

The role of non-coding RNAs in cancer progression and therapy.

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Abstract

Cancer is a complex disease that results from the accumulation of genetic and epigenetic alterations in cells. Over the years, several studies have identified various molecular mechanisms that contribute to the initiation, progression, and metastasis of cancer. One such mechanism involves the deregulation of non-coding RNAs (ncRNAs), which have emerged as important regulators of gene expression in cancer cells. In this article, we will discuss the role of ncRNAs in cancer progression and therapy.

Keywords: Non-coding RNAs, Cancer progression, Cancer therapy, Antisense oligonucleotides, Delivery strategies.

Introduction

Non-coding RNAs (ncRNAs) are RNA molecules that are transcribed from DNA but do not code for proteins. They are broadly classified into two main categories: long non-coding RNAs (lncRNAs) and small non-coding RNAs (sncRNAs). The latter category includes microRNAs (miRNAs), small interfering RNAs (siRNAs), and piwi-interacting RNAs (piRNAs). These molecules are involved in a wide range of cellular processes, including gene regulation, chromatin remodeling, and protein synthesis. Several studies have shown that ncRNAs play important roles in cancer progression. For example, lncRNAs such as HOTAIR, MALAT1, and ANRIL have been shown to promote cancer cell proliferation, invasion, and metastasis by regulating the expression of various genes involved in these processes [1].

Similarly, miRNAs such as miR-21, miR-155, and miR-221/222 have been shown to promote cancer progression by targeting tumor suppressor genes and/or genes involved in apoptosis and cell cycle regulation. One of the ways in which ncRNAs contribute to cancer progression is by regulating the expression of genes involved in the epithelial-mesenchymal transition (EMT). EMT is a process by which epithelial cells lose their cell-cell contacts and acquire mesenchymal-like characteristics, such as increased motility and invasiveness. This process plays a critical role in cancer metastasis, as it allows cancer cells to invade surrounding tissues and migrate to distant sites in the body. Several lncRNAs and miRNAs have been shown to regulate EMT by modulating the expression of genes involved in this process [2].

In addition to their role in cancer progression, ncRNAs also have therapeutic potential. Several studies have shown that targeting ncRNAs can inhibit cancer cell growth and metastasis in preclinical models. For example, inhibition of HOTAIR, MALAT1, or ANRIL has been shown to reduce tumor growth and metastasis in various cancer types. Similarly, inhibition of

miR-21, miR-155, or miR-221/222 has been shown to reduce cancer cell proliferation, invasion, and metastasis. One of the advantages of targeting ncRNAs is their specificity. Unlike traditional chemotherapy drugs, which target rapidly dividing cells, ncRNA-based therapies can target specific cancer cells without affecting normal cells. This can reduce the side effects associated with traditional chemotherapy drugs, such as hair loss, nausea, and fatigue [3].

Several ncRNA-based therapies are currently in development or clinical trials. For example, a phase II clinical trial is currently underway to evaluate the safety and efficacy of a miR-34a mimic in patients with advanced solid tumors. MiR-34a is a tumor suppressor miRNA that is downregulated in various cancer types. The mimic is designed to restore the expression of miR-34a in cancer cells, which is expected to inhibit cancer cell proliferation and promote apoptosis.

Another promising ncRNA-based therapy is the use of antisense oligonucleotides (ASOs) to target lncRNAs. ASOs are short RNA molecules that can bind to specific RNA sequences and induce their degradation. Several studies have shown that ASOs targeting lncRNAs can effectively inhibit cancer cell growth and metastasis in preclinical models. For example, ASOs targeting HOTAIR have been shown to reduce tumor growth and metastasis in breast cancer and pancreatic cancer models. Similarly, ASOs targeting MALAT1 have been shown to reduce tumor growth and metastasis in lung cancer and colorectal cancer models [4].

However, there are several challenges associated with ncRNA-based therapies. One of the main challenges is the delivery of the therapeutic molecules to cancer cells. Since ncRNAs are large and charged molecules, they cannot easily cross the cell membrane and reach their target site. Various delivery strategies have been developed to overcome this challenge, including the use of lipid nanoparticles, viral vectors, and cell-penetrating peptides. Another challenge is the specificity

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of ncRNA-based therapies. While ncRNAs are generally considered to be specific regulators of gene expression, they can also have off-target effects. This can result in unintended consequences, such as the inhibition of genes involved in normal cellular processes. To address this challenge, it is important to carefully select the target ncRNA and validate its specificity in preclinical models [5].

Conclusion

In, ncRNAs play important roles in cancer progression and therapy. They are involved in a wide range of cellular processes, including gene regulation, chromatin remodeling, and protein synthesis. Targeting ncRNAs can inhibit cancer cell growth and metastasis in preclinical models, and several ncRNA-based therapies are currently in development or clinical trials. However, there are several challenges associated with ncRNA-based therapies, including the delivery of the therapeutic molecules to cancer cells and the specificity of the therapies. Future research in this field is needed to overcome these challenges and develop effective ncRNA-based therapies for cancer.

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