IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 3, December 2023

Review on Gene Therapy for Cancer

Sayali Arun Ingle, Farah Khan, Reshma Sawale
New Montfort Institute of Pharmacy, Asht, Wardha, Maharashtra
inglesayali10@gmail.com

Abstract: *Advances in our understanding of the mechanisms by which tumor cells detect drug-induced DNA damage leading to apoptotic death have aided in the design of novel, potentially more selective strategies for cancer treatment. Several of these strategies use proapoptotic factors and have shown promise in sensitizing tumor cells to the cytotoxic actions of traditional cancer chemotherapeutic drugs. Although antiapoptotic factors are generally regarded as poor prognostic factors for successful cancer chemotherapy, strategies that use antiapoptotic factors in combination with suicide or other gene therapies can also be considered. The introduction of antiapoptotic factors that act downstream of drug-induced mitochondrial transition delays, but does not block, the ultimate cytotoxic response to cancer chemotherapeutic drugs that activate a mitochondrial pathway of cell death.*

Keywords: Angiogenesis; Cancer; Gene therapy; Interferon; Angiostatin; Endostatin

I. INTRODUCTION

Cancer is the most common cause of death in developed countries. Many patients, by the time of presentation, have already developed secondary tumors (metastases), which are generally responsible for fatalities. Conventional therapies for cancer such as chemotherapy and radiotherapy are characterized by poor survival rates due to multiple factors including tumor development of drug-resistance and their lack of tumor specificity, resulting in undesirable side effects on healthy cells and therefore limitations on therapeutic dose[1,2].

II. TYPES OF GENE THERAPY

TUMOR SUPPRESSOR GENE THERAPY

Tumor suppressor genes are involved in cellular checkpoint control, preventing the passage of cells with damaged DNA or other cellular damage through the cell cycle. The p53 tumor suppressor gene plays a critical regulatory role in determining the fate of a cell after apoptotic signaling and DNA damage, through its transcriptional activation of p21, a potent inhibitor of cyclin D1–mediated G1/S transition[3.]

SUICIDE GENE THERAPY

Suicide genes, so called because they induce cell death, encode an enzyme product capable of converting a prodrug into a cytotoxic compound. Suicide gene therapy involves delivering the suicide gene (not normally present) to the target cells and then administering the prodrug. Delivery of the suicide gene is generally accomplished by injecting a viral vector containing the suicide gene directly into the tumor mass, thereby infecting tumor cells, though variations exist. An inherent limitation of all viral-based cancer gene therapy protocols is the inability to transduce the entire tumor cell population[4.]

ANTIANGIOGENIC GENE THERAPY

Tumor growth and survival depend on angiogenesis to provide a path for delivery of oxygen and nutrients to tumor cells. Without this process of blood vessel recruitment, tumor growth is limited to 1–2 mm2, the diffusion limit of oxygen. In 1971,Folkman proposed that tumor growth could be arrested by blocking angiogenesis[20]. Furthermore, metastasis may also be prevented, since the formation of tumor vasculature seems to be a requisite for it. This promoted a widespread search for proangiogenic factors associated with neovascularization and tumor vessel maturation5.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 3, December 2023

Strategies for vector-mediated cancer gene therapy :

Toxic transgene products :

- Transfer of tumor suppressor genes.
- Suicide genes-Enzyme/pro-drug approach.
- Expression of antisense, ribozymes or siRNAs for dominant oncogenes.

Immunomodulatory approaches :

- Expression of cytokines
- Expression of costimulatory molecules
- Expression of tumor specific antigens

Other strategies :

Expression of molecules that affect angiogenesis, cell adhesion and metastasis

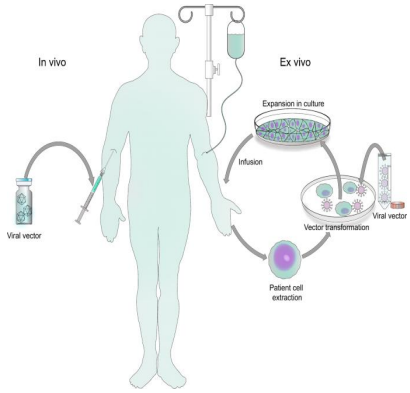
- Chemoprotection of stem cells.
- Expression of cell surface receptors/ligands to target cancer cells.
- Tumor-specific promoter driven transgene expression.
- Replicating (oncolytic) vectors[6].

Gene Transfer Methods and Vectors Used for Gene Therapy :

The challenge in gene therapy is to deliver an adequate amount of genetic material into target cells or tissues and to maintain gene expression for a desired period of time. Genetic material can be introduced to their target cells or tissues via different methods of delivery. In principle, we can group them into: (1) physical; (2) viral; (3) non-viral methods; and (4) bacterial or yeast. Electroporation, ultrasound, and gene gun deliveries are examples of physical methods that have been used. As the name already implies, with viral vectors a biological (*i.e.*, virus) vector is used as a vehicle to deliver the genetic material into the cells, whereas with non-viral gene transfer methods a synthetic carrier (liposomes or nanoparticles) is used. Different vectors have different properties inrelation to their transduction efficiency and their efficacy to express the introduced genes. In addition, they differ in respect of the duration of expression of the transgene, as well as their safety profile[7].

1.Viral Vectors :

The most commonly used viral vectors used for gene transfer are adenoviruses, and retroviruses (including the human immunodeficiency virus (HIV)), vaccinia viruses, adeno associated viruses (AAV), and baculoviruses. These vectors differ from each other regarding their cell tropisms, expression profiles, transgene capacities, immunogenicity, as well as different duration of transgene expression. In addition to their origin, viral vectors can be divided into integrating and non-integrating vectors. Adenoviruses and baculoviruses are examples of non-integratingvectors[8].

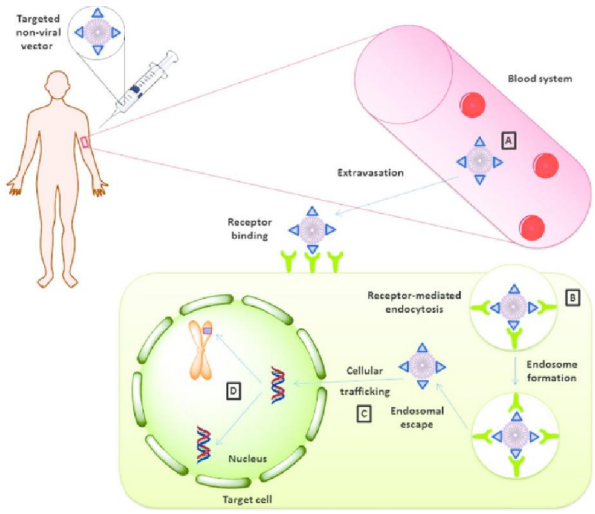


IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 3, December 2023

2. Non Viral Vectors :

The simplest form of a non-viral system is anaked plasmid DNA. The advantage of naked plasmid is that it poses the lowest form of toxicity or other unwanted reactions. In addition, it is easy to formulate and inexpensive to produce. However, its disadvantage is the low transfection efficiency compared to viral-mediated gene transfer . As a result, to improve transfection efficiency, cationic polymers, or lipids formulations have been developed to condense plasmid DNA to protect the degradation of DNA and to enhance uptake and transfection of plasmids.

The advantage with those formulations is that polymers or lipids can comparatively easily be designed toattain certain properties. For example, non-viral vectors can easily be targeted to a target tissue or cell by coupling of cell- or tissue-specific targeting moieties on the carrier[9].



III. CONCLUSION

Once gene delivery problems are solved, RNAi gene therapy of brain cancer, and gene therapy of cancer in general, can move from monogenic to polygenic forms of therapy. Cancer arises from the mutation of multiple genes within a single cell.

Therefore, it is unlikely that the targeting of a single mutated gene will result in a cancer cure. Rather, gene therapy should be directed at multiple gene targets simultaneously, just as chemotherapy of cancer employs multiple drugs simultaneously. Polygenic gene therapy may simultaneously knockdown oncogenic genes, as with RNAi-based gene therapy or replace mutated tumor suppressor genes with replacement gene therapy. However, gene therapy of cancer has not moved beyond the monogenic phase because progress in this area has been slowed by the gene delivery problem[10].

REFERENCES

[1]. Russell RCG, Williams NS, Bulstrode CJK. Bailey & Love's short practice of surgery. Arnold 2000.

[2]. Walther W, Stein U. Viral vectors for gene transfer: A review of their use in the treatment of human diseases. Drugs 2000; 60(2):249-71.

[3]. Springer CJ, Niculescu-Duvaz I. 2000.Prodrug-activating systems in suicide gene therapy. *J. Clin. Invest.* 105:1161–67

[4]. Thomas CE, Ehrhardt A, Kay MA. Progress and problems with the use of viral vectors for gene therapy. Nat Rev Genet 2003; 4:346-58.

[5]. Pathak, A.; Patnaik, S.; Gupta, K.C. Recent trends in non-viral vector-mediated gene delivery. *Biotechnol0gy. J.* **2009**, *4*, 1559–1572.

[6]. Escoffre, J.M.; Teissie, J.; Rols, M.P. Gene transfer: How can the biological barriers be overcome? *J. Membr. Biol.* **2010**, *236*, 61–74