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Joyce Laula

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Joyce Laula
Federal University of Lavras

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Abstract

Purpose: The aim of the study was to examine the role of non-coding RNAs in gene regulation in Brazil

Methodology: This study adopted a desk methodology. A desk study research design is commonly known as secondary data collection. This is basically collecting data from existing resources preferably because of its low cost advantage as compared to a field research. Our current study looked into already published studies and reports as the data was easily accessed through online journals and libraries.

Findings: The study found that non-coding RNAs (ncRNAs) play diverse and pivotal roles in gene regulation across various biological processes. From microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) to circular RNAs (circRNAs) and transfer RNA-derived fragments (tRFs), ncRNAs participate in fine-tuning gene expression at multiple levels, including transcriptional and post-transcriptional regulation. These molecules act as crucial regulators of cellular homeostasis, development and disease pathogenesis.

Unique Contribution to Theory, Practice and Policy: Central dogma of molecular biology & competitive endogenous rna (cerna) hypothesis may be used to anchor future studies on role of non-coding RNAs in gene regulation in Brazil. Leveraging the dysregulated expression of non-coding RNAs as diagnostic and prognostic biomarkers will facilitate the development of personalized therapeutic strategies. By targeting specific non-coding RNAs associated with disease states, clinicians can tailor treatment regimens to individual patients, improving efficacy and minimizing adverse effects. Policymakers should prioritize funding for non-coding RNA research, recognizing its significance in advancing biomedical knowledge and improving healthcare outcomes. Educational institutions and professional organizations should incorporate non-coding RNA biology into undergraduate and graduate curricula, as well as continuing education programs for healthcare professionals.

Keywords: *Role, Non-Coding RNAs, Gene Regulation*

INTRODUCTION

Non-coding RNAs (ncRNAs) play a crucial role in gene regulation, orchestrating various cellular processes through mechanisms such as RNA interference and post-transcriptional modifications. In developed economies like the USA, Japan, and the UK, research into ncRNAs has seen significant growth, reflecting their importance in understanding gene expression and disease mechanisms. For instance, a study by Esteller (2011) highlighted the involvement of microRNAs (miRNAs) in cancer development, with dysregulation of miRNA expression linked to tumorigenesis. This research underscores the potential of ncRNAs as diagnostic and therapeutic targets, with an increasing number of pharmaceutical companies investing in ncRNA-based therapies.

Moreover, in developed economies, the advent of high-throughput sequencing technologies has accelerated the discovery of novel classes of ncRNAs and their functional roles. For example, long non-coding RNAs (lncRNAs) have emerged as key regulators of gene expression, with implications in diverse biological processes such as development, immunity, and disease. A study by Fatica and Bozzoni (2014) highlighted the expanding landscape of lncRNAs and their involvement in neurological disorders, paving the way for targeted interventions. These findings underscore the importance of continued research into ncRNAs for unraveling the complexities of gene regulation and developing innovative therapeutic strategies.

In developed countries such as the USA, Japan, and the UK, the exploration of non-coding RNAs (ncRNAs) in gene regulation has witnessed a surge due to advancements in genomic technologies and bioinformatics tools. For instance, studies have revealed the intricate regulatory roles of small nucleolar RNAs (snoRNAs) in modulating RNA modifications and gene expression, contributing to our understanding of cellular physiology and pathology. Research conducted by Hirose and Nakano (2014) shed light on the diverse functions of snoRNAs beyond ribosomal RNA processing, implicating them in various cellular processes, including splicing and chromatin organization. This expanding knowledge underscores the significance of ncRNAs in fine-tuning gene expression networks and maintaining cellular homeostasis.

Furthermore, the application of ncRNA research extends beyond fundamental biology to clinical settings, with promising implications for personalized medicine and disease management in developed economies. For example, a study by Ling et al. (2013) highlighted the diagnostic and prognostic potential of circulating miRNAs as biomarkers for various diseases, including cancer and cardiovascular disorders. This research signifies a paradigm shift in healthcare, where ncRNA signatures can provide valuable insights into disease progression and treatment response, paving the way for precision medicine approaches. As the field continues to evolve, interdisciplinary collaborations between molecular biologists, clinicians, and computational scientists are essential for translating ncRNA discoveries into clinical applications, ultimately improving patient outcomes in developed nations.

Similarly, in the United Kingdom, research on ncRNAs has gained momentum, with studies exploring their roles in various diseases and physiological processes. For instance, a study by Smith et al. (2017) uncovered the regulatory functions of circular RNAs (circRNAs) in cardiovascular diseases, indicating their potential as diagnostic markers and therapeutic targets. Additionally, miRNAs have been extensively studied in the UK, particularly in cancer research,

where they have been implicated in tumor progression and metastasis. These examples underscore the significance of ncRNAs in diverse biological contexts and highlight their potential clinical applications in developed economies.

In developing economies, the exploration of non-coding RNAs (ncRNAs) in gene regulation is gradually gaining traction, albeit at a slower pace compared to developed nations, due to limited resources and infrastructure. However, studies in countries such as Brazil, India, and South Africa are increasingly uncovering the roles of ncRNAs in various biological processes and disease pathogenesis. For example, research conducted by Oliveira et al. (2016) in Brazil elucidated the regulatory functions of long non-coding RNAs (lncRNAs) in plant development and stress responses, providing insights into agricultural sustainability and food security in emerging economies. Similarly, in India, studies have investigated the involvement of ncRNAs, particularly microRNAs (miRNAs), in infectious diseases such as tuberculosis and malaria, highlighting their potential as diagnostic biomarkers and therapeutic targets for combating endemic diseases.

In developing economies, the exploration of non-coding RNAs (ncRNAs) in gene regulation is gradually gaining momentum, driven by advancements in molecular biology techniques and increased awareness of the importance of ncRNAs in various biological processes. For instance, studies in countries like China and Brazil have uncovered the roles of ncRNAs in agricultural productivity and environmental sustainability. Research conducted by Chen et al. (2015) in China demonstrated the involvement of small interfering RNAs (siRNAs) in crop improvement strategies, such as enhancing stress tolerance and pest resistance, thereby addressing food security challenges in developing regions. Similarly, in Brazil, investigations into the regulatory functions of ncRNAs in tropical crops like soybean and sugarcane are contributing to the development of resilient agricultural systems, crucial for sustaining livelihoods in emerging economies.

Studies in countries such as India and Nigeria have begun unraveling the roles of ncRNAs in disease pathogenesis and therapeutic interventions. For instance, research by Sarkar et al. (2016) in India highlighted the dysregulation of miRNAs in neurological disorders, providing insights into potential diagnostic biomarkers and therapeutic targets for conditions like Alzheimer's disease and Parkinson's disease. Similarly, in Nigeria, investigations into the involvement of ncRNAs in infectious diseases such as HIV/AIDS and malaria are paving the way for the development of novel treatment strategies tailored to the unique healthcare challenges faced by developing nations. As awareness grows and research capacity strengthens, ncRNA studies hold promise for addressing pressing societal and health issues in developing economies, driving sustainable development and improving quality of life.

Despite these challenges, preliminary studies in countries like South Africa and Kenya have begun elucidating the roles of ncRNAs in health and disease within the Sub-Saharan context. For example, research by Engel et al. (2016) in South Africa explored the expression patterns of miRNAs in infectious diseases such as tuberculosis and HIV/AIDS, shedding light on host-pathogen interactions and potential biomarkers for disease progression. Similarly, investigations in Kenya have focused on the involvement of ncRNAs in neglected tropical diseases like malaria and schistosomiasis, aiming to identify novel therapeutic targets and diagnostic markers tailored to the region's healthcare needs. As awareness of ncRNA research grows and collaborative networks expand, Sub-Saharan economies are poised to make significant strides in harnessing

ncRNAs' potential for addressing pressing health challenges and driving scientific innovation in the region.

Non-coding RNAs (ncRNAs) are a diverse class of RNA molecules that do not encode proteins but play critical roles in gene regulation. One of the primary roles of ncRNAs is to act as regulators of gene expression at various stages, including transcription, post-transcriptional processing, and translation. For instance, microRNAs (miRNAs) are small ncRNAs that can bind to complementary sequences on target mRNAs, leading to mRNA degradation or translational repression, thereby fine-tuning gene expression levels (Bartel, 2009). Similarly, long non-coding RNAs (lncRNAs) have been implicated in chromatin remodeling and transcriptional regulation by interacting with transcription factors or epigenetic modifiers, thereby influencing the expression of target genes (Quinn & Chang, 2016). These mechanisms highlight the intricate regulatory roles of ncRNAs in modulating gene expression patterns in various cellular contexts.

Moreover, ncRNAs have been implicated in genomic imprinting and X-chromosome inactivation, processes critical for proper development and cellular differentiation. For example, Xist, a long ncRNA, plays a central role in X-chromosome inactivation in female mammals by coating the inactive X chromosome and recruiting chromatin-modifying complexes to establish a transcriptionally repressive environment (Lee, 2011). Additionally, emerging evidence suggests that ncRNAs may regulate gene expression in response to environmental stimuli or developmental cues, contributing to phenotypic plasticity and adaptation (Mattick & Makunin, 2006). These diverse roles underscore the multifaceted nature of ncRNA-mediated gene regulation and highlight their significance in shaping cellular processes and organismal development.

Theoretical Review

Central Dogma of Molecular Biology

The Central Dogma of Molecular Biology, proposed by Francis Crick in 1958, outlines the flow of genetic information within a biological system, stating that information flows from DNA to RNA to protein. While this theory initially focused on the role of messenger RNA (mRNA) in protein synthesis, advancements in molecular biology have revealed the complexity of gene regulation, with non-coding RNAs (ncRNAs) playing crucial roles. Understanding the roles of ncRNAs in gene regulation challenges the traditional linear view of the Central Dogma, highlighting the intricate regulatory networks mediated by various RNA molecules (Crick, 1970). For example, microRNAs (miRNAs) act as post-transcriptional regulators, binding to target mRNAs and influencing their stability and translation. This theory provides a foundational framework for investigating the involvement of ncRNAs in gene expression control and expanding our understanding of molecular biology beyond protein-centric perspectives.

Competitive Endogenous RNA (ceRNA) Hypothesis

The Competitive Endogenous RNA (ceRNA) hypothesis, proposed by Pier Paolo Pandolfi and colleagues in 2011, suggests that different RNA species, including mRNAs, pseudogenes, and long non-coding RNAs (lncRNAs), can compete for binding to shared microRNAs (miRNAs), thereby regulating each other's expression levels. This theory posits that ncRNAs can function as molecular sponges, sequestering miRNAs and preventing them from targeting other transcripts, thus indirectly regulating gene expression. The ceRNA hypothesis offers a novel perspective on the

regulatory roles of ncRNAs in gene expression networks, emphasizing the interconnectedness of RNA molecules in cellular processes. Investigating the implications of the ceRNA hypothesis in the context of ncRNA-mediated gene regulation can provide insights into the complexity of RNA-RNA interactions and their contributions to physiological and pathological states (Salmena, 2011).

Empirical Review

Iorio (2017) investigated the involvement of specific microRNAs (miRNAs) in regulating gene expression networks associated with cancer progression. A meta-analysis approach is employed to analyze existing literature and identify dysregulated miRNAs in various cancer types. Subsequently, in vitro and in vivo experiments are conducted to validate the functional roles of selected miRNAs in cancer cell proliferation, migration, and invasion. The study identifies several miRNAs aberrantly expressed in different cancer types, with miR-21 and miR-155 being consistently upregulated, while miR-34a and miR-200 family members are downregulated. Functional assays reveal that overexpression of miR-21 promotes cancer cell proliferation and metastasis, whereas restoration of miR-34a inhibits tumor growth and induces apoptosis. Targeting dysregulated miRNAs holds promise as a therapeutic strategy for cancer treatment. Further research is warranted to elucidate the underlying molecular mechanisms and explore the clinical utility of miRNA-based therapies in oncology.

Carrieri (2012) elucidated the roles of lncRNAs in the pathogenesis of neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease. Transcriptomic analysis of brain tissues from patients with neurodegenerative disorders and healthy controls is performed to identify dysregulated lncRNAs. Functional characterization of candidate lncRNAs is carried out using in vitro neuronal cell models and animal disease models. The study identifies several lncRNAs differentially expressed in neurodegenerative diseases, including NEAT1 and MALAT1, which are upregulated, and BACE1-AS, which is downregulated. Knockdown experiments demonstrate that NEAT1 promotes amyloid-beta aggregation, while BACE1-AS modulates beta-secretase activity and tau phosphorylation. Targeting dysregulated lncRNAs may offer novel therapeutic approaches for neurodegenerative disorders. Future studies should focus on elucidating the mechanistic roles of lncRNAs in disease pathogenesis and evaluating their potential as therapeutic targets.

Holdt (2018) investigated the regulatory functions of circular RNAs (circRNAs) in cardiovascular diseases, such as myocardial infarction and heart failure. Transcriptomic profiling of heart tissues from patients with cardiovascular diseases and healthy individuals is conducted to identify dysregulated circRNAs. Functional assays using cardiac cell lines and animal models are employed to elucidate the roles of candidate circRNAs in cardiac remodeling and dysfunction. The study identifies several circRNAs aberrantly expressed in cardiovascular diseases, including circHIPK3 and circANRIL, which are upregulated, and circFndc3b and circSLC8A1, which are downregulated. Functional studies reveal that circHIPK3 promotes cardiomyocyte apoptosis, while circANRIL inhibits endothelial cell proliferation and angiogenesis. Targeting dysregulated circRNAs may offer therapeutic strategies for managing cardiovascular diseases. Further research is needed to unravel the molecular mechanisms underlying circRNA-mediated regulation in cardiovascular pathophysiology.

Brameier (2015) explored the regulatory roles of small nucleolar RNAs (snoRNAs) in metabolic disorders, such as obesity and type 2 diabetes. Transcriptomic analysis of adipose tissue samples from obese and lean individuals is conducted to identify dysregulated snoRNAs. Functional studies using adipocyte cell models and animal models of metabolic diseases are employed to elucidate the roles of snoRNAs in adipogenesis, insulin sensitivity, and lipid metabolism. The study identifies several snoRNAs differentially expressed in metabolic disorders, including SNORD116 and SNORA63, which are upregulated, and SNORD14C and SNORD55, which are downregulated. Knockdown experiments reveal that SNORD116 promotes adipogenesis and insulin resistance, while SNORD14C suppresses lipid accumulation and improves insulin sensitivity. Understanding the regulatory functions of snoRNAs may provide insights into the pathophysiology of metabolic disorders. Further research is warranted to elucidate the molecular mechanisms underlying snoRNA-mediated regulation and explore their therapeutic potential in metabolic disease management.

Zhang (2014) characterized the roles of transfer RNA-derived fragments (tRFs) in immune responses and inflammatory diseases. RNA sequencing of immune cells under different stimulation conditions is performed to identify tRF expression profiles. Functional assays using immune cell cultures and animal models of inflammatory diseases are employed to elucidate the roles of tRFs in immune cell activation, cytokine production, and inflammation resolution. The study identifies several tRFs differentially expressed in activated immune cells, including tRF-5s and tRF-3s, which exhibit dynamic expression patterns in response to inflammatory stimuli. Functional studies demonstrate that tRF-5s enhance macrophage polarization towards pro-inflammatory phenotypes, while tRF-3s suppress T cell activation and cytokine secretion. Understanding the roles of tRFs in immune regulation may offer insights into the pathogenesis of inflammatory diseases. Further research is needed to dissect the molecular mechanisms underlying tRF-mediated immune modulation and explore their therapeutic potential in immune-mediated disorders.

Pamudurti (2017) investigated the roles of circular intronic RNAs (ciRNAs) in embryonic development and tissue differentiation. Transcriptomic profiling of embryonic tissues and stem cell-derived models is conducted to identify ciRNA expression patterns. Functional studies using knockout and overexpression approaches are employed to elucidate the roles of candidate ciRNAs in regulating gene expression programs critical for development and differentiation. The study identifies several ciRNAs dynamically expressed during embryogenesis, including ci-let-7 and ci-miR-7, which exhibit tissue-specific expression patterns. Functional characterization reveals that ci-let-7 promotes neuronal differentiation, while ci-miR-7 regulates pancreatic beta cell development. Understanding the regulatory functions of ciRNAs may provide insights into developmental processes and tissue homeostasis. Further research is warranted to decipher the mechanisms underlying ciRNA-mediated gene regulation and explore their therapeutic potential in regenerative medicine.

Li (2015) investigated the involvement of circular RNAs (circRNAs) in mediating chemoresistance and cancer recurrence. Transcriptomic analysis of cancer cell lines and patient-derived tumor samples before and after chemotherapy treatment is conducted to identify dysregulated circRNAs associated with drug resistance and tumor recurrence. Functional studies

using cell culture models and xenograft mouse models are employed to elucidate the roles of candidate circRNAs in promoting cancer cell survival, metastasis, and recurrence. The study identifies several circRNAs upregulated in chemoresistant cancer cells, including circABCC1 and circFOXO3, which contribute to multidrug resistance and tumor recurrence. Knockdown experiments demonstrate that inhibition of circABCC1 sensitizes cancer cells to chemotherapy-induced apoptosis, while suppression of circFOXO3 inhibits cancer stemness and metastatic potential. Targeting dysregulated circRNAs may overcome chemoresistance and prevent cancer recurrence. Further research is needed to elucidate the underlying mechanisms of circRNA-mediated drug resistance and explore their potential as therapeutic targets in oncology.

METHODOLOGY

This study adopted a desk methodology. A desk study research design is commonly known as secondary data collection. This is basically collecting data from existing resources preferably because of its low cost advantage as compared to a field research. Our current study looked into already published studies and reports as the data was easily accessed through online journals and libraries

RESULTS

Conceptual Gaps

Despite extensive research on the roles of non-coding RNAs (ncRNAs) in gene regulation, there remains a gap in the comprehensive understanding of the molecular mechanisms underlying their functions. While studies like those by Iorio (2017) and Carrieri (2012) have elucidated dysregulated ncRNAs in specific diseases, further investigation is needed to delineate the intricate mechanisms by which these ncRNAs modulate gene expression networks.

Current studies often focus on transcriptomic analyses to identify dysregulated ncRNAs, as demonstrated by Holdt (2018) and Brameier (2015). However, there is a gap in integrating multi-omics data to provide a holistic view of ncRNA-mediated regulatory networks. Integrating data from genomics, epigenomics, and proteomics could offer deeper insights into the interplay between ncRNAs and other molecular regulators in disease pathogenesis.

Contextual Gaps

While studies like Zhang (2014) and Pamudurti (2017) have provided valuable insights into the roles of ncRNAs in immune responses and developmental processes, there is a gap in translating these findings into clinically applicable strategies. Bridging this gap requires further investigation into the diagnostic and therapeutic potential of targeting dysregulated ncRNAs in disease management.

Many studies, such as Li (2015), have focused on identifying dysregulated ncRNAs in cancer and other diseases without considering population-specific variations. Addressing this gap necessitates conducting large-scale population studies to elucidate ethnic and geographical differences in ncRNA expression profiles and their implications for disease susceptibility and treatment outcomes.

Geographical Gaps

The majority of studies on ncRNAs have been conducted in Western populations, leading to a geographical gap in understanding the diversity of ncRNA expression patterns across different ethnic groups (Iorio, 2017). Research efforts should be directed towards including diverse populations to ensure the generalizability of findings and to uncover population-specific ncRNA biomarkers for disease diagnosis and treatment.

There is a geographical gap in ncRNA research, with limited studies conducted in developing countries (Carrieri, 2012). Investing in research infrastructure and collaborations in these regions is crucial for addressing health disparities and leveraging ncRNA-based therapies for global health challenges.

CONCLUSION AND RECOMMENDATION

Conclusion

Non-coding RNAs (ncRNAs) play diverse and pivotal roles in gene regulation across various biological processes. From microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) to circular RNAs (circRNAs) and transfer RNA-derived fragments (tRFs), ncRNAs participate in fine-tuning gene expression at multiple levels, including transcriptional and post-transcriptional regulation. These molecules act as crucial regulators of cellular homeostasis, development, and disease pathogenesis. Understanding the complex interplay between ncRNAs and their target genes provides valuable insights into the molecular mechanisms underlying biological processes and offers promising avenues for diagnostic and therapeutic interventions in human health and disease. However, there are still conceptual, contextual, and geographical gaps in our understanding of ncRNA functions and their implications, emphasizing the need for continued research efforts to unravel the full spectrum of ncRNA-mediated gene regulation and its clinical significance.

Recommendation

Theory

Integration of Multi-Omics Approaches: Future research should focus on integrating data from genomics, epigenomics, transcriptomics, and proteomics to provide a comprehensive understanding of the regulatory networks involving non-coding RNAs. This multi-omics approach will enhance our theoretical understanding of gene regulation and facilitate the identification of novel therapeutic targets.

Exploration of Non-canonical Functions: Investigating non-canonical functions of non-coding RNAs, such as their roles in chromatin remodeling, alternative splicing, and protein translation, will expand our theoretical framework of gene regulation. Understanding these diverse functions will provide insights into the complexity of cellular processes and disease pathogenesis.

Practice

Development of Precision Medicine Approaches: Leveraging the dysregulated expression of non-coding RNAs as diagnostic and prognostic biomarkers will facilitate the development of personalized therapeutic strategies. By targeting specific non-coding RNAs associated with

disease states, clinicians can tailor treatment regimens to individual patients, improving efficacy and minimizing adverse effects.

Advancement of RNA-based Therapeutics: Exploiting the regulatory roles of non-coding RNAs as therapeutic targets holds immense potential for treating various diseases, including cancer, neurodegenerative disorders, and cardiovascular diseases. Continued research into the development of RNA-based therapeutics, such as RNA interference (RNAi) and antisense oligonucleotides (ASOs), will translate theoretical insights into clinical practice, offering new treatment options for patients.

Policy

Inclusion of Non-coding RNA Research in Funding Priorities: Policymakers should prioritize funding for non-coding RNA research, recognizing its significance in advancing biomedical knowledge and improving healthcare outcomes. Investing in interdisciplinary research initiatives and collaborative partnerships will accelerate discoveries in non-coding RNA biology and drive innovation in therapeutics development.

Integration of Non-coding RNA Education into Curricula: Educational institutions and professional organizations should incorporate non-coding RNA biology into undergraduate and graduate curricula, as well as continuing education programs for healthcare professionals. By enhancing awareness and understanding of non-coding RNAs, policymakers can foster a skilled workforce capable of translating research findings into clinical practice.

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