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# Research on Target Peptides and siRNA Delivery Systems in Lung Cancer Targeted Therapy

**Hongsen Ye**

Chengdu lie Wu Middle school, Chengdu, Sichuan, 610056, China
Email: Jason211111ye@gmail.com

**Abstract:**

With the development of gene silencing technology and siRNA, significant potential has been demonstrated in cancer treatment, garnering widespread attention. siRNA specifically targets and degrades certain mRNA, thereby inhibiting the expression of corresponding proteins. It has shown great promise in applications such as cancer, viral infections, and genetic diseases. However, the effective delivery of siRNA has been a major challenge for its clinical application. This paper focuses on discussing the mechanisms and advantages of siRNA delivery systems and introduces the current challenges and research issues faced by siRNA, such as the application mechanisms, dosage, and toxicity of targeted peptides and siRNA delivery systems.

**Keywords:** siRNA therapy, lung cancer, targeted peptides, treatment safety, nanoparticles

## 1. Introduction

Lung cancer is one of the most common cancers worldwide and a leading cause of death. According to data from the World Health Organization, estimates by the International Agency for Research on Cancer (IARC) in GLOBOCAN 2020 show that lung cancer remains the leading cause of cancer death, with an estimated 1.8 million deaths (18%) in 2020[1]. A study published on Springer Link indicates that, with high and rising smoking rates in many Asian and developing countries, the incidence of lung cancer and the resulting deaths are expected to increase in the coming decades. By 2030, it is estimated that 70% of tobacco-related deaths will occur in developing and low-income countries [2]. Currently, conventional treatment methods include surgical resection, radiation therapy, and chemotherapy, but these approaches are limited by various factors such as significant side effects, drug resistance, and suboptimal treatment outcomes.

## 2. Application of Target Peptides in Lung Cancer Targeted Therapy

The primary approach involves utilizing specific small peptides to selectively target and inhibit the proliferation and metastasis of lung cancer cells. These peptide molecules demonstrate high selectivity, enabling them to recognize and bind to specific molecular targets expressed on the surface of lung cancer cells. This binding facilitates the induction of apoptosis or inhibits cellular functions in tumor cells, while minimally affecting normal cells.

### 2.1 . Types and Advantages of Target Peptides

Targeting peptides can be broadly categorized into three types: diagnostic peptides, therapeutic peptides, and imaging peptides.

Diagnostic Peptides: These are used for disease diagnosis and can specifically bind to disease markers.

Therapeutic Peptides: These are used in treatment to directly intervene in the pathological processes.

Imaging Peptides: Used in medical imaging, these peptides help in labeling and observing specific cells or tissues within imaging techniques.

Targeting peptides offer several advantages. They demonstrate high specificity to their targets at nanomolar concentrations and are inherently low in toxicity, causing negligible harm to the normal tissues surrounding tumors. These peptides are quickly cleared at non-target sites. Moreover, they are easily synthesized and can be optimized to better bind to targets. Their structures can be modified to increase stability against proteolytic degradation, extend their half-life in the bloodstream, and enhance permeability through capillaries[3].

### 2.2 . Mechanism of Target Peptides Binding to Lung Cancer Cells

Targeting peptides are typically designed to recog-

nize and bind to molecules specific to lung cancer cells. These target proteins are either overexpressed or play a crucial role in the progression of lung cancer. When targeting peptides bind to their specific receptors or surface molecules, they can induce conformational changes in the receptors, triggering a series of downstream signaling events. These events may lead to inhibition of cell growth, cell death, or other anti-tumor responses. Some targeting peptides may induce lung cancer cell death by activating the apoptotic pathways of the cells. Furthermore, targeting peptides can also inhibit tumor growth and metastasis. They can affect the migration and invasion capabilities of tumor cells by interfering with the degradation of the extracellular matrix, affecting the expression of cell adhesion molecules, and thereby inhibiting tumor growth and metastasis.

3.Application of siRNA Delivery Systems in Lung Cancer Targeted Therapy

The delivery of siRNA requires safe and efficient carrier systems. Therefore, various types of carriers are needed, which can be either viral, such as adenovirus or retrovirus systems, or non-viral, such as nanoparticles, liposomes, and polymers. Additionally, siRNA delivery systems can be used alone or in combination with other treatment methods (such as chemotherapy or radiation therapy) to enhance therapeutic effects.

## 3.1 . Advantages of siRNA

Compared to traditional treatment methods, siRNA therapy offers the advantages of strong specificity, improved therapeutic effects, and fewer side effects. siRNA has high specificity and can precisely target specific genes, reducing the impact on normal cells [3]. Additionally, the therapeutic effect is enhanced; by using targeting peptides, siRNA accumulates at lung cancer target sites, enhancing the silencing effect, increasing the sensitivity of lung cancer to drugs, reducing resistance, and thus enhancing the therapeutic outcome. siRNA also features high stability. Inhalable siRNA nanoparticle drugs have shown significant potential in treating KRAS-mutated lung cancer. These drugs have good nebulization stability, lung mucosa penetrability, and targeting of lung tumors, successfully achieving anti-tumor effects against in situ KRAS-mutated non-small cell lung cancer [4].

## 3.2 . Various siRNA Delivery Systems

The purpose of siRNA delivery systems is to efficiently transport siRNA molecules into cells, thereby achieving the silencing of specific genes. There are various types of siRNA delivery systems, such as viral delivery systems, lipid-based delivery systems, targeted delivery systems, and carrier-free direct delivery. These methods aim to enhance the bioavailability and stability of anticancer drugs in targeted lung areas.

### 3.2.1 . Viral Delivery Systems

Viral vectors have become a popular tool for gene delivery due to their high efficiency in transducing target cells. Modified viruses such as adenoviruses, adeno-associated viruses (AAV), retroviruses, and lentiviruses are commonly used in these systems [5].

### 3.2.2 . Targeted Delivery Systems

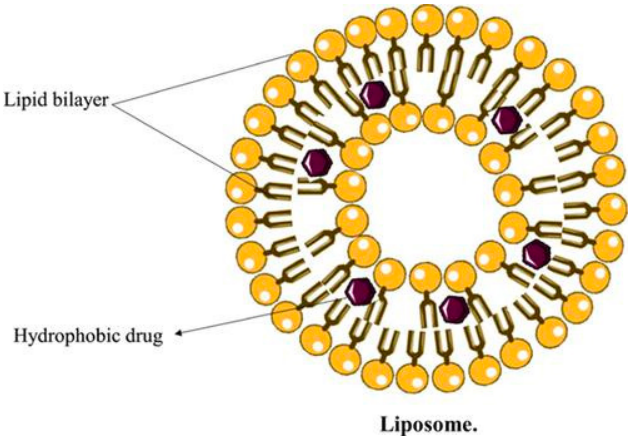
Targeted delivery systems aim to increase the therapeutic efficacy and reduce side effects by directing drugs or genes specifically to the target cells or tissues. This can be achieved through ligand-receptor interactions, antibody targeting, or the use of magnetic nanoparticles [6].

### 3.2.3 . Carrier-Free Direct Delivery

Carrier-free direct delivery methods, such as electroporation, gene gun, ultrasound, and naked DNA injection, involve the direct introduction of therapeutic agents into cells. These techniques circumvent carrier-associated toxicity and immunogenicity but often require optimization to improve efficiency [7].

### 3.2.4 . Lipid-Based Delivery Systems

Lipid-based delivery systems, including liposomes and lipid nanoparticles, have emerged as promising carriers for drug and gene delivery. These systems offer advantages such as biocompatibility, low immunogenicity, and the ability to encapsulate both hydrophilic and hydrophobic agents [8].




Liposome.

**Figure 1**

Figure 1 describes a typical siRNA delivery system known as the lipid-based delivery system. Liposomes are tiny artificial vesicles consisting of one or more lipid

bilayers formed by phospholipid molecules. The heads of these phospholipid molecules are hydrophilic, facing the aqueous environment inside and outside the vesicle, while their tails are hydrophobic, located inside the bilayer. In this model, liposomes are used to encapsulate hydrophobic drugs, which are embedded within the lipid bilayer.

## 4. Combined Application of Target Peptides and siRNA Delivery Systems

The combined application of peptides and siRNA delivery systems often faces several challenges, such as the selection of targeting peptides, the design and synthesis of siRNA, and the construction of the delivery system.

Selection of Targeting Peptides: The choice of targeting peptides is based on their ability to recognize and bind to specific receptors or markers associated with disease cells. This selection ensures that the delivery system can accurately transport siRNA to the target cells.

Design and Synthesis of siRNA: siRNA works through the RNA interference (RNAi) mechanism to silence disease-related genes. Designing the appropriate siRNA sequence is crucial for ensuring effective gene silencing.

Construction of the Delivery System: It is generally necessary to construct a delivery carrier that can load both the targeting peptide and siRNA. Common carriers include lipid nanoparticles, polymer nanoparticles, and others. The carrier needs to have good biocompatibility and sufficient protective properties to prevent the degradation of siRNA in the body.

### 4.1. Advantages of Combined Application of Target Peptides and siRNA Delivery Systems

Targeting peptides are a class of small molecule peptides that can be used in conjunction with siRNA, utilizing their specific binding to tumor surface substances to achieve targeted effects. By combining the specificity of targeting peptides with the therapeutic action of siRNA, the accumulation of siRNA at the target site is increased, enhancing the silencing effect. This can improve the sensitivity of lung cancer to drugs and reduce resistance, thereby enhancing the effectiveness of lung cancer treatment.[3]

5.conclusion

Research on targeting peptides and siRNA delivery systems for lung cancer targeted therapy has improved significantly, but still faces several challenges:

1.High Cost and Long Production Cycles: The chemical synthesis of siRNA is costly, and the customization cycle is typically long, depending on the synthesis and purification options.

2.Susceptibility to Degradation: Chemically synthesized siRNA shares the normal characteristics of RNA, which makes it prone to degradation, thereby limiting its durability of action.

3.Dependence on Viral Vectors with High Infectivity Diversity: Some siRNA expression vectors rely on viral carriers with high infectivity diversity, which demands high gene transfer requirements. Additionally, producing high-efficiency recombinant adenoviruses is challenging, increasing the complexity of operations.

Addressing these issues presents significant challenges that need to be overcome to enhance the effectiveness and feasibility of siRNA-based therapies for lung cancer.

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