

Chapter 3

Gene Drug Delivery for the Treatment of Cancer

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ABSTRACT

Gene drug delivery is a pivotal approach in modern cancer treatment, offering targeted therapies that overcome the limitations of conventional methods. This chapter delves into the significance of gene therapy in oncology, highlighting key mechanisms like gene silencing, suicide genes, and tumor suppressor gene replacement to inhibit cancer progression. Advanced delivery systems are essential for effective gene therapy. The chapter explores nanocarriers and both viral and nonviral gene delivery methods as critical tools for improving precision. Gene editing technologies like CRISPR-Cas9 are also investigated for their potential to transform treatment. The integration of gene therapy with other modalities, such as immunotherapy and personalized medicine, is proposed as a way to improve patient outcomes. Future directions and developing trends in gene therapy, including innovations in delivery technologies and the persistent obstacles in clinical translation, are also explored. This chapter offers a concise overview of the current and future prospects of gene therapy in cancer treatment.

1. INTRODUCTION

Since the beginning of the 21st century, tumors continue to pose a significant and serious danger to human life and well-being. There is a pressing need for additional research in cancer detection and treatment. Currently, chemotherapy is the main therapeutic approach used in clinical practice to treat tumors. Nevertheless, despite the evident therapeutic impact, chemotherapy also generates unavoidable

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side effects, including harm to healthy tissues/cells and intense pain, which greatly afflict patients. Hence, it is of paramount importance to design treatments that effectively cater to the needs and preferences of cancer patients. Researchers must comprehend the fundamental process of tumors (Li et al., 2023). In 2001, two separate preliminary copies of the human genome sequence were published, along with the simultaneous discovery of some 30,000 genes (Lander et al., 2001). Subsequently, there was a comprehensive investigation in molecular genetics, employing sophisticated techniques to analyze gene activity and investigate the biological mechanisms underlying genetic abnormalities and the development of cancer (Dulbecco, 1986). The recent growth in understanding of cancer has led to the development of novel treatment techniques in cancer management, particularly gene therapy (Strachan & Read, 1999). Theodore Friedmann first introduced the idea 45 years ago that a gene might be transplanted into specific cell types and its activation could lead to therapeutic efficacy, greatly improving patient outcomes. George Stamatoyannopoulos, a founding member of the American Society of Gene and Cell Therapy, enthusiastically supported and implemented this notion afterwards. In this scenario, the medicine, referred to as a gene in the context of gene therapy, is enclosed within a vector that facilitates its delivery into the patient's cells. Undoubtedly, the concept of gene therapy has expanded, and in broad terms, gene therapy is used to describe a treatment method that involves altering the genetic composition of a patient's cells using nucleic acid (Papanikolaou & Bosio, 2021).

Gene therapy became possible due to the revolutionary recombinant DNA technology developed in 1970. Initially, various techniques, such as physical methods (hydrodynamic pressure, electroporation, gene guns, and ultrasound), chemical methods (peptide-mediated and lipid-mediated), and viral vectors (adenoviruses, helper-dependent adenoviruses, retroviruses, and lentiviruses), were created with therapeutic purposes in mind (Niidome & Huang, 2002).

The FDA recently approved a gene therapy for ADA-SCID (a severe combined immunodeficiency caused by an ADA gene mutation). This therapy inserts a functional ADA gene into the patient's stem cells, allowing them to produce a crucial enzyme that restores immune function. It provides a longer-lasting alternative to bone marrow transplants and enzyme replacement therapies, which have limitations, especially if no matching donor is available (Aiuti et al., 2017).

Chemotherapy is a conventional and widely employed approach for treating cancer. Chemotherapy functions through multiple mechanisms, but its primary purpose is to eliminate actively dividing cells, both cancerous and healthy, which leads to significant side effects such as alopecia, myelosuppression, and gastrointestinal complications (Zitvogel et al., 2008). Hence, the primary focus of a significant portion of cancer research in the past few decades has been to discover drugs that specifically target tumour cells rather than healthy ones. Despite the

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