

Gene Therapy VS Chemotherapy

Joshyitha Arun Kumar

Abstract: To date, cancer remains one of the most formidable diseases known to humankind, with its multifaceted nature demanding innovative and personalized treatment strategies. Chemotherapy has long been a cornerstone of cancer therapy, targeting rapidly dividing cells with cytotoxic agents. However, its limitations, including toxicity to healthy tissues and the development of drug resistance, have led to the exploration of alternative approaches. One such includes gene therapy, providing a promising frontier to the future of cancer treatment while offering the potential to correct genetic abnormalities and bolster the body's innate defenses against malignancies.

Chemotherapy focuses more on drugs that lead to several painful side effects such as loss of hair, fatigue, constipation and much more. Gene therapy works around these unnecessary side effects provided by conventional treatments by harnessing genetic engineering techniques. This approach offers the potential for enhanced therapeutic efficacy, reduced side effects, and the ability to overcome drug resistance by targeting specific genes or pathways involved in cancer progression.

This research paper aims to provide a comprehensive overview of cancer, the mechanisms underlying chemotherapy, and the evolving role of gene therapy in cancer treatment. Additionally, it explores the mechanisms of action and limitations of traditional chemotherapy agents, highlighting the need for more targeted and personalized therapies. Furthermore, it explores the challenges, ethical considerations, and regulatory aspects associated with the clinical implementation of gene therapy. By understanding the molecular intricacies of cancer and harnessing the power of genetic manipulation, we move closer to a future where cancer can be effectively controlled, if not eradicated, offering renewed hope to individuals battling this devastating disease.

1. Introduction:

Everyone here today is familiar with the concept of cancer. An impossible challenge for medical professionals, the darkest of days for its victims, a feeling of hopelessness for the family and a cause for pity and sympathy among bystanders, cancer has been invading lives for a long time now. It is characterized by the uncontrolled growth and spread of abnormal cells in the body and can affect any part of the body. This leads to its many stages and its several types depending on the area it affects and the extent to which it does. Due to its severity, it is crucial we find an appropriate cure that can ensure the sure survival of the victim.

Chemotherapy is a powerful and widely used cancer treatment that involves the administration of drugs to target and destroy cancer cells. These medications work by interfering with the growth and division of rapidly multiplying cancer cells, aiming to shrink

or eradicate the tumor. On the other hand, a more suitable approach refers to gene therapy. It involves the introduction, modification, or replacement of genes within a patient's cells to correct or mitigate the underlying genetic cause of a condition. By harnessing the power of genetics, gene therapy aims to offer potential cures for once-incurable diseases thus providing a beacon of hope for patients and medical staff alike. The purpose is to study the relationship between the two and establish certain advantages and disadvantages while convincing the majority to investigate gene therapy instead.

2. What is Cancer

To put it in simple words, cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. Normally, human cells grow and multiply (through a process called cell division) to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. Sometimes this orderly process breaks down, and abnormal or damaged cells grow and multiply when they should not. These cells may form tumors, which are lumps of tissue. Tumors can be cancerous or not cancerous.

Cancer is the second most common cause of death in the U.S., but fewer people are dying of cancer now than 20 years ago. Early detection and innovative treatments are curing cancer and helping people with cancer live longer. At the same time, medical researchers are identifying independent risk factors linked to developing cancer to help prevent people from developing it.

The most terrifying aspect of cancer for some individuals is the survival rates which are usually just estimates based on the experiences of large groups of people who have various kinds of cancer. The body normally eliminates cells with damaged DNA (Deoxyribo Nucleic Acid) before they turn cancerous. But the body's ability to do so goes down as we age. This is part of the reason there is a higher risk of cancer later in life. Cancer survival rates vary based on cancer type, stage, and treatment. According to the most recent data from the National Cancer Institute, 68% of people with any kind of cancer were alive five years after their diagnosis.

Some common early cancer symptoms include:

- Unexplained weight loss.
- Chronic tiredness.
- Persistent pain.
- Fever that occurs mostly at night.
- Skin changes, particularly moles that change shape and size or new moles.

Left untreated, cancer may cause additional symptoms, including:

- Bruising or bleeding more easily.
- Lumps or bumps under your skin that do not go away.
- Difficulty breathing.
- Difficulty swallowing.

Most cancers have four stages. The specific stage is determined by a few varied factors, including the tumor's size and location:

- Stage I: The cancer is localized to a small area and has not spread to lymph nodes or other tissues.
- Stage II: The cancer has grown, but it has not spread.
- Stage III: The cancer has grown larger and has spread to lymph nodes or other tissues.
- Stage IV: The cancer has spread to other organs or areas of your body.

As mentioned above, sometimes, cancer can spread from the place where it first formed to another place in the body. It is called metastatic cancer. Metastatic cancer has the same name and the same type of cancer cells as the original, or primary, cancer. For example, breast cancer that forms a metastatic tumor in the lung is metastatic breast cancer, not lung cancer.

2.1 Differences between normal cells and cancerous cells

There are numerous differences between normal cells and cancerous cells. Firstly, cancerous cells grow in the absence of signals telling them to grow. Normal cells only grow when they receive such signals. They also ignore signals that normally tell cells to stop dividing or to die (a process known as programmed cell death or apoptosis). This is what leads to the uncontrolled division of these cells that results in the formation of tumors.

These tumors then invade into nearby areas and spread to other areas of the body. Normal cells stop growing when they encounter other cells, and most normal cells do not move around the body. Blood vessels mistake them for normal cells and supply tumors with oxygen and nutrients and remove waste products from tumors. They hide from the immune system which normally eliminates damaged or abnormal cells by convincing immune cells to protect the tumor instead of attacking it. Moreover, they rely on various kinds of nutrients than normal cells. In addition, some cancer cells make energy from nutrients in a unique way than most normal cells. This lets cancer cells grow more quickly.

2.2 Causes

Cancer is a genetic disease—that is, it is caused by changes to genes that control the way our cell's function, especially how they grow and divide. Medical researchers estimate 5% to 12% of all cancers are caused by inherited genetic mutations that you cannot control.

Genetic changes that cause cancer can happen because:

- of errors that occur as cells divide.
- of damage to DNA caused by harmful substances in the environment, such as the chemicals in tobacco smoke and ultraviolet rays from the sun.
- They were inherited from our parents.

The genetic changes that contribute to cancer tend to affect three main types of genes—proto-oncogenes, tumor suppressor genes and DNA repair genes. These changes are sometimes called “drivers” of cancer. Proto-oncogenes are involved in normal cell growth and division. Tumor suppressor genes are also involved in controlling cell growth and division. DNA repair genes are involved in fixing damaged DNA.

Gene mutations occur frequently during normal cell growth. The gene mutations you are born with and those that you acquire throughout your life work together to cause cancer. However, cells contain a mechanism that recognizes when a mistake occurs and repairs the mistake. Occasionally, a mistake is missed. This could cause a cell to become cancerous.

The incidence, geographic distribution, and behavior of specific types of cancer are related to multiple factors, including sex, age, race, genetic predisposition, and exposure to environmental carcinogens. Of these factors, **environmental exposure** is the most important. Exposure to ionizing radiation has been well documented as a significant risk factor for many cancers, including acute leukemias, thyroid cancer, breast cancer, lung cancer, soft tissue sarcoma, and basal cell and squamous cell skin cancers.

Medical researchers have identified several risk factors that increase your chance of developing cancer.

Cancer risk factors include:

- Smoking
- Diet
- Environment
- Radiation exposure
- Hormone therapy

2.3 Effects

Cancer and its treatments can introduce a range of side effects that vary depending on the type and stage of cancer, as well as the specific therapies involved. Common side effects include:

- Difficulty breathing
- Nausea
- Diarrhea or constipation
- Weight loss

Some cancer treatments have lasting side effects that may cause pain. One study found that 39% of people who completed cancer treatment had chronic pain. Peripheral neuropathy is an example of pain that may persist after treatment. Another side effect includes Cancer fatigue,

an overwhelming sense of tiredness that is not helped by getting more rest. Some people have chronic cancer fatigue that continues after they have finished treatment.

Chemotherapy brain fog (chemo brain) happens when cancer or cancer treatment affects your ability to remember or act on information. About 75% of people receiving cancer treatment tell their healthcare providers that they have issues with memory, concentration, and their ability to complete tasks. Moreover, the immune system can be compromised, making individuals more susceptible to infections. Emotional and psychological effects are prevalent, encompassing anxiety, depression, and the stress of managing a chronic illness. Each person's experience with cancer is unique, and the side effects can significantly impact their quality of life during and after treatment.

2.4 Types

There are more than 100 types of cancer. Types of cancer are usually named for the organs or tissues where the cancers form. For example, lung cancer starts in the lung, and brain cancer starts in the brain. Cancers also may be described by the type of cell that formed them, such as an epithelial cell or a squamous cell.

Carcinomas are the most common type of cancer. They are formed by epithelial cells, which cover the inside and outside surfaces of the body.

Sarcomas are cancers that form in bone and soft tissues, including muscle, fat, blood vessels, lymph vessels, and fibrous tissue (such as tendons and ligaments).

Cancers that begin in the blood-forming tissue of the bone marrow are called leukemias. These cancers do not form solid tumors. Instead, large numbers of abnormal white blood cells (leukemia cells and leukemia blast cells) build up in the blood and bone marrow, crowding out normal blood cells.

Lymphoma is cancer that begins in lymphocytes (T cells or B cells). These are disease-fighting white blood cells that are part of the immune system. In lymphoma, abnormal lymphocytes build up in lymph nodes, lymph vessels, and other organs of the body.

Melanoma is cancer that begins in cells that become melanocytes, which are specialized cells that make melanin (the pigment that gives skin its color). Most melanomas form on the skin, but melanomas can also form in other pigmented tissues, such as the eye.

3. What is chemotherapy

Treatment of cancer with chemicals goes back several hundred years, but it was not until the 1940s that the first successful and documented use of systemic chemotherapy took place. Cancer chemotherapy refers to the administration of cyto- toxic chemicals, i.e., chemicals

with cell killing properties, with the aim to, in some cases, eradicate the tumor or, at least, reduce the tumor burden and, thereby, reduce the tumor-related symptoms and prolong life.

With present methods of treatment, when the tumor remains localized at the time of diagnosis, about one-third of patients are cured with local treatment strategies, such as surgery or radiotherapy. In the remaining cases, however, early micro metastasis is a characteristic feature, indicating that a systemic approach with chemotherapy is required for effective cancer management. In patients with locally advanced disease, chemotherapy is often combined with radiotherapy to allow for subsequent surgical resection to take place, and such a combined modality approach has led to improved clinical outcomes. At present, about 50% of patients who are initially diagnosed with cancer can be cured. In contrast, chemotherapy alone can cure less than 10% of all cancer patients when the tumor is diagnosed at an advanced stage. Moreover, it is impossible to achieve tumour remission without a risk for potentially life-threatening adverse effects.

3.1 Mechanism on the body

The term ‘chemotherapy’ is confusing since it suggests therapy with a chemical, and most drugs could easily be considered as chemicals even though they might not be used in cancer therapy. ‘Cytotoxic’ therapy is a better description of what is meant. The treatment aims at killing the cancer cell through a direct effect.

Cytotoxic drugs are mostly given in specialized combinations of two or more drugs with the aim to increase the possibility to overcome tumour cell resistance, procure the activity of the regimen against different tumor cell clones and to avoid pronounced toxicity from normal tissues.

The selection of a chemotherapeutic regimen for an individual patient has so far been based on tumour histology and data from clinical trials including many patients, indicating which therapeutic option is the best for the average patient. According to this concept, the individual patient’s treatment response can only be determined after some cycles of chemotherapy have been attempted. This is problematic in that a patient with an often short, expected survival has an elevated risk of contracting serious side-effects, leading to decreasing quality of life before a gain from the therapy can be evaluated.

A chemotherapy regimen is specialized with respect to cytotoxic drugs included the doses to be used, mostly expressed as $\text{mg} \cdot \text{m}^2$ body surface, and relative time-points for, and methods of, administration. The time between the start days for each course of chemotherapy, i.e., the cycle time, is mostly 21 or 28 days (about 4 weeks) but, weekly administration of various drug combinations is frequently used in, e.g., chemotherapy for lymphomas. The drugs included in the regimen are often administered as intravenous injections or infusions during 1 – 5 days in the beginning of each course, but additional administration later in the course, is included in some regimens. The mechanisms by which cytotoxic drugs act at the cells to induce cell death and stop cell growth, have mostly been investigated in the laboratory in continuously growing tumour cell lines. Most cytotoxic drugs act inside the cell by interaction with cellular functions necessary for cell growth and survival.

Chemotherapy can be distinguished as three main types:

Primary chemotherapy refers to chemotherapy administered as the primary treatment in patients who present with advanced cancer for which no alternative treatment exists. This has been the main approach in treating patients with advanced metastatic disease, and in most cases, the goals of therapy are to relieve tumor-related symptoms, improve overall quality of life, and prolong time to tumor progression.

Neoadjuvant chemotherapy refers to the use of chemotherapy in patients who present with localized cancer for which alternative local therapies, such as surgery, exist but which have been shown to be less than completely effective. It is most often administered in the treatment of anal cancer, bladder cancer, breast cancer and gastroesophageal cancer.

Adjuvant chemotherapy is one of the most important roles for cancer chemotherapy to local treatment modalities such as surgery. The goal of chemotherapy is to reduce the incidence of both local and systemic recurrence and to improve the overall survival of patients. Adjuvant chemotherapy is effective in prolonging both disease-free survival (DFS) and overall survival (OS) in patients with breast cancer, colon cancer and gastric cancer.

Chemotherapy can also be given as instillations, usually as an add-on to general therapy, into sanctuaries with the aim to increase the chance for tumour cell eradication and control at that site.

3.2 Advantages and disadvantages

Chemotherapy, despite its formidable reputation for causing side effects, plays a crucial role in cancer treatment and has several advantages. One of its primary strengths lies in its ability to target rapidly dividing cancer cells, impeding their growth and preventing the spread of the disease. Chemotherapy is versatile, capable of treating several types of cancers, and often serves as a powerful tool in combination with other treatment modalities like surgery or radiation therapy. Additionally, its systemic nature allows it to reach cancer cells that may have spread to other parts of the body. While the side effects can be challenging, many individuals successfully undergo chemotherapy and achieve remission, highlighting its effectiveness in combating cancer and improving overall survival rates.

Unfortunately, the negative effects are greater than the positive ones. The tumour types in which cytotoxic drugs may provide cure from metastatic disease are few and encompass a minority of patients with advanced disease. A considerable proportion of patients will not achieve a substantial tumour response but will only experience side-effects. For some tumour types, the proportion of patients that benefit may be as low as 20%, even when choosing the best-established therapeutic regimen. Moreover, the several-fold difference in systemic drug exposure after standard dosing could mean that patients with a high clearance of the drugs would risk a too low exposure to the drugs given and, thus, a reduced chance of an antitumor effect. On the other hand, patients with low clearance would risk excessively high drug exposure. This would increase the chance of an antitumor effect but also increase the risk for unacceptable toxic effects

Another fundamental problem in cancer chemotherapy is the development of cellular drug resistance. Primary or inherent resistance refers to drug resistance without prior exposure to

available standard agents. Many tumour types, e.g., cancer of the lung (non- small cell type), kidney and gastrointestinal tract often show resistance to most cytotoxic drugs already from the beginning. Other tumour types, e.g., cancer of the breast, ovary, and hematological malignancies, may respond initially but later appear resistant also to drugs not used earlier. Knowledge of the mechanisms for drug resistance at cellular level is, therefore, of importance for understanding the failure of chemotherapy in patients.

Another major factor preventing chemotherapy from establishing a permanent cure is dose intensity. In experimental animal models, the dose-response curve is usually steep in the linear phase, and a reduction in dose when the tumor is in the linear phase of the dose-response curve always results in a loss in the capacity to cure the tumor effectively before a reduction in the antitumor activity is observed. Although complete remissions may continue to be observed with dose reductions down to as low as 20% of the optimal dose, residual tumor cells may not be eliminated thereby allowing for eventual relapse. Because toxicities are usually associated with anticancer drugs, it is often appealing for clinicians to avoid acute toxicity by simply reducing the dose and/or by increasing the time interval between each cycle of treatment. However, such modifications in dose represent a major cause of treatment failure, especially in patients with drug-sensitive tumors.

Not only do these disadvantages of chemotherapy affect the patients but rather pose a threat encompassing the staff that deal with these chemicals too. For example, most cytotoxic drugs bear the risk of induction of secondary malignancies. This could pose an employee-protection problem if the handling in the clinic is associated with repeated exposure to these drugs. In fact, mutagenic activity was observed in the urine from nurses involved in the preparation of cytotoxic drugs.

3.3 Effects on the body

Of immense importance is the consideration that the side effects of chemotherapy frequently limit the amount of drug that can be given safely to treat an individual with cancer. Furthermore, antineoplastic agents are currently not highly specific for cancer cells, they also damage normal cells, albeit to differing degrees.

The side effects most frequently reported were hair loss, nausea, and tiredness. Each of these side effects was experienced by more than 80% of patients at some time up through cycle 6, and by close to two or three of the group in any single cycle. In addition, vomiting, sleep disturbance, weight gain, mouth sores, and numbness/tingling were each a consequence for more than 40% of the patients.

The patients do find chemotherapy to be difficult and distressing. Ninety-five and five tenths' percent of patients indicated some difficulty with chemotherapy (Le., rated difficulty as non-zero for at least one of the first six cycles), 90.3% reported some emotional distress from chemotherapy, 75.0% reported some disruption in their social life, and 80.6% reported some disruption in their work life. The mere presence of side effects is not the only factor related to distress; an inability to manage or cope with side effects is also important.

Emotional upset and functional disruption are even more pronounced when these side effects prove to be resistant to coping efforts. Failures in coping may be responsible for the increase in reported distress and disruption from chemotherapy over time, an effect that occurred although the total number of side effects remained constant from cycle to cycle. That patients failed to adapt or “get used to” chemotherapy also may be due to the development of anticipatory nausea.

3.4 Future

It is quite clear from the above that there is a need for new and more active drugs in cancer chemotherapy.

A bearing principle in the development process for new cytotoxic drugs is the hope that there may be tumour cells that are not present in normal cells and the exploitation of which may confer a more advantageous therapeutic index for cytotoxic drugs. Regarding the process of drug development, there is reason to believe it will become more efficient. By the addition of laboratory testing systems with good correlation to activity in the patients, the preclinical part of new drug development may become more rapid and efficient than so far. Besides rational drug design, there will also be space in the future for progress in drug development based on analog-synthesis, unprejudiced drug screening and exploitation of serendipitous findings.

Advances in genetic and molecular understanding of cancer will enable oncologists to tailor therapies based on an individual's unique genetic profile, optimizing efficacy while minimizing side effects. Additionally, the development of novel drug delivery systems and nanotechnology may refine the precision and efficiency of chemotherapy, allowing for more potent treatments with fewer systemic repercussions. Collaborative efforts between medical researchers, pharmaceutical companies, and technology innovators are likely to reshape the landscape of chemotherapy, offering patients not just improved survival rates but also a higher quality of life during and after treatment.

4. What is Gene therapy

Gene therapy is the administration of foreign genomic material into the host tissue to modify the expression of a gene product or to change the biological properties of cells for therapeutic use which fulfils the following two characteristics: (a) it contains an active substance which contains or consists of a recombinant nucleic acid used in or administered to human beings with a view to regulating, repairing, replacing, adding or deleting a genetic sequence; (b) its therapeutic, prophylactic or diagnostic effect relates directly to the recombinant nucleic acid sequence it contains, or to the product of genetic expression of this sequence

Five decades ago, visionary scientists hypothesized that genetic modification by exogenous DNA might be an effective treatment for inherited human diseases. This “gene therapy” strategy offered the theoretical advantage that a durable and curative clinical benefit would be achieved by a single treatment. Although the journey from concept to clinical application has been long and tortuous, gene therapy is now bringing new treatment options to multiple fields of medicine.

Gene therapy can be categorized into two categories — germ line gene therapy and somatic gene therapy. The difference between these two approaches is that in somatic gene therapy genetic material is inserted in some target cells, but the change is not passed along to the next generation, whereas in germ line gene therapy the therapeutic or modified gene will be passed on to the next generation.

Currently, more than 1800 approved gene therapy clinical trials worldwide have been conducted or are still ongoing. Up to date, cancer is by far the most common disease treated by gene therapy. It composes over 60% of all ongoing clinical gene therapy trials worldwide, followed by monogenetic and cardiovascular diseases. Gene therapy in various forms has also produced clinical benefits in patients with blindness, neuromuscular disease, hemophilia, immunodeficiencies, and cancer. To date, over 3000 genes are associated with disease-causing mutations, and about 2600 gene therapy trials are undergoing for the management of various disorders.

4.1 Mechanism on the body

The type and mode of gene therapy will be determined based on an individual’s genomic constituents, as well as his or her tumor specifics, genetics, and host immune status, to design a multimodality treatment that is unique to each individual’s specific needs.

Gene transfer therapy can be conducted either as in vivo or ex vivo approaches. In the in vivo approach, targeted cells are approached directly, such as the intradermal injection of a metastatic nodule, or intravesical therapy for superficial bladder cancer. In the ex vivo approach, targeted cells from a tumor are selected, then collected, grown in culture media at a controlled microenvironment, manipulated genetically by the insertion of a new gene or protein (transgene) in the cell genome, then introduced back into the host. Cancer gene therapy has focused instead on using recombinant DNA constructs to augment existing therapies.

Immunotherapy

Currently gene therapy is being used to create recombinant cancer vaccines. Unlike vaccines for infectious agents, these vaccines are not meant to prevent disease, but to cure or contain it by training the patient’s immune system to recognize the cancer cells by presenting it with highly antigenic and immunostimulatory cellular debris. Initially cancer cells are harvested from the patient (autologous cells) or from established cancer cell lines (allogeneic) and then are grown in vitro. These cells are then engineered to be more recognizable to the immune

system by the addition of one or more genes and the cellular contents are incorporated into a vaccine. Another unique immunotherapy strategy facilitated by gene therapy is to directly alter the patient's immune system to sensitize it to the cancer cells. Vaccines using engineered cells are showing great promise for the treatment of many cancers that respond poorly to conventional therapy. Vaccine therapy for non-small cell lung cancer is an example of an autologous vaccine therapy that has had satisfactory results in clinical trials.

Oncolytic agents

Another growing area of gene therapy treatment for cancer is the use of oncolytic vectors for cancer destruction. Like immunotherapy, this is a concept that has been around for a century, and, like immunotherapy, it is undergoing a renaissance due to gene therapy. Oncolytic gene therapy vectors are viruses that have been genetically engineered to target and destroy cancer cells while remaining innocuous to the rest of the body. Oncolytic vectors are designed to infect cancer cells and induce cell death through the propagation of the virus, expression of cytotoxic proteins and cell lysis. In murine models, both colon and bladder cancer have shown survival benefits and reduced metastasis using oncolytic viral agents. However, there are several unique obstacles for oncolytic virotherapy in humans. Most people have antibodies to the common viruses used for therapy development which often leads to an immune response that clears the viral agent before it has had time to infect cells.

Gene transfer

One of the most exciting treatments to emerge from the concept of gene therapy is that of gene transfer or insertion. This is a radically new treatment paradigm involving the introduction of a foreign gene into the cancer cell or surrounding tissue. Solid tumors such as prostate, lung and pancreatic tumors have been treated successfully in animal models using a variety of genes and transfer methods. However, delivery of the therapeutic gene to the target cells must be effective enough to elicit a response and has been difficult to achieve with many current technologies. In addition, extra precautions must be taken to ensure the therapeutic gene does not integrate into unwanted cell types, such as reproductive tissues.

4.2 Advantages and disadvantages

Cancer occurs due to disrupting the normal cell proliferation and apoptosis process. Advances in cancer therapy need a novel therapeutic agent with novel mode of action, several mechanisms of cell death, and constructive collaboration with conventional management. Gene therapies possess all these profiles. Gene therapies are bringing new treatment options to multiple fields of medicine. Growing interest in gene therapy was inspired by the recognition that—at least in principle—a single treatment might achieve durable, potentially curative clinical benefit.

Investigators hypothesized that in contrast to protein-based drugs that may require repeated infusion, gene-based therapies delivered to long-lived cells might afford sustained production

of endogenous proteins, such as clotting factors in hemophilia. Moreover, long-term cell replacement afforded by genetically engineered hematopoietic stem cells (HSCs) may durably alleviate a range of conditions, obviating, for example, the need for lifelong enzyme administration or transfusion therapy.

Despite these advantages, gene therapy comes with its share of disadvantages. One significant drawback is its non-specific nature, as it targets rapidly dividing cells, affecting not only cancerous ones but also healthy cells with high turnover rates, such as those in the digestive system and hair follicles. This can lead to a range of side effects, including nausea, hair loss, and compromised immune function. Additionally, chemotherapy often causes fatigue, making it challenging for patients to maintain their normal daily activities. The treatment's systemic impact on the entire body may result in long-term complications, such as increased risk of infection and potential damage to vital organs. Moreover, some individuals may experience psychological distress due to the uncertainty of its outcomes and the toll it takes on their quality of life. Balancing the benefits and drawbacks of chemotherapy is a complex decision that patients and healthcare providers must carefully navigate.

4.3 Effects on the body

Gene therapy, while holding immense promise for treating genetic disorders, is not without its share of potential side effects. One concern revolves around the possibility of unintended genetic changes, where therapeutic genes may disrupt normal gene function or activate oncogenes, potentially leading to the development of cancer. Additionally, the body's immune response to the introduced genetic material can result in inflammation and other immune reactions. Adverse reactions to the delivery system, such as viral vectors used to transport therapeutic genes, can also occur.

Moreover, the long-term effects of gene therapy remain a topic of ongoing research, as the durability and stability of the introduced genetic changes over time are not yet fully understood. Careful monitoring and continued research are crucial to mitigate these side effects and unlock the full potential of gene therapy. However, the most frequent side effects are fever and symptoms that resemble a cold. If the agent is injected, there is often localized swelling and inflammation at the site of the injection.^{14,16-18} However, when compared with the side effects of conventional chemotherapeutic treatments, these side effects are minimal.

4.4 Future

Building on decades of scientific, clinical, and manufacturing advances, gene therapies have begun to improve the lives of patients with cancer and a variety of inherited genetic diseases. Partnerships with biotechnology and pharmaceutical companies with expertise in manufacturing and scale-up will be required for these therapies to have a broad impact on human disease. Many challenges remain, including understanding and preventing

genotoxicity from integrating vectors or off-target genome editing, improving gene transfer, or editing efficiency to levels necessary for treatment of many targets' diseases.

Several overly exciting cancer vaccine treatments are in late-stage trials, thanks to the advent of genetic engineering. In addition, gene transfer technology for cancer treatment holds great promise for increasing the effectiveness of current chemotherapeutic treatment regimens. Significant advances have been made in oncolytic virotherapy, and trials are in progress that incorporate this technique for precancerous and cancerous treatment. Many of the past obstacles to treatment are being actively overcome and current second and third generation therapeutics are being tested. Key areas for future research include modifying viral vectors to reduce toxicity and immunogenicity, increasing the transduction efficiency of nonviral vectors, enhancing vector targeting and specificity, regulating gene expression, and identifying synergies between gene-based agents and other cancer therapeutics.

Importantly, a societal consensus must be reached on the ethics of germline genome editing considering rapid scientific advances that have made this a real, rather than hypothetical, issue. Finally, payers and gene therapy clinicians and companies will need to work together to design and test new payment models to facilitate delivery of expensive but potentially curative therapies to patients in need. The ability of gene therapies to provide durable benefits to human health, exemplified by the scientific advances and clinical successes over the past several years, justifies continued optimism and increasing efforts toward making these therapies part of our standard treatment armamentarium for human disease.

5. Which is better? Chemotherapy? Gene therapy?

To conclude, the choice between chemotherapy and gene therapy depends on numerous factors, including the type and stage of cancer, as well as individual patient characteristics. Chemotherapy is a well-established treatment that uses drugs to kill or inhibit the growth of cancer cells. It is often effective in treating a wide range of cancers and can rapidly reduce tumor size. However, it can also cause significant side effects, including nausea, fatigue, and damage to healthy cells.

On the other hand, gene therapy is a promising, innovative approach that targets the genetic mutations responsible for cancer. It has the potential to provide more targeted and precise treatment with fewer side effects. Gene therapy aims to correct or replace faulty genes that drive cancer growth. While it shows great promise, it is still an evolving field with ongoing research and clinical trials.

The choice between chemotherapy and gene therapy should be made in consultation with healthcare professionals who can consider the specific circumstances of the patient and the current state of medical knowledge. In some cases, a combination of both therapies may offer the best outcome by leveraging the strengths of each approach.

References

1. <https://www.cancer.gov/about-cancer/understanding/what-is-cancer#:~:text=Pittsburgh%20Cancer%20Institute-,The%20Definition%20of%20Cancer,up%20of%20trillions%20of%20cells.>
2. <https://www.mayoclinic.org/diseases-conditions/cancer/symptoms-causes/syc-20370588>
3. <https://my.clevelandclinic.org/health/diseases/12194-cancer>
4. <https://www.tandfonline.com/doi/pdf/10.1080/02841860151116204>
5. https://books.google.ae/books?hl=en&lr=&id=6Nz_87OLrtC&oi=fnd&pg=PR7&dq=chemotherapy&ots=oeQYZs2-Eq&sig=Bluakd2yoblvmB7lpJoS2dmA2kc&redir_esc=y#v=onepage&q=chemotherapy&f=false
6. <https://www.sciencedirect.com/science/article/abs/pii/S0378111913004344>
7. <https://www.science.org/doi/full/10.1126/science.aan4672>
8. <http://www.clinmedres.org/content/4/3/218.full.pdf+html>
9. <https://www.tandfonline.com/doi/full/10.2147/BTT.S302095>
10. <https://molcelltherapies.biomedcentral.com/articles/10.1186/2052-8426-2-27>
11. <https://academic.oup.com/jnci/article/89/1/21/2526155?login=false>
12. <https://www.sciencedirect.com/sdfe/pdf/download/eid/1-s2.0-0749208189900806/first-page-pdf>
13. <https://acsjournals.onlinelibrary.wiley.com/doi/epdf/10.1002/1097-0142%2819890201%2963%3A3%3C604%3A%3AAID-CNCR2820630334%3E3.0.CO%3B2-2>
14. <https://www.sciencedirect.com/science/article/abs/pii/S0959804900001337>