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Dual effects of circular RNAs in thyroid and breast cancer: A complex interplay

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INTRODUCTION

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. Cancer is a multifaceted and complex disease that involves a multitude of genetic and molecular factors. Thyroid cancer and breast cancer are two of the most common cancer types affecting individuals worldwide. Recent research has shed light on the involvement of circular RNAs (circRNAs) in the development and progression of these cancers. CircRNAs are a unique class of non-coding RNAs that have garnered significant attention due to their intricate regulatory roles in various biological processes, including cancer. In this article, we will explore the dual effects of circRNAs in thyroid and breast cancer. We will discuss how circRNAs can act both as oncogenic drivers and tumor suppressors, depending on their specific molecular functions and targets. Understanding this duality is crucial for developing more targeted and effective cancer therapies.

DESCRIPTION

Circular RNAs: An overview

Circular RNAs, a class of non-coding RNAs, were once considered byproducts of pre-mRNA splicing errors. However, recent studies have revealed their critical roles in regulating gene expression at various levels. Unlike linear RNAs, circRNAs form closed loops and lack 5' caps and 3' polyadenylated tails, making them highly stable and resistant to exonucleases. These unique properties contribute to their long half-lives and functional significance.

CircRNAs are produced through a process known as back-splicing, where a downstream splice donor site joins an upstream splice acceptor site, resulting in a covalently closed loop structure. They can be categorized into three main types: Exonic circRNAs (ecircRNAs), circular intronic RNAs (ciRNAs) and Exon-Intron circRNAs (EIciRNAs), depending on the regions from which they are derived. CircRNAs are involved in diverse cellular processes and their dysregulation has been linked to various diseases, including cancer.

CircRNAs in thyroid cancer

Thyroid cancer is one of the fastest-growing cancer types worldwide, with a rising incidence over the past few decades. The role of circRNAs in thyroid cancer is still a

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topic of ongoing research, but recent findings have revealed their complex involvement in this disease. CircRNAs can exert both oncogenic and tumor-suppressive effects in thyroid cancer.

Oncogenic circRNAs in thyroid cancer

CircFOXO3: CircFOXO3 has been found to be upregulated in thyroid cancer tissues and cell lines. It promotes thyroid cancer cell proliferation, migration and invasion by sponging miR-149-5p, which, in turn, derepresses the oncogene FZD4. High expression of CircFOXO3 is associated with advanced tumor stages and poor prognosis in thyroid cancer patients.

CircRNA_100290: CircRNA_100290 is overexpressed in thyroid cancer and promotes cell proliferation and migration. It acts as a sponge for miR-29b-3p, which leads to increased expression of the oncogene PHLDB2. Silencing of CircRNA_100290 reduces tumor growth and metastasis in thyroid cancer.

Tumor-suppressive circRNAs in thyroid cancer

Circ-ITCH: Circ-ITCH is downregulated in thyroid cancer and negatively regulates the Wnt/β-catenin pathway. It functions as a sponge for miR-22-3p and miR-7-5p, leading to the inhibition of thyroid cancer cell proliferation and invasion. Restoring Circ-ITCH expression can suppress tumor growth and improve the prognosis of thyroid cancer patients.

CircRNA-0067934: CircRNA-0067934 acts as a tumor suppressor in thyroid cancer. It functions by sponging miR-1323, which targets the oncogene ZEB2. CircRNA-0067934 inhibits cell proliferation and migration, highlighting its potential as a therapeutic target.

CircRNAs in breast cancer

Breast cancer is the most common cancer among women and research into the roles of circRNAs in this disease has intensified in recent years. Just like in thyroid cancer, circRNAs play a dual role in breast cancer, acting as both oncogenic drivers and tumor suppressors.

Oncogenic circRNAs in breast cancer

CircHIPK3: CircHIPK3 is upregulated in breast cancer and promotes cancer cell proliferation, migration and invasion. It acts as a sponge for multiple miRNAs, such as miR-124 and miR-124-3p, which relieve the inhibition of oncogenes. High levels of CircHIPK3 are associated with poor prognosis in breast cancer patients.

Circ_0006528: Circ_0006528 is overexpressed in breast cancer tissues and cell lines. It promotes cell proliferation and inhibits apoptosis by sponging miR-7. Silencing Circ_0006528 inhibits tumor growth and metastasis in breast cancer.

Tumor-suppressive circRNAs in breast cancer

CircRNA-000911: CircRNA-000911 is downregulated in breast cancer and inhibits cell proliferation and migration. It acts as a sponge for miR-449a, which targets the oncogene HDAC1. Restoring circRNA-000911 expression can suppress tumor growth and improve the prognosis of breast cancer patients.

Circ-DB: Circ-DB acts as a tumor suppressor in breast cancer by sponging miR-34a and miR-21. It inhibits cell proliferation, migration and invasion by regulating the Wnt/β-catenin pathway. Overexpression of circ-DB reduces tumor growth and metastasis in breast cancer.

CONCLUSION

Circular RNAs, once considered genetic anomalies, have emerged as critical regulators of gene expression with a complex dual role in cancer, particularly in thyroid and breast cancer. These small, stable RNA molecules can function as either oncogenic drivers or tumor suppressors, depending on their specific targets and the cellular context. The oncogenic circRNAs promote cancer progression by sponging miRNAs that would otherwise inhibit the expression of oncogenes. In contrast, tumor-suppressive circRNAs act as negative regulators of cancer cell growth and migration by sequestering miRNAs that target oncogenic pathways.

The duality of circRNAs in thyroid and breast cancer underscores the importance of understanding the intricate regulatory networks within cancer cells. Harnessing the potential of circRNAs for therapeutic interventions, either by modulating their expression or targeting their downstream effectors, holds promise for more effective and personalized cancer treatments. Further research is needed to uncover the full spectrum of circRNA functions in cancer and to develop innovative strategies for diagnosing, treating and ultimately preventing thyroid and breast cancer.