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REVIEW ON CANCER GENE THERAPY

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ABSTRACT: -

Over the years, the main objective of gene therapy research has been the treatment of cancer.
Despite the lack of a cancer gene therapy medication on the market yet, significant advancements have been made recently in the identification of putative targets and the creation of viral and nonviral gene delivery methods. To date, many genes have been investigated as potential targets for cancer gene therapy. Numerous gene therapy approaches have been developed, such as oncolytic viral therapies, antiangiogenesis, suicide gene therapy, and gene therapy vaccines. The effectiveness of treatment has been further enhanced by the combination of gene therapy with more traditional techniques like radiotherapy, chemotherapy, and immunotherapy.There are still not many gene therapy agents in phase III trials, in spite of the very favorable outcomes of preclinical and experimental studies. We will go over gene transfer mechanisms, targets, gene targeting tactics, and cancer gene therapy in clinical settings in this chapter. One of the leading causes of death in the world today is cancer. The World Health Organization (WHO) observations that deaths from cardiovascular disease account for the majority of deaths worldwide, with cancer coming in second.in charge of one in every six fatalities. However, it is thought it might eventually turn out to be the primary cause of death. High levels of academic achievement are not exclusive to cancer. economies at the global level; developing nations provide slightly more than half (56%) of annual new cancer diagnoses and 64% of cancer-related deaths globally.

Therefore, it is regarded as an important obstacle to international social and economic development. According to WHO estimates, the annual number of cancer cases could exceed 20 million by 2030. Due to the current demographic explosion and the rise in the elderly population, individuals. However, the

Key words :- Cancer, immunotherapy,Antiabgiogesis,Nonviral, Medication, Diagnosis

INTRODUCTION: -

The improvements in the past 20 years in the molecular biology have evoked optimism in the treatment of cancer and yielded a number of targeted drugs in the market. However, the curative treatment of the cancer has still been possible with only the early diagnosis and early intervention in the vast majority of the solid tumors. Almost half of the cancer patients diagnosed each year have been dying of the disease throughout the world. In particular, the patients with distant metastasis have no hope of cure with the current treatment modalities. Around the world, cancer is the second most common cause of death. Overall, there has been a rise in the prevalence of cancer; by 2014, 585,720 persons had died from cancer in the United States of America alone, accounting for about 1,665,540 cases of the disease. Consequently, cancer is a severe issue that has an impact on everyone's health in human societies. Regretfully, the disease exhibits variability at the tissue level, which poses significant challenges to its precise diagnosis and treatment efficacy 2, 3. The prostate, lung and bronchus, colon and rectum, and urinary tract have the highest percentages of cancer types in men, respectively.Cancer is the second leading cause of death worldwide. Overall, the prevalence of cancer has increased; in the United States alone, 585,720 people had passed away from the disease in 2014, making up roughly 1,665,540 cases. Thus, in human societies, cancer is a serious problem that affects everyone's health. Unfortunately, the disease is variable at the tissue level, which creates major obstacles to accurate diagnosis and effective treatment 2, 3. Men's cancer rates are highest in the prostate, lung as well as bronchus, colon and rectum, and urinary tract, in that order.

Epidemiology

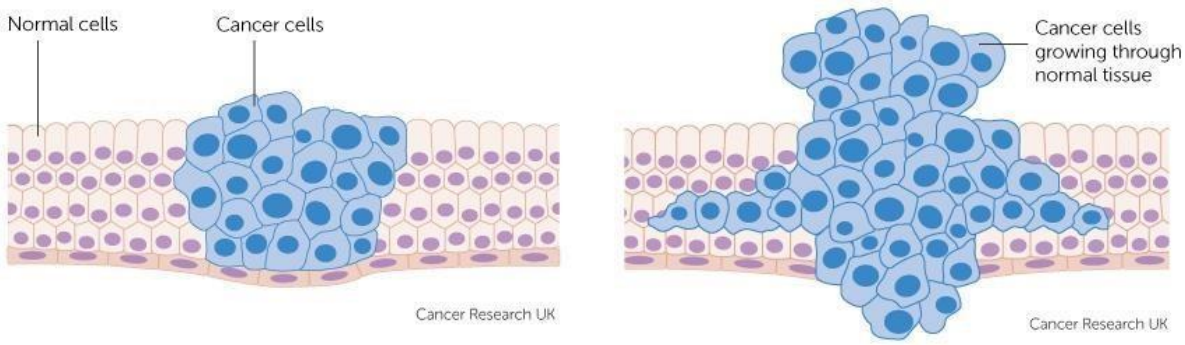
Clinical cancer is the result of a multi-phase process that includes the individual cell and its micro-environment in a series of biochemical and biophysical events. These include epigenetic events like modifications to membranes and receptors, shifts in the host's immunologic and metabolic state, and mutations, gene damage and repair, additions, and activations and repressions. Generally speaking, it is uncertain whether many of these events are sequential or irreversible, nor is it known with certainty what their molecular makeup is. While some events are thought to be epi-phenomena, others are thought to be limiting steps that are essential or necessary for the induction of cancer.Broadly speaking, the molecular makeup of several such

Whether an event is sequential or irreversible is unknown with certainty. Typically,
believed that certain occurrences are essential or crucial for the induction of cancer and serve as limiting steps;
Others could be epiphenomena. Modifications to specific oncogenes could be a crucial mechanism
step in certain cancers, while in others they might be relevant as biomarkers for diagnosis and
forecast.It has been recognized that any number of exogenous or endogenous, including genetic, factors might either directly or indirectly initiate the entire process. The statement in the IARC monographs that 'cancer can be induced by a range of different mechanisms which cannot as yet be defined or accurately measured' (IARC, 1982) probably still holds true for the majority of tumors. These stimuli vary from defined complete carcinogens to multiple as yet poorly identified enhancing factors.

WHAT IS CANCER

Cancer is a disease in which some of the body's cells grow
uncontrollably and spread to other parts of the body.

FIGURE NO.1



METHODS OF TREATMENT OF CANCER

- ✓ Surgery.
- ✓ Chemotherapy.
- ✓ Radiation Therapy.
- ✓ Targeted Therapy.
- ✓ Immunotherapy.
- ✓ Stem Cell or Bone Marrow Transplant.
- ✓ Hormone Therapy.
- ✓ Gene Therapy

HISTORY AND DEVELOPMENT OF GENE THERAPY

- ✓ Gene therapy is being studied as a treatment for several illnesses, including severe combined immunodeficiencies (SCID). Hemophilia Parkinson's illness Cancer HIV 1960:
- ✓ Gene therapy concepts were first presented 1970:
- ✓ In 1990, the National Institute of Health in the United Kingdom approved the first gene therapy case. Friedmann and Roblin, authors of a paper in Science titled "Gene treatment for human genetic disease?", mention this as the first attempt at performing gene therapy. Ashanti DaSilva, a four-year-old girl, was the patient. She was receiving treatment for a genetic defect that caused a deficiency in her immune system.
  The reference: (https://www.intechopen.com/chapters/49480)

WHAT IS GENE THERAPY:

Since the damaged or absent genes can contribute to cancer, gene therapy is an experimental treatment that involves introducing genetic material into your cells to give them a new function or restore a function that has been lost.
Gene therapy is the process of delivering genetic elements to immune response cells or cancer cells in order in order to stimulate an immune response against the cancer cells or correct abnormalities in the cancer tissue.Gene therapy aims to introduce a healthy gene in place of a defective or absent one, changing the molecular makeup of cancer cells. A "Vector," which is typically an inactive virus or liposome, transports the new gene to the target cell.

Approaches:

- Modification of tumour cells
- Sensitization of normal tissues or tumour cells
- Modulation of tumour invasiveness
- Enhancement of the antitumor immune response

HOW IT WORKS??

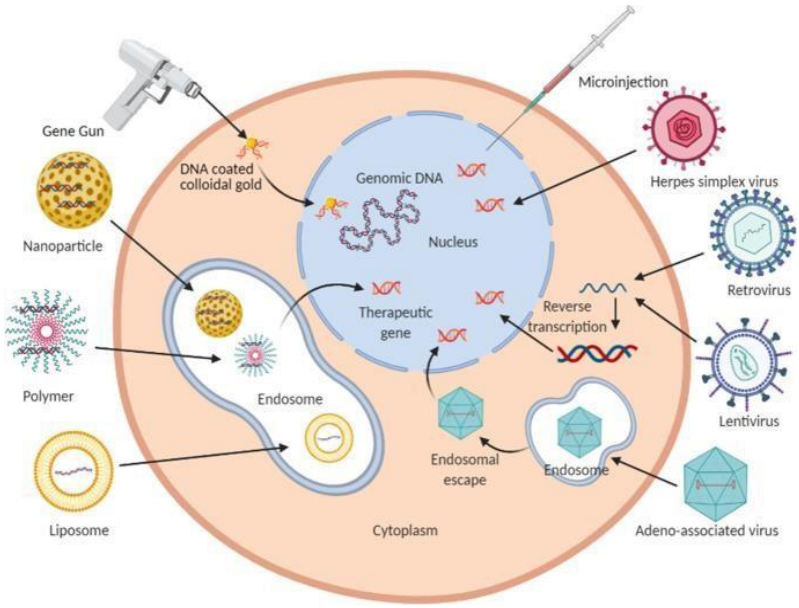
A. Local anesthetic was applied, and an inert virus (AAV-2 GAD) was used. Introduce the GAD gene into the patient's subthalamic nucleus. As the disease worsens, the gene causes cells to start producing GABA neurotransmitters, which help to restore the normal chemical balance.
B. implementing a suitable gene into the target cell is the second step in gene therapy after it has been identified. The genes have been inserted into the cells using a variety of vehicles, or vectors, including cell-based carriers, nonviral vectors, and viral vectors. In cancer gene therapy, retroviruses, adenoviruses, and adenoassociated viruses are the most frequently used viral vectors.
A different approach is to use fat droplets known as liposomes or nanoparticles to introduce the therapeutic genetic elements into the cancer cells. The genes themselves can be administered locally or systemically in the form of unpackaged DNA or DNA in the form of particles.

Targets for gene therapy of cancer:

The primary goal of current gene therapy research has been inserting the genes into the tumor.
cells to forestall the development of tumor vasculature and the function of oncogene expression, or to elicit the immune system to react unfavorably to the cancerous tissue. The primary objectives of Gene therapy is demonstrated as
1. Genes known as tumor suppressors (p53, RB, APC, BRCA1)
2. Oncogenes, such as HPV E6E7, MET, RAS, BCL-2, MYC, and ERBB2.
3. Enzymes involved in the metabolism of drugs, such as carboxypeptidase A, cytochrome p450, purine nucleoside phosphorylase, and HSV-thymidine kinase.
4. Using oncolytic vectors to directly kill cells
5. Angiogenesis (tissue factor, Tie2, endostatin, angiostatin, VEGF, etc.)
6. Cytokines (GM-CSF vb, IL-12, and IL-2)
7. Immune system (T-cell receptor)/cancer vaccines (polynucleotide vaccines, transgenic dendritic cell-based vaccines, adoptive immunotherapies, and antigens specific to a given tumor)

Gene transfer systems of cancer gene therapy

Figure no2



- ✓ Genes can enter tumor cells through three main methods: cell-based vehicles, viral vectors, and nonviral vectors.
- ✓ In the majority of tumors, the tumor cells may be killed by the relatively short-term expression of therapeutic genes. Synthetic gene delivery vectors have been made possible by the quick removal of viral vectors from the bloodstream. Nonetheless, transporting the relevant DNA to the far-off metastatic deposits is a significant disadvantage of these methods.

- ✓ Typically, local tumor injections have been used to introduce nonviral gene delivery vectors.
  Whilst local injection makes sense for certain tumors like melanoma, head and neck cancers, or peritoneal carcinomatosis, patients with hematogenous metastases should not use it.
- ✓ The nonviral gene therapy vectors have the same limitations as the viral vectors.
  In order to be stopped in the target tumor tissue, they must endure through the bloodstream, spread, attach to particular cells, enter those cells, and eventually make their way to the nucleus.

CONCLUSION

Gene therapy is a cutting-edge treatment option for illnesses for which there is currently no effective treatment. In the past three decades, gene therapy has made significant strides in the treatment of cancer; some drugs have been approved, while others are still in clinical trials. When it comes to cancer treatment, gene therapy is generally safer and has more manageable side effects than chemotherapy. Future advancements in tumor genomic analysis, host humoral and immune cell evaluation, and patient matching will improve the process of choosing the best candidates for gene therapy. Advances in the creation of secure and efficient gene delivery vectors and comprehension of nuclease activity pave the way for the potential use of genome editing in the treatment of incurable illnesses such as cancer.

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