genetic tweaks. Next-generation cancer treatments are anticipated to heavily rely on personalised gene therapy in conjunction with immunotherapy and nanotechnology. [22]

CONCLUSION

In the field of cancer treatment, gene therapy has become a revolutionary and extremely promising strategy that offers a paradigm shift from traditional medicines toward more individualised and focused interventions. Gene therapy offers a more targeted approach to treatment that reduces harm to healthy cells while increasing therapeutic efficacy by treating the underlying genetic defects that cause cancer formation and progression. In both experimental and clinical settings, techniques like gene replacement, gene silencing, suicide gene therapy, and immunogene therapy have shown great promise, especially in the treatment of haematological malignancies and some solid tumours.

REFERENCES

1. Anderson, W. F. (1992). Human gene therapy. *Science*, 256(5058), 808–813.
2. Naldini, L. (2015). Gene therapy returns to centre stage. *Nature*, 526(7573), 351–360.
3. Ginn, S. L., Amaya, A. K., Alexander, I. E., Edelstein, M., & Abedi, M. R. (2018). Gene therapy clinical trials worldwide. *Journal of Gene Medicine*, 20(5), e3015.
4. Kay, M. A. (2011). State-of-the-art gene-based therapies. *Nature Reviews Genetics*, 12(5), 316–328.
5. Hacein-Bey-Abina, S., et al. (2003). LMO2-associated clonal T cell proliferation. *Science*, 302(5644), 415–419.
6. June, C. H., & Sadelain, M. (2018). Chimeric antigen receptor therapy. *New England Journal of Medicine*, 379(1), 64–73.
7. Rosenberg, S. A., et al. (2008). Adoptive cell transfer therapy. *Nature Reviews Cancer*, 8(4), 299–308.
8. Mullard, A. (2017). FDA approves CAR-T therapy. *Nature Reviews Drug Discovery*, 16(10), 669–670.

9. Maude, S. L., et al. (2014). CAR-T cells in leukemia. *New England Journal of Medicine*, 371(16), 1507–1517.
10. Porter, D. L., et al. (2011). CAR-T cell therapy persistence. *New England Journal of Medicine*, 365(8), 725–733.
11. Doudna, J. A., & Charpentier, E. (2014). Genome editing CRISPR-Cas9. *Science*, 346(6213), 1258096.
12. Cong, L., et al. (2013). Multiplex genome engineering. *Science*, 339(6121), 819–823.
13. Jinek, M., et al. (2012). CRISPR-Cas9 programmable DNA cleavage. *Science*, 337(6096), 816–821.
14. Barrangou, R., et al. (2007). CRISPR immunity. *Science*, 315(5819), 1709–1712.
15. Mali, P., et al. (2013). RNA-guided genome engineering. *Science*, 339(6121), 823–826.
16. Cavazzana-Calvo, M., et al. (2000). Gene therapy for immunodeficiency. *Science*, 288(5466), 669–672.
17. Thomas, C. E., Ehrhardt, A., & Kay, M. A. (2003). Viral vectors. *Nature Reviews Genetics*, 4(5), 346–358.
18. Lundstrom, K. (2018). Viral vectors in gene therapy. *Diseases*, 6(2), 42.
19. Mintzer, M. A., & Simanek, E. E. (2009). Nonviral vectors. *Chemical Reviews*, 109(2), 259–302.
20. Yin, H., et al. (2014). Non-viral gene delivery. *Nature Reviews Genetics*, 15(8), 541–555.
21. Sheridan, C. (2011). Gene therapy finds its niche. *Nature Biotechnology*, 29(2), 121–128.
22. Aiuti, A., et al. (2013). Gene therapy for ADA-SCID. *Science*, 341(6148), 1233151.
23. Check, E. (2002). Gene therapy death. *Nature*, 420(6912), 116–118.
24. Wilson, J. M. (2009). Lessons from gene therapy. *Molecular Therapy*, 17(2), 203–205.
25. High, K. A., & Roncarolo, M. G. (2019). Gene therapy. *New England Journal of Medicine*, 381(5), 455–464.
26. Hacein-Bey-Abina, S., et al. (2010). Gene therapy outcomes. *Journal of Clinical Investigation*, 120(3), 924–933.
27. Cavazzana, M., et al. (2014). Gene therapy success. *Nature*, 507(7490), 329–332.
28. Naldini, L. (2011). Ex vivo gene therapy. *Nature Reviews Genetics*, 12(5), 301–315.
29. Hacein-Bey-Abina, S., et al. (2002). Gene therapy in SCID. *New England Journal of Medicine*, 346(16), 1185–1193.
30. Hacein-Bey-Abina, S., et al. (2008). Insertional oncogenesis. *Nature*, 455(7214), 871–876.
31. Robbins, P. F., et al. (2015). Cancer immunotherapy. *Nature Medicine*, 21(7), 740–746.

32. Restifo, N. P., et al. (2012). Adoptive immunotherapy. *Nature Reviews Immunology*, 12(4), 269–281.
33. June, C. H., et al. (2015). CAR-T therapy advances. *Science*, 348(6230), 56–61.
34. Grupp, S. A., et al. (2013). CAR-T in children. *New England Journal of Medicine*, 368(16), 1509–1518.
35. Park, J. H., et al. (2018). Long-term CAR-T outcomes. *New England Journal of Medicine*, 378(5), 449–459.
36. Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of cancer. *Cell*, 144(5), 646–674.
37. Vogelstein, B., et al. (2013). Cancer genome landscapes. *Science*, 339(6127), 1546–1558.
38. Stratton, M. R., et al. (2009). Cancer genome. *Nature*, 458(7239), 719–724.
39. Garraway, L. A., & Lander, E. S. (2013). Precision oncology. *Cell*, 153(1), 17–37.
40. Sawyers, C. (2004). Targeted therapy. *Nature*, 432(7015), 294–297.