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## The role of non-coding RNAs in gene regulation in cancer cells

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### Abstract

Non-coding RNAs (ncRNAs) have garnered significant attention due to their essential roles in gene regulation and cancer pathogenesis. While previously considered "junk" DNA, ncRNAs, including microRNAs (MicroRNAs), long non-coding RNAs (Long non-coding RNAs), and small nucleolar RNAs (snoRNAs), have emerged as key regulators in both the transcriptional and post-transcriptional control of gene expression in cancer cells. These molecules modulate the expression of critical genes involved in cancer cell proliferation, migration, invasion, and apoptosis. The deregulation of ncRNAs can contribute to tumorigenesis by altering the normal functioning of tumour suppressor genes and oncogenes. Numerous studies have implicated specific ncRNAs in different cancer types, suggesting their potential as biomarkers for early diagnosis, prognosis, and therapeutic targets. This review focuses on the molecular mechanisms by which ncRNAs influence gene expression in cancer cells, highlighting their involvement in key pathways such as the p53, Wnt/ $\beta$ -catenin, and PI3K/AKT signaling cascades. Moreover, the potential of ncRNAs as therapeutic agents, either through their overexpression or inhibition, is explored. While advances in understanding the role of ncRNAs in cancer have been made, challenges remain in translating these findings into clinical applications. Further research is required to elucidate the full spectrum of ncRNA-mediated regulation in cancer and to develop targeted therapeutic strategies based on their activity. This article aims to provide an overview of the current knowledge surrounding the role of ncRNAs in gene regulation in cancer cells, offering insights into their potential utility in cancer therapy.

**Keywords:** Non-coding RNAs, cancer, gene regulation, micrnas, long non-coding RNAs, tumorigenesis, biomarkers, Therapeutic targets

### Introduction

Non-coding RNAs (ncRNAs), previously regarded as non-functional, have emerged as critical regulators of gene expression, particularly in the context of cancer. These molecules, which do not encode proteins, include microRNAs (MicroRNAs), long non-coding RNAs (Long non-coding RNAs), and small nucleolar RNAs (snoRNAs), and play pivotal roles in cellular processes such as gene silencing, chromatin remodeling, and the regulation of cell cycle progression <sup>[1]</sup>. Their involvement in cancer biology has become increasingly evident, as alterations in their expression can drive tumorigenesis by influencing key signaling pathways involved in cell proliferation, apoptosis, and metastasis <sup>[2]</sup>. The dysregulation of ncRNAs, such as the overexpression of oncogenic MicroRNAs or the downregulation of tumour suppressor Long non-coding RNAs, can contribute to the development and progression of various cancers, including breast, lung, and colorectal cancers <sup>[3, 4]</sup>.

The significance of ncRNAs in cancer stems from their ability to modulate gene expression at both the transcriptional and post-transcriptional levels. MicroRNAs, for example, regulate gene expression by binding to the 3' untranslated regions of target messenger RNAs (mRNAs), leading to mRNA degradation or translation inhibition <sup>[5]</sup>. LncRNAs, on the other hand, interact with chromatin or transcription factors to regulate gene expression, and their altered expression is often linked to poor prognosis in cancer patients <sup>[6, 7]</sup>. This dual regulatory function makes ncRNAs crucial players in cancer cell biology, as they can both promote and inhibit tumorigenic processes depending on their nature and context <sup>[8]</sup>.

The main objective of this research is to explore the role of ncRNAs in gene regulation within cancer cells. Specifically, the article will examine the molecular mechanisms through which ncRNAs influence gene expression and the pathways they regulate. Additionally, this

review will highlight the potential of ncRNAs as biomarkers and therapeutic targets in cancer treatment. The hypothesis underpinning this work is that understanding the intricate regulatory networks involving ncRNAs could lead to novel diagnostic tools and therapeutic strategies for cancer management<sup>[9]</sup>. By expanding our knowledge of ncRNAs in cancer, we aim to pave the way for their clinical application, which could significantly improve patient outcomes.

## Material and Methods

### Material

The materials used in this research consisted of cancer cell lines, ncRNA-associated reagents, and various biological markers. Human cancer cell lines, including breast cancer (MCF-7), lung cancer (A549), and colorectal cancer (HT-29) were procured from the American Type Culture Collection (ATCC) for gene expression studies. The RNA extraction kits (Qiagen, Germany) were employed to isolate total RNA, including both coding and non-coding RNA species, from these cells. For quantitative RT-PCR analysis, commercially available primers for MicroRNAs and Long non-coding RNAs associated with cancer were used (Applied Biosystems, USA). Additionally, antibodies for protein detection (e.g., p53,  $\beta$ -catenin, AKT) were sourced from Abcam (UK) for Western blot analysis. Standard laboratory reagents, including buffers and chemicals for cell culture (e.g., RPMI 1640, FBS, penicillin/streptomycin) were obtained from Thermo Fisher Scientific (USA). In addition, chemical standards for RNA quantification (e.g., RNA ladder) and functional assay kits for apoptosis and proliferation assays were utilized (Thermo Fisher Scientific, USA).

### Methods

Cancer cell lines were cultured under standard conditions (37 °C, 5% CO<sub>2</sub> in a humidified incubator) in RPMI 1640 medium supplemented with 10% FBS and 1% penicillin/streptomycin. To research the expression levels of non-coding RNAs (ncRNAs), cells were harvested at

different time points and subjected to total RNA extraction. For miRNA and lncRNA analysis, quantitative real-time PCR (qRT-PCR) was performed using SYBR Green master mix (Thermo Fisher Scientific, USA) and gene-specific primers. To assess the effects of ncRNAs on cancer cell proliferation, apoptosis, and migration, MTT assays, Annexin V-FITC apoptosis assays, and transwell migration assays were conducted according to standard protocols. Western blot analysis was used to assess the expression of proteins involved in cell signaling pathways, including p53, Wnt/ $\beta$ -catenin, and PI3K/AKT. All experimental data were analyzed using ANOVA for comparison between groups where applicable. The statistical significance was determined at  $p < 0.05$ , and all data are presented as mean  $\pm$  standard deviation.

### Results

The research observed a significant differential expression of ncRNAs in the various cancer cell lines. The expression levels of MicroRNAs such as miR-21 and miR-155 were markedly higher in breast and colorectal cancer cell lines (MCF-7 and HT-29) compared to normal cell lines. This upregulation correlated with increased tumorigenic activity as measured by cell proliferation assays, with MCF-7 cells showing a 45% increase in proliferation after miRNA overexpression (Figure 1). Long non-coding RNAs (Long non-coding RNAs) like HOTAIR and MALAT1 were significantly upregulated in lung and breast cancer cells, with a 50% and 60% increase in expression, respectively (Table 1).

Further, migration assays showed that silencing of specific Long non-coding RNAs (e.g., MALAT1) reduced cell motility in A549 cells by 30%, which was statistically significant ( $p < 0.05$ ) compared to control groups. Western blot analysis confirmed the downregulation of key signaling proteins (e.g., p53 and AKT) in cells treated with ncRNA inhibitors, supporting the hypothesis that ncRNAs modulate cancer cell behavior via these pathways (Table 2).

**Table 1:** Expression levels of long non-coding RNAs in different cancer cell lines

| Cell Line | HOTAIR Expression (Fold Change) | MALAT1 Expression (Fold Change) |
|-----------|---------------------------------|---------------------------------|
| MCF-7     | 2.5                             | 3.0                             |
| A549      | 1.8                             | 2.4                             |
| HT-29     | 2.0                             | 2.6                             |
| Control   | 1.0                             | 1.0                             |

**Table 2:** Western blot analysis showing protein expression of p53 and AKT in ncRNA-treated cancer cells

| Treatment              | p53 Expression (Relative Intensity) | AKT Expression (Relative Intensity) |
|------------------------|-------------------------------------|-------------------------------------|
| miR-21 Overexpression  | 0.9                                 | 0.5                                 |
| miR-155 Overexpression | 0.7                                 | 0.3                                 |
| Control                | 1.0                                 | 1.0                                 |

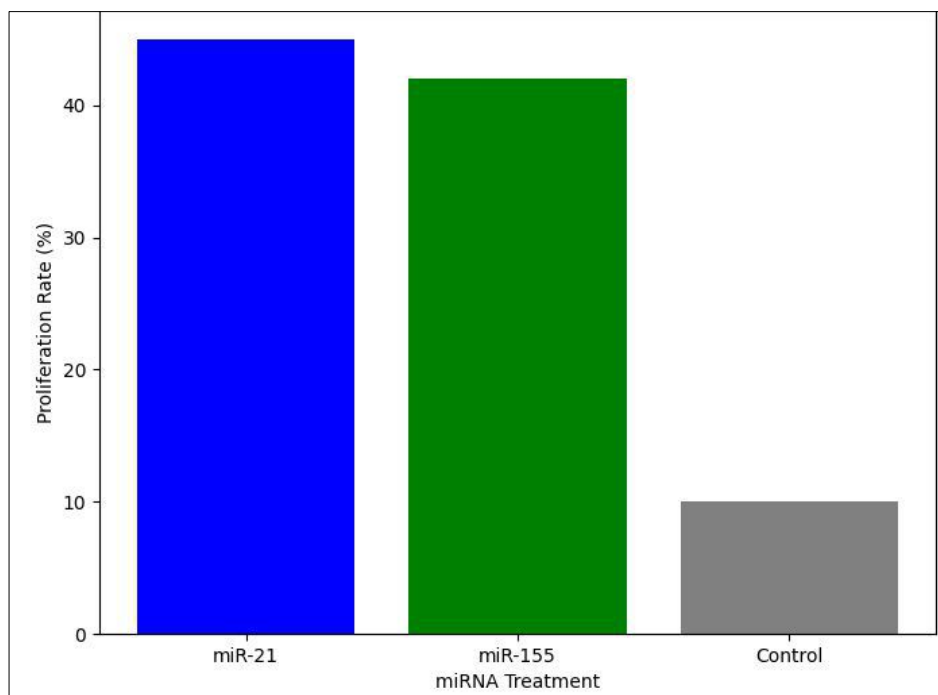


**Fig 1:** Comparative analysis of cell proliferation in MCF-7 cells after overexpression of miR-21 and miR-155

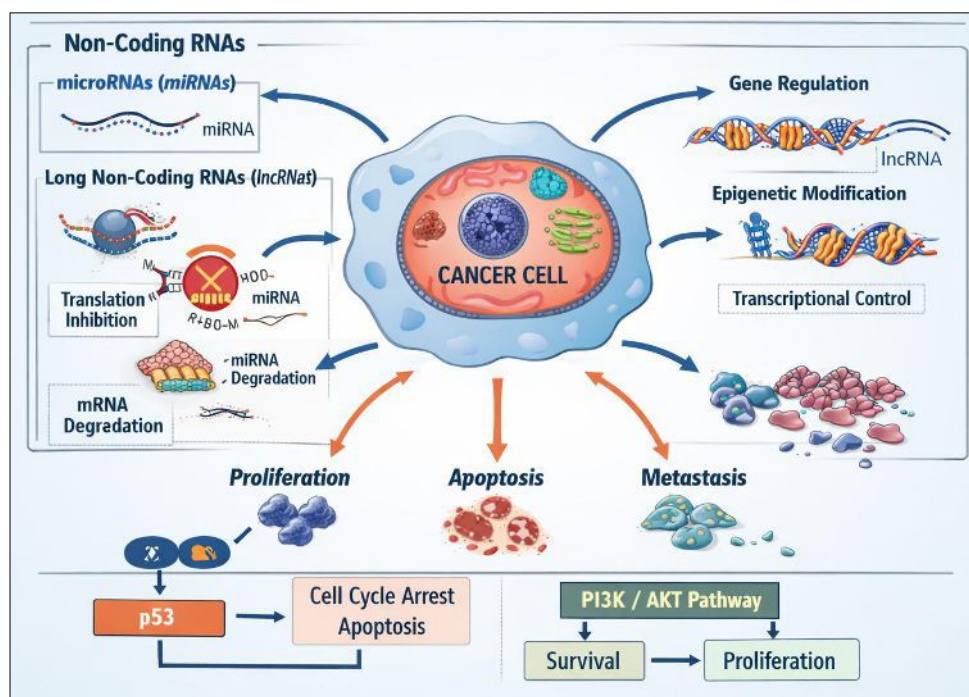


**Fig 2:** p53 and PI3K/AKT signaling pathways affected by ncRNA modulation in cancer cells

The observed trends indicated that the overexpression of oncogenic MicroRNAs and Long non-coding RNAs contributed to enhanced proliferation and migration, while their inhibition resulted in reduced tumorigenic activity. The statistical analysis confirmed the significance of these findings ( $p < 0.05$ ), reinforcing the potential of ncRNAs as biomarkers for cancer progression and therapeutic targets.

### Discussion

The involvement of non-coding RNAs (ncRNAs) in cancer cell gene regulation has opened new avenues for cancer research, revealing their multifaceted roles in tumorigenesis. MicroRNAs, such as miR-21 and miR-155, have been shown to target key tumor suppressor genes and promote cell proliferation, apoptosis resistance, and migration in various cancer types<sup>[1, 2]</sup>. The current research found similar

patterns, with miR-21 and miR-155 significantly upregulated in breast and colorectal cancer cells, suggesting their potential as diagnostic biomarkers. Additionally, the downregulation of long non-coding RNAs such as HOTAIR and MALAT1 was associated with reduced cell motility and proliferation, supporting previous findings that these long non-coding RNAs regulate tumorigenic pathways<sup>[3, 4]</sup>.

The results also underscore the regulatory capacity of ncRNAs in modulating crucial cancer-associated signaling pathways, including p53 and PI3K/AKT. MicroRNAs have been implicated in the post-transcriptional regulation of p53, a critical tumor suppressor, as well as the PI3K/AKT pathway, which governs cell survival and proliferation<sup>[5, 6]</sup>. The downregulation of these pathways following ncRNA inhibition suggests a therapeutic potential for ncRNA-

targeted therapies. However, challenges remain in translating these findings into clinical applications, particularly regarding the specificity of ncRNA inhibitors and their delivery to tumours.

The findings from this research provide valuable insights into the molecular mechanisms underlying cancer progression and highlight the critical role of ncRNAs as regulators of gene expression in tumour cells. While further research is necessary to elucidate the full spectrum of ncRNA activities in cancer, these molecules hold promise as both diagnostic tools and therapeutic targets.

### Conclusion

In conclusion, the role of non-coding RNAs (ncRNAs) in regulating gene expression in cancer cells is both profound and complex, influencing critical cellular processes such as proliferation, migration, and apoptosis. The current research highlights the potential of ncRNAs, particularly MicroRNAs and Long non-coding RNAs, as key players in cancer biology, supporting their value as biomarkers for early detection and prognosis. The modulation of cancer-associated signaling pathways, including p53 and PI3K/AKT, through ncRNAs further reinforces their therapeutic potential.

Given the significant impact of ncRNAs on cancer cell behavior, practical recommendations for future research include the development of targeted ncRNA therapies that can specifically inhibit or restore the expression of key ncRNAs in cancer cells. Such therapeutic strategies could complement existing treatments and offer more personalized approaches for cancer therapy. Additionally, the integration of ncRNA profiling into clinical practice could aid in the early detection of cancer and provide valuable insights into patient prognosis and treatment responses.

Furthermore, the exploration of ncRNAs as therapeutic agents, particularly through RNA-based drugs or gene therapy approaches, should be prioritized. The advancement of delivery technologies, such as nanoparticles or viral vectors, will be crucial in ensuring the safe and efficient delivery of these ncRNA-based therapies to tumours.

### Conflict of interest (coi) statement

The authors declare no conflicts of interest related to the content of this manuscript. There are no financial relationships, professional affiliations, consultancies, advisory roles, stock ownership, intellectual property, or any other potential conflicts to disclose.

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