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Circular RNAs: Characteristics and their potential applications in thyroid cancer

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INTRODUCTION

Thyroid cancer is one of the most common endocrine malignancies, with its incidence steadily rising in recent years. Although the prognosis for most thyroid cancer patients is favorable, there are subsets of cases that exhibit aggressive behavior and resistance to conventional therapies. Understanding the molecular mechanisms that underlie thyroid cancer is crucial for developing more effective diagnostic and therapeutic strategies. Circular RNAs (circRNAs), a class of non-coding RNAs, have emerged as significant players in various biological processes and diseases, including cancer. In this article, we will delve into the characteristics, functions, mechanisms and potential applications of circRNAs in the context of thyroid cancer.

DESCRIPTION

Circular RNAs: An overview

Circular RNAs, also known as circRNAs, are a class of non-coding RNAs that have attracted considerable attention in recent years. Unlike the more commonly known linear RNAs, circRNAs form a closed loop structure due to a covalent bond between the 3' and 5' ends, making them resistant to exonuclease degradation and more stable compared to linear RNAs. The circular structure is formed through a process known as back-splicing, where a downstream 3' splice site joins an upstream 5' splice site, resulting in a circular molecule devoid of free ends.

Characteristics of circRNAs

CircRNAs are distinguished by several notable characteristics that set them apart from other RNA species:

Stability: CircRNAs are more stable than linear RNAs because of their closed-loop structure, making them resistant to degradation by exonucleases.

Abundance: CircRNAs are widely expressed in various tissues and cell types and their expression profiles can be tissue-specific.

Conservation: Some circRNAs are highly conserved across species, suggesting their evolutionary significance.

Diverse biogenesis: CircRNAs can be derived from exonic, intronic or intergenic regions, providing a diverse source of potential functional elements.

Functions of circRNAs

CircRNAs have been implicated in various cellular processes and functions, including gene expression

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regulation, protein interaction and molecular signaling. In the context of thyroid cancer, the functions of circRNAs can be broadly categorized as follows:

MicroRNA sponging: CircRNAs can act as competitive endogenous RNAs (ceRNAs) to sequester microRNAs (miRNAs) away from their target mRNAs. This mechanism can indirectly regulate gene expression by preventing miRNAs from binding to their mRNA targets.

Protein binding: CircRNAs can interact with proteins, such as RNA-binding proteins and influence their activity. This interaction may lead to the regulation of protein function, stability or subcellular localization.

Splicing regulation: CircRNAs can modulate alternative splicing of mRNA transcripts by binding to splicing factors, thereby influencing the diversity of gene products.

Transcriptional regulation: CircRNAs can influence t he transcription of their parent genes by acting as enhancers or by sequestering transcription factors.

Translation: While circRNAs were initially considered non-coding, some recent studies have proposed that specific circRNAs may undergo translation, producing functional peptides or proteins.

CircRNAs in thyroid cancer

Several studies have explored the role of circRNAs in thyroid cancer, shedding light on their involvement in tumorigenesis, progression and potential clinical applications.

Tumor promotion: Certain circRNAs have been identified as oncogenic in thyroid cancer. For instance, circRNA_100395 has been shown to promote cell proliferation, migration and invasion in thyroid cancer by sponging miR-1228 and upregulating ADAM10.

Tumor suppression: Conversely, some circRNAs function as tumor suppressors in thyroid cancer. CircHIPK3, for example, inhibits thyroid cancer cell proliferation and invasion by acting as a miR-653 sponge and downregulating FOXM1.

Diagnostic markers: CircRNAs have demonstrated potential as diagnostic biomarkers for thyroid cancer. CircRNA_101364 has been found to be significantly upregulated in thyroid cancer tissues and is associated with lymph node metastasis, making it a potential diagnostic indicator.

Prognostic factors: The expression levels of specific circRNAs have been linked to patient prognosis in thyroid cancer. High levels of circRNA_0005728 are associated with worse overall survival, while low expression of circRNA_0000711 is linked to poorer disease-free survival.

Mechanisms of circRNAs in thyroid cancer

The mechanisms underlying the involvement of circRNAs in thyroid cancer are diverse and include miRNA sponging, protein interactions and splicing regulation.

miRNA sponging: CircRNAs in thyroid cancer often function as miRNA sponges, influencing the expression of target genes. For example, circRNA_101364 acts as a sponge for miR-149, which, in turn, modulates ZBTB7A expression and promotes tumor growth.

Protein interactions: CircRNAs can bind to proteins involved in thyroid cancer pathogenesis. For instance, circRNA_100290 interacts with the splicing factor SF3A3, leading to enhanced tumor growth and migration in thyroid cancer.

Splicing regulation: Some circRNAs regulate alternative splicing of genes associated with thyroid cancer. CircHIPK3, mentioned earlier, affects splicing events, thereby influencing the expression of genes involved in cell proliferation and invasion.

Potential applications of circRNAs in thyroid cancer

The study of circRNAs in thyroid cancer has opened up several potential applications that can be beneficial for both research and clinical settings.

Diagnostic biomarkers: CircRNAs show promise as diagnostic markers for thyroid cancer. Analyzing the expression levels of specific circRNAs in thyroid nodules or tissues can aid in early cancer detection and differentiation between benign and malignant lesions.

Prognostic indicators: CircRNAs can serve as prognostic factors for thyroid cancer patients. Their expression profiles may help predict disease progression, recurrence and overall survival, aiding in patient management and treatment decisions.

Therapeutic targets: CircRNAs involved in thyroid cancer pathogenesis can be explored as therapeutic targets. Modulating their expression or activity could potentially halt or slow down the progression of the disease.

Personalized medicine: The unique expression patterns of circRNAs in thyroid cancer suggest that they can be utilized in personalized treatment approaches. Tailoring therapies based on a patient's circRNA profile may enhance treatment outcomes.

CONCLUSION

Circular RNAs, with their unique characteristics and multifaceted functions, have emerged as pivotal players in thyroid cancer. Their involvement in tumorigenesis, progression and clinical applications opens up exciting avenues for research and potential therapeutic interventions. While the study of circRNAs in thyroid cancer is still in its infancy, ongoing research is likely to unravel their full potential in improving the diagnosis, treatment and management of this increasingly prevalent endocrine malignancy. As we continue to delve deeper into the world of circular RNAs, their implications in thyroid cancer are likely to expand, offering new insights and opportunities for patients and clinicians alike.