



Non-coding RNA: From gene expression regulation to precision medicine and modern therapeutic applications – A comprehensive scientific review

Zahraa Qasim Mousa

General Directorate for Education in the province of Maysan ,Ministry of Education, Iraq.

Email corresponding author's: zahraa.qasim.mousa@ec.edu.iq

Received: 7/7/2026

Accepted: 12/9/2026

Published:16/9/2026

Abstract

Recently, there has been a surge of interest in understanding gene regulation following the discovery that a significant portion of the human genome does not code for proteins but rather produces molecules of non-coding RNA (ncRNA) that perform complex and essential regulatory functions in various cellular processes. This discovery overturned the previously held belief that ncRNA was a functionless nucleic acid. Modern studies have demonstrated that these molecules are among the most important regulators of gene expression at the transcriptional, post-transcriptional, and epigenetic levels, and are involved in controlling cell growth, differentiation, apoptosis, immune response, and maintaining homeostasis. These molecules are diverse, including microRNA, long ncRNA, circular RNA, small interfering RNA, and other types that play specialized roles in regulating gene networks. Recent research has shown that disruptions in the expression of these molecules are closely linked to the development of many diseases, including cancer, cardiovascular diseases, neurodegenerative disorders, and immune and metabolic diseases. In recent years, ncRNA has become a major focus in precision medicine due to its great potential as a highly sensitive and specific biomarker for early diagnosis, predicting disease course, and assessing therapeutic response, as well as its role as a promising therapeutic target in the development of modern molecular therapies.

Keyword : *Non-coding RNA, precision medicine, gene therapy, microRNA, circular RNA, siRNA therapeutics, RNA delivery.*

Doi : <https://doi.org/10.64943/ljacs.2026.010209>

INTRODUCTION

The regulation of gene expression is one of the most complex biological processes, as it relies on molecular mechanisms that control the level of gene expression to ensure the maintenance of normal cellular functions [1], [2]. Scientific attention has focused on protein-coding genes because they are responsible for producing proteins that regulate various biological processes [3]. Advances in gene sequencing technologies, particularly the Human Genome Project, have revealed that less than 2% of the human genome codes for proteins, while the majority is transcribed into RNA molecules that are not translated into proteins and are known as ncRNA [4]. These molecules play essential regulatory roles in controlling gene expression and maintaining cellular homeostasis. They are not a byproduct of transcription or a non-functional part of the genome, but rather among the most important regulatory elements that control many biological processes such as cell growth, division, cell differentiation, apoptosis, DNA repair, and the regulation of immune and inflammatory responses[5], [6]. These molecules exert their functions through interaction with DNA, proteins, and messenger RNA (mRNA), enabling the formation of complex regulatory networks that influence gene expression at the transcriptional, post-

transcriptional, and epigenetic levels [7]. The ncRNA family includes species that differ in their molecular structure, mechanisms of action, and biological functions. Among the most prominent are microRNA, long ncRNA, circular RNA, and small interfering RNA, in addition to other types [8]. Studies have shown a close relationship between impaired ncRNA expression and the development of many human diseases [9]. It has been shown that abnormal expression levels of some of its molecules lead to disruptions in cellular signaling pathways,[10]cell cycle disruption,[11] increased oxidative stress,[12] and the development of chronic inflammation,[13]. which contribute to the development of cancer [14] and cardiovascular diseases [15]. Neurodegenerative diseases [16], autoimmune diseases, and many genetic disorders [17] have all contributed to the development of ncRNA in precision medicine, which relies on personalized diagnostic and therapeutic strategies[18]. Numerous studies have demonstrated that certain ncRNA molecules exhibit high stability in blood and other body fluids, making them promising biomarkers for early disease detection, assessment of disease severity, prediction of treatment response, and monitoring disease progression[19]. Modern technologies have paved the way for the development of therapies that inhibit or enhance the expression of these molecules using gene therapy techniques, representing a significant advancement in molecular medicine [20]. This scientific review aims to provide a comprehensive analysis of the latest research on ncRNA, focusing on its classification, its mechanisms of action in regulating gene expression, its role in the development of human diseases, and its potential as a biomarker and therapeutic tool in precision medicine. It also discusses the most prominent challenges and future trends that may contribute to enhancing its clinical applications.

THE CONCEPT OF NCRNA AND ITS HISTORICAL DEVELOPMENT

The ncRNA is defined as a group of RNA molecules that are transcribed from the genome but are not translated into proteins. Instead, they perform regulatory, structural, and catalytic functions within the cell [21]. These molecules do not participate directly in protein synthesis and play a pivotal role in controlling gene expression, maintaining genome stability, and regulating vital processes that ensure normal cell growth [22], [23]. Scientists believed that most of the human genome consisted of non-functional sequences and termed it "junk DNA" because the focus was on protein-coding genes, which represent only a small percentage of the genome [24]. This concept began to change with the development of molecular biology techniques and high-throughput sequencing, which revealed that most of the genome is transcribed into RNA molecules that perform complex regulatory functions, leading to a radical shift in the understanding of gene regulation mechanisms[25] The discovery of microRNA in the 1990s represented a major turning point in this field[26] Studies have shown that small RNA molecules can regulate gene expression by binding to messenger RNA (mRNA), preventing its translation or inducing its degradation[27] Further discoveries have led to the identification of numerous types of ncRNA, such as long ncRNA (lncRNA), circular RNA (circRNA), small interfering RNA (siRNA), and others[8] Recent studies have shown that ncRNA is involved in regulating gene expression at multiple levels[7] Genomic studies indicate that over 98% of the human genome does not code for proteins, but a significant portion is transcribed into ncRNA molecules with diverse functions, as shown in Figure 1 [28]. Understanding these molecules is fundamental to explaining many biological and pathological phenomena, as any disruption in their production or expression can lead to genetic network disturbances and the emergence of numerous diseases [9]. Therefore, ncRNA has become a central focus in molecular biology and precision medicine research, representing one of the most rapidly developing scientific fields in the last.

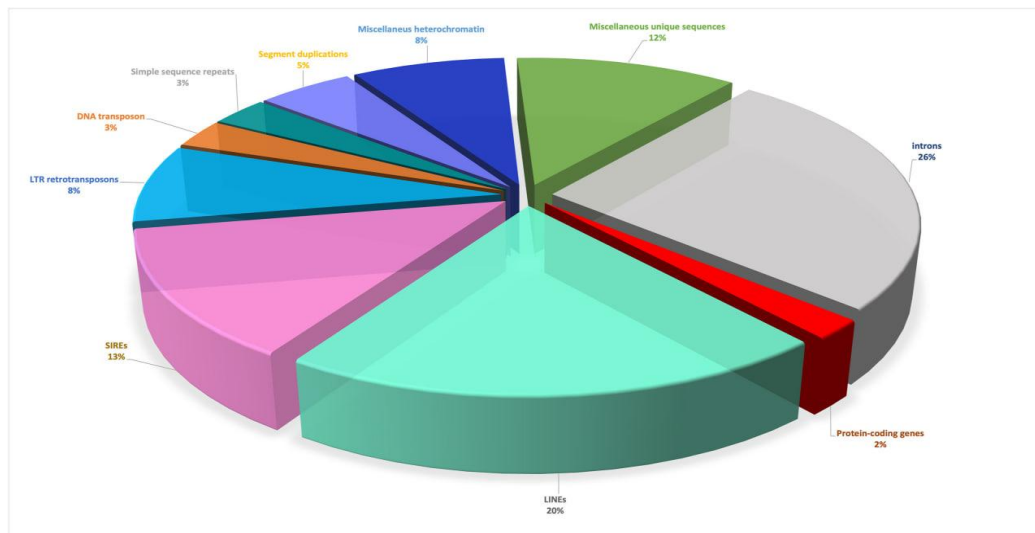


Figure 1. The relative distribution of the components of the human genome, showing the ratio of protein-coding genes to non-coding elements such as introns, mobile elements, and repetitive sequences [29].

CLASSIFICATION AND TYPES OF NCRNA

MicroRNA (miRNA)

MicroRNA, or miRNA, is the most studied type of ncRNA. It consists of short molecules, typically 20 to 24 nucleotides in length [29]. These molecules act post-transcriptionally, binding to specific sequences in messenger RNA (mRNA), thereby inhibiting its translation or promoting its degradation and reducing the production of target proteins [30]. Studies have shown that miRNA molecules regulate thousands of human genes and are involved in controlling the cell cycle, cell division, apoptosis, cell differentiation, immune response, and angiogenesis [31]. Disruptions in their expression are associated with the development of many diseases, particularly cancer, as some miRNA molecules may act as tumor suppressors while others may promote tumor growth and spread [32].

Long ncRNA (lncRNA)

This type includes molecules longer than 200 nucleotides and is characterized by great diversity in its structure and function [33]. It was previously thought to have no function, but recent research has shown that it participates in regulating gene transcription, epigenetic modifications, chromatin remodeling, and regulating messenger RNA stability, in addition to its role in regulating protein synthesis [34]. lncRNA affects gene expression through interaction with DNA, proteins, and transcription factors. It also sometimes acts as aggregation of several regulatory proteins within the cell or as molecular structures that bind to miRNA molecules and prevent them from binding to their targets, thus indirectly altering the level of gene expression [35].

Circular RNA

Circular RNA (circRNA) is characterized by a closed-loop structure that makes it more resistant to degradation compared to other types of RNA. This stability has led to increased interest in it as a promising biomarker for various diseases [8]. Recent studies indicate that circRNA plays an important role in regulating gene expression by binding to microRNA molecules and acting as a molecular sponge that reduces their regulatory effect. It also participates in regulating transcription and translation processes and is associated with the development of many diseases, especially cancer, neurological diseases, and heart disease [8].

Small Interfering RNA (siRNA)

Small interfering RNA (siRNA) consists of short, double-stranded molecules, approximately 21–23 nucleotides in length. It plays a key role in gene silencing by binding to specialized proteins to form a complex that recognizes and breaks down target mRNA molecules, thus preventing the production of encoding proteins. This property has been used in the development of modern therapeutic techniques based on silencing disease-causing genes and has become a promising tool in gene therapy and precision medicine [36], [37].

Other Types of ncRNA

Other types of RNA perform specialized functions, such as: PIWI-interacting RNA (piRNA), which contributes to maintaining genome stability, particularly in germ cells, by inhibiting mobile genetic elements; small nucleolar RNA (snoRNA), which is involved in modifying and processing ribosomal RNA; and small nuclear RNA (snRNA), which [38]. It plays a key role in the process of removing introns (RNA splicing) during messenger RNA maturation [39]. See Table 1 summarizes the key differences among major ncRNA classes and Figure 2.

Table 1. comparison of major non-coding RNA classes

ncRNA type	Typical size
miRNA	18-25 nt
siRNA	20-25 nt
piRNA	24-31 nt
lncRNA	>200 nt
circRNA	Hundreds-thousands nt
snoRNA	60-300 nt
snRNA	~150 nt
tRNA-derived fragments	18-40 nt

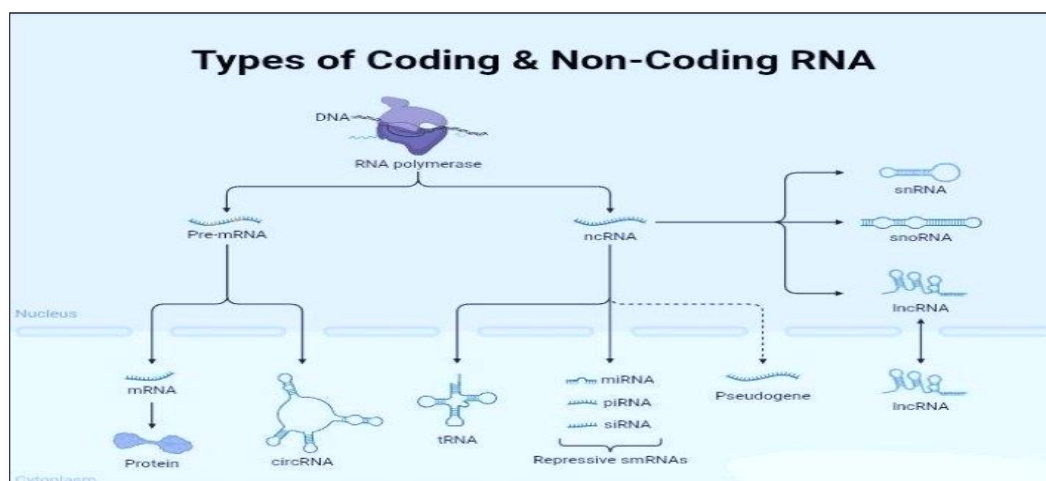


Figure 2. Classification of RNA molecules into major types according to their sizes and regulatory functions in gene expression [40].

MECHANISMS OF GENE EXPRESSION REGULATION BY NCRNA

This regulation operates through a complex network of molecular interactions that control gene activity at multiple stages, starting with the regulation of transcription within the nucleus, extending to the processing of messenger RNA (mRNA), regulating its translation, and finally

determining its lifespan within the cell [34] These mechanisms ensure the cell's response to environmental and physiological changes and the maintenance of homeostasis [41].

Transcriptional Regulation

The ncRNA participates in the control of transcription by interacting with transcription factors and enzymes responsible for gene transcription, such as RNA polymerase II. Some lncRNA molecules attract or inhibit transcription factors at specific regions of the genome, leading to an increase or decrease in the transcription rate of target genes [42]. Additionally, some lncRNA molecules can bind directly to chromatin and direct regulatory protein complexes to specific sites in the genome, thus activating or inhibiting certain genes according to the cell's needs [34].

Epigenetic Regulation

Epigenetic regulation is one of the most important pathways through which ncRNA influences gene expression without altering the DNA sequence. This occurs through DNA methylation, histone modification, and chromatin remodeling [43]. These modifications alter the accessibility of transcription factors to genes, leading to their activation or silencing. Studies have shown that disruption of these mechanisms is associated with the development of many diseases, particularly cancer and neurological disorders [44].

Post-Transcriptional Regulation

After messenger RNA (mRNA) is produced, a new regulatory phase begins, primarily driven by microRNA molecules. These microRNA molecules bind to complementary sequences, often at the untranslated end (3'UTR) of mRNA molecules. This leads to one of two possibilities: inhibition of mRNA translation into protein or stimulation of mRNA degradation and a reduction in its intracellular quantity [45]. This mechanism allows the cell to precisely regulate the amount of proteins produced, which is crucial in regulating cell division, stress response, inflammation, and the immune response [46].

Interaction Between ncRNA Types

The ncRNA forms an integrated regulatory network and does not function independently. For example, circular RNA (circRNA) or long ncRNA (lncRNA) can bind to microRNA (miRNA) molecules and prevent them from reaching their targets, a process called miRNA sponging (competing endogenous RNA, ceRNA, activity). This results in increased gene expression rather than suppression by the microRNA. This is where the importance of these molecules in the development of cancer and many chronic diseases lies [47].

Cell Cycle Regulation and Apoptosis

The ncRNA (nRNA) contributes to cell cycle regulation by controlling the expression of genes responsible for cell division, DNA repair, and apoptosis. When the expression of certain miRNA or lncRNA molecules is disrupted, cells may continue to divide uncontrollably or fail to undergo apoptosis when damaged, which is one of the most important steps leading to the development of cancerous tumors [48].

Regulation of The Immune and Inflammatory Response

Recent research has shown that ncRNA plays a crucial role in regulating the immune system by controlling the production of cytokines and inflammatory factors, as well as regulating the activity of various immune cells. It also participates in regulating the innate and adaptive immune response. Disruption in the expression of some of its molecules has been linked to an increased risk of autoimmune and chronic inflammatory diseases [15].

Maintaining Genome Stability

The ncRNA contributes to the protection of genetic material stability by regulating the activity of mobile genetic elements, participating in DNA repair, and maintaining chromosome integrity during cell division. This is a key reason for preventing the accumulation of genetic mutations that could lead to cancer [49].

APPLICATIONS OF NCRNA IN PRECISION MEDICINE

Precision medicine is one of the most significant transformations in modern healthcare. It relies on designing diagnostic, treatment, and prevention strategies based on the genetic and molecular characteristics of each patient, rather than following a standardized treatment approach for all patients [50]. In this context, ncRNA has emerged as one of the most important tools contributing to the development of precision medicine due to its high sensitivity in detecting molecular changes associated with diseases, in addition to its role in predicting disease progression and response to treatment [18].

ncRNA as a biomarker

Molecular biomarkers are fundamental to precision medicine. Studies have shown that many ncRNA molecules possess properties that make them ideal biomarkers, including: their detectability in blood, urine, saliva, cerebrospinal fluid, and other body fluids; their relative stability in biological samples compared to many other molecules; their direct correlation with the early stages of disease; and the fact that their levels change in proportion to disease severity and response to treatment [51]. For these reasons, these molecules have become a primary target for developing accurate, non-invasive diagnostic tests that can be used in clinical practice.

Early Disease Diagnosis

Early diagnosis is one of the most important factors in improving treatment outcomes [52]. Studies have shown that changes in the levels of certain microRNA and lncRNA molecules can occur long before the onset of clinical symptoms. This has led to the development of diagnostic models based on the expression patterns of these molecules for the early detection of cancer, heart disease, diabetes, and neurological diseases, thus increasing the chances of therapeutic intervention in the early stages of the disease [53].

Predicting Disease Course

The role of ncRNA is not limited to disease diagnosis but extends to predicting its clinical behavior. Certain gene expression patterns are associated with the rate of disease progression, the likelihood of complications, survival rates, and the probability of disease recurrence after treatment. This information helps the physician identify patients most susceptible to complications and choose the most appropriate treatment plan for each case [54].

Predicting Treatment Response

Patients respond to treatment differently due to genetic and molecular differences. Studies have shown that certain ncRNA molecules are associated with the degree of cell sensitivity to drugs [55]. Decreased or increased expression of certain miRNA molecules may be related to factors such as targeted therapy, immunotherapy in some types of cancer, or resistance to chemotherapy, allowing for the selection of the most effective treatment for each patient [56].

Personalized Medicine and Targeted Therapy

Understanding the regulatory networks driven by ncRNA has enabled the design of targeted therapies that directly target the molecules responsible for disease progression [57]. This is crucial

for tailoring treatment plans based on a patient's molecular profile. This strategy contributes to increased treatment efficacy, reduced side effects, and improved patient quality of life [58].

Artificial Intelligence and ncRNA Data Analysis

With the expansion of high-throughput gene sequencing technologies, the volume of data generated from ncRNA studies has become enormous, leading to reliance on artificial intelligence and machine learning techniques to analyze this data and discover complex molecular patterns [59]. These techniques are used to build models capable of predicting disease risk, classifying patients, discovering new biomarkers, and supporting clinical decision-making—a key future trend in precision medicine.

MODERN THERAPEUTIC APPLICATIONS OF ncRNA

Recent years have witnessed significant advancements in the therapeutic use of ncRNA. It has transitioned from a tool for understanding the molecular mechanisms of disease to a promising therapeutic target for precisely modulating gene expression. Advances in genetic engineering and nanotechnology have accelerated the development of miRNA, lncRNA, and siRNA-based therapies, with some of these strategies reaching early clinical trial phases [60].

miRNA-Based Therapy

This approach relies on restoring or inhibiting the function of microRNAs, depending on the nature of the disease. In cases where tumor suppressor miRNAs are underexpressed, mimics (miRNAs) can be used to restore the normal activity of genes regulating cell growth [61]. Conversely, in cases of overexpression of oncogenic miRNAs, specific inhibitors (antagomiRs or anti-miRs) can be used to disrupt their activity and reduce their pathogenic effects. These strategies have demonstrated promising results. Promising in several early clinical trials [62].

siRNA Therapy

Small Interfering RNA (siRNA) is one of the most advanced therapeutic applications of RNA. It relies on silencing disease-causing genes by stimulating the degradation of targeted mRNA molecules and preventing the production of harmful proteins [63]. This approach has led to the development of RNA interference (RNAi)-based drugs, and some siRNA-based therapies have demonstrated clinical success, confirming the great potential of RNA-based therapy in modern medicine [64].

Targeting lncRNA and circRNA

lncRNA and circRNA molecules have become promising therapeutic targets, particularly in cancer, heart disease, and neurological diseases. Technologies are currently being developed that utilize antisense oligonucleotides, which are short, synthetically produced strands of DNA or RNA designed to bind to specific gene sequences, and gene-editing techniques that target these pathogenic RNA molecules within cells to modify their expression [65]. Gene therapy and small molecules capable of modulating the activity of certain types of lncRNA. Although most of these applications are still in early clinical trials, their initial results are encouraging and open new horizons for molecular therapy [66].

RNA Delivery Systems

Delivering RNA molecules to target cells is one of the biggest challenges facing gene therapy, as these molecules are subject to rapid degradation within the body [67]. To overcome this, several methods have been developed, the most important of which are: lipid nanoparticles [68], modified viral vectors [69], natural exosomes [70], and bio-nanoparticles. These technologies have

contributed to improving the stability of RNA molecules and increasing their efficiency of delivery to target tissues [71]. Several representative strategies illustrate this potential, including miRNA mimics, antagomiRs, siRNA therapeutics such as patisiran and inclisiran, and RNA delivery systems based on lipid nanoparticles and GalNAc conjugates.

Current Challenges

Several challenges limit the widespread clinical application of ncRNA-based therapies, the most important of which are: the difficulty of delivering molecules to target tissues with high efficiency, the possibility of unintended effects on other genes, the stimulation of an immune response in some cases, and the high costs of production and development. To long-term clinical studies to prove safety and efficacy [72].

STRENGTHS AND LIMITATIONS:

- Covers multiple ncRNA types.
- Links molecular mechanisms to medical applications.
- Emphasizes precision medicine.
- Discusses therapeutic applications.
- Highlights AI and bioinformatics integration.
- Varying strength of evidence across ncRNA types.
- Limited clinical studies for certain types, especially lncRNAs and circRNAs.
- Differences in measurement and analysis methods across studies.
- Delivery efficiency, off-target effects, immunogenicity, and long-term safety remain challenges.

FUTURE PROSPECTS

Recent research trends indicate that integrating artificial intelligence and bioinformatics with gene sequencing and genetic engineering will contribute to the discovery of new therapeutic targets based on ncRNA. Furthermore, the development of nano-delivery systems and gene editing technologies is expected to improve treatment efficacy and reduce side effects, thus enhancing the role of ncRNA in disease diagnosis and treatment within the framework of precision and personalized medicine in the future [73].

DISCUSSION

Available scientific evidence has shown that ncRNA is one of the most important molecular regulators of gene expression, and its functions have challenged traditional notions that emphasize the importance of the genome in protein-coding genes [74]. Most recent studies confirm that miRNA, lncRNA, and circRNA molecules play complementary roles in regulating many cellular processes, such as cell division, differentiation, apoptosis, immune response, and homeostasis [75]. The majority of studies agree that disruptions in the expression of these molecules are closely linked to the development of many diseases, although the nature of this link varies. Depending on the type of disease and the affected tissue, in cancer, ncRNA molecules play a dual role, with some being tumor suppressors and others tumor promoters, reflecting the great complexity of regulatory networks within the cell [76]. Evidence also indicates that the use of ncRNA as a biomarker offers significant advantages over traditional markers, including the

possibility of early disease detection, high sensitivity and specificity, and the possibility of measuring it in non-invasive samples such as blood, plasma, or saliva [77]. The difference in measurement methods, the variation in sample characteristics, and the small sample sizes in some studies limit the widespread adoption of these markers in clinical practice [78]. Preclinical studies and early clinical trials have shown promising potential for therapies based on modifying the expression of ncRNA molecules by enhancing molecules with a protective effect or inhibiting molecules associated with the disease [79]. Studies agree that the challenges related to delivery methods, biostability, and off-target effects still require further development before full clinical adoption [80]. A significant development in recent years has been the integration of artificial intelligence and bioinformatics with ncRNA studies. This has contributed to the analysis of vast amounts of genomic data, the discovery of new biomarkers, and a better understanding of the complex relationships between different molecules [81].

CONCLUSION

The ncRNA (nRNA) is a fundamental component in regulating gene expression and cellular processes. Its various types contribute to RNA modification, transcriptional control, and the regulation of disease-associated gene activity. Rapid advancements in gene sequencing technologies and artificial intelligence are enhancing our understanding of the functions of these molecules and their use as biomarkers and therapeutic targets in precision medicine. However, challenges remain in defining the functions of many types of nRNA and their clinical applications, necessitating continued research to achieve more precise and effective therapeutic applications.

RECOMMENDATIONS

- Fundamental and Translational Research: Prioritize mechanistic investigations into the regulatory networks of nRNAs and their interactions with coding genes across diverse physiological and pathological contexts
- Implement universal protocols for biospecimen handling, RNA extraction, and data normalization (e.g., qPCR/sequencing).
- Leverage advanced bioinformatics pipelines and machine learning algorithms to mine high-dimensional genomic datasets .
- Advanced Delivery Systems: Intensify research into next-generation delivery platforms (e.g., modified lipid nanoparticles, targeted exosomes, and tissue-specific conjugates) to overcome biological barriers, ensure cell-type-specific targeting, and minimize off-target toxicity and immunogenicity, thereby addressing the principal translational bottleneck
- Foster collaborative consortia bridging molecular biology, clinical medicine, pharmacology, bioengineering, and data science. A critical objective is the seamless integration of multi-omics nRNA data with comprehensive genomic and phenotypic clinical records to design tailored therapeutic regimens.

REFERENCES

1. Pope, S. D., & Medzhitov, R. (2018). Emerging Principles of Gene Expression Programs and Their Regulation. *Molecular Cell*, 71(3), 389–397. <https://doi.org/10.1016/j.molcel.2018.07.017>
2. Mousa, Z. Q. (2022). *Genetic Polymorphisms in β -Thalassemia Major in Misan*. Ministry of Higher Education.
3. Maroto, M., Torvisco, S. N., García-Merino, C., Fernández-González, R., & Pericuesta, E. (2025). Mechanisms of Hormonal, Genetic, and Temperature Regulation of Germ Cell Proliferation, Differentiation, and Death During Spermatogenesis. *Biomolecules*, 15(4), 500. <https://doi.org/10.3390/biom15040500>
4. Amaral, P., Carbonell-Sala, S., De La Vega, F. M., Faial, T., Frankish, A., Gingeras, T., Guigo, R.,

- Harrow, J. L., Hatzigeorgiou, A. G., Johnson, R., Murphy, T. D., Pertea, M., Pruitt, K. D., Pujar, S., Takahashi, H., Ulitsky, I., Varabyou, A., Wells, C. A., Yandell, M., ... Salzberg, S. L. (2023). The status of the human gene catalogue. *Nature*, 622(7981), 41–47. <https://doi.org/10.1038/s41586-023-06490-x>
5. Alzarea, S. I. (2025). Non-coding RNA-mediated gene regulation in Alzheimer's disease pathogenesis: molecular insights and emerging innovations. *Saudi Pharmaceutical Journal*, 33(5), 33. <https://doi.org/10.1007/s44446-025-00026-2>
 6. Mousa, Z. Q., & Dragh, M. A. (2023). *The Study of BCL11A Gene in Patients with Beta-Thalassemia Major and Intermedia by Random Amplephed Polymorphism DNA in Iraq*.
 7. Li, Y. (2023). Non-Coding RNA Performs Its Biological Function by Interacting with Macromolecules. In *International Journal of Molecular Sciences* (Vol. 24, Issue 22, p. 16246). MDPI. <https://doi.org/10.3390/ijms242216246>
 8. Márton, É., Varga, A., Domoszlai, D., Buglyó, G., Balázs, A., Penyige, A., Balogh, I., Nagy, B., & Szilágyi, M. (2025). Non-Coding RNAs in Cancer: Structure, Function, and Clinical Application. *Cancers*, 17(4), 579. <https://doi.org/10.3390/cancers17040579>
 9. Nemeth, K., Bayraktar, R., Ferracin, M., & Calin, G. A. (2024). Non-coding RNAs in disease: from mechanisms to therapeutics. *Nature Reviews Genetics*, 25(3), 211–232. <https://doi.org/10.1038/s41576-023-00662-1>
 10. Nadhan, R., Isidoro, C., Song, Y. S., & Dhanasekaran, D. N. (2022). Signaling by LncRNAs: Structure, Cellular Homeostasis, and Disease Pathology. *Cells*, 11(16), 2517. <https://doi.org/10.3390/cells11162517>
 11. Pathania, A. S., Chava, H., Balusu, R., Pasupulati, A. K., Coulter, D. W., & Challagundla, K. B. (2024). The crosstalk between non-coding RNAs and cell-cycle events: A new frontier in cancer therapy. *Molecular Therapy Oncology*, 32(2). <https://doi.org/10.1016/j.omton.2024.200785>
 12. Ginckels, P., & Holvoet, P. (2022). Oxidative Stress and Inflammation in Cardiovascular Diseases and Cancer: Role of Non-coding RNAs. *Yale Journal of Biology and Medicine*, 95(1), 129–152.
 13. Zhang, Y., Liu, H., Niu, M., Wang, Y., Xu, R., Guo, Y., & Zhang, C. (2024). Roles of long noncoding RNAs in human inflammatory diseases. *Cell Death Discovery*, 10(1), 235. <https://doi.org/10.1038/s41420-024-02002-6>
 14. Afroze, N., Sundaram, M. K., Haque, S., & Hussain, A. (2025). Long non-coding RNA involved in the carcinogenesis of human female cancer - a comprehensive review. *Discover Oncology*, 16(1), 122. <https://doi.org/10.1007/s12672-025-01848-1>
 15. Xie, Y., & Wei, Y. (2021). A novel regulatory player in the innate immune system: Long non-coding RNAs. *International Journal of Molecular Sciences*, 22(17), 9535. <https://doi.org/10.3390/ijms22179535>
 16. Kumar, L., Shamsuzzama, Haque, R., Baghel, T., & Nazir, A. (2017). Circular RNAs: the Emerging Class of Non-coding RNAs and Their Potential Role in Human Neurodegenerative Diseases. *Molecular Neurobiology*, 54(9), 7224–7234. <https://doi.org/10.1007/s12035-016-0213-8>
 17. Lodde, V., Murgia, G., Simula, E. R., Steri, M., Floris, M., & Idda, M. L. (2020). Long noncoding RNAs and circular RNAs in autoimmune diseases. *Biomolecules*, 10(7), 1–22. <https://doi.org/10.3390/biom10071044>
 18. Smith, E. S., Whitty, E., Yoo, B., Moore, A., Sempere, L. F., & Medarova, Z. (2022). Clinical Applications of Short Non-Coding RNA-Based Therapies in the Era of Precision Medicine. *Cancers*, 14(6), 1588. <https://doi.org/10.3390/cancers14061588>
 19. Anfossi, S., Babayan, A., Pantel, K., & Calin, G. A. (2018). Clinical utility of circulating non-coding RNAs — an update. *Nature Reviews Clinical Oncology*, 15(9), 541–563. <https://doi.org/10.1038/s41571-018-0035-x>
 20. Abuhaliema, A., Gharaibeh, L., Jaradat, E., Hammad, M., & Alshaer, W. (2026). Non-coding RNAs in gene therapy: mechanisms, delivery strategies, and clinical translation. *Pharmacia*, 73(73), 1–25. <https://doi.org/10.3897/pharmacia.73.e173259>
 21. Mattick, J. S., & Makunin, I. V. (2006). Non-coding RNA. *Human Molecular Genetics*, 15(suppl_1), R17–R29.

22. Oo, J. A., Brandes, R. P., & Leisegang, M. S. (2022). Long non-coding RNAs: novel regulators of cellular physiology and function. *Pflugers Archiv European Journal of Physiology*, 474(2), 191–204. <https://doi.org/10.1007/s00424-021-02641-z>
23. Abdul-Sahib, R. J., & Faraj, S. H. (2023). Molecular Analysis Of Cyp17 Gene Promoter In Iraqi Infertile Women. *Ann. For. Res*, 66(1), 2518–2525.
24. Walter, N. G. (2024). Are non-protein coding RNAs junk or treasure?: An attempt to explain and reconcile opposing viewpoints of whether the human genome is mostly transcribed into non-functional or functional RNAs. *BioEssays*, 46(4), 2300201. <https://doi.org/10.1002/bies.202300201>
25. Marguerat, S., & Bähler, J. (2010). RNA-seq: From technology to biology. *Cellular and Molecular Life Sciences*, 67(4), 569–579. <https://doi.org/10.1007/s00018-009-0180-6>
26. Sempere, L. F. (2019). Celebrating 25 years of microRNA research: From discovery to clinical application. In *International Journal of Molecular Sciences* (Vol. 20, Issue 8, p. 1987). MDPI. <https://doi.org/10.3390/ijms20081987>
27. Werstruck, G., & Green, M. R. (1999). Controlling gene expression in living cells through small molecule-RNA interactions. *Chemtracts*, 12(11), 803–807.
28. Ruffo, P., Traynor, B. J., & Conforti, F. L. (2025). Unveiling the regulatory potential of the non-coding genome: Insights from the human genome project to precision medicine. *Genes and Diseases*, 12(6), 101652. <https://doi.org/10.1016/j.gendis.2025.101652>
29. Charan, P., Joseph, A., Ebenezer, P., Sankar, V., Suravajhala, R., Rao, R. S. P., & Suravajhala, P. (2025). An introduction to non-coding RNAs. *Progress in Molecular Biology and Translational Science*, 214, 1–17.
30. Fabian, M. R., Sonenberg, N., & Filipowicz, W. (2010). Regulation of mRNA translation and stability by microRNAs. *Annual Review of Biochemistry*, 79(1), 351–379. <https://doi.org/10.1146/annurev-biochem-060308-103103>
31. Li, M., Marin-Muller, C., Bharadwaj, U., Chow, K. H., Yao, Q., & Chen, C. (2009). MicroRNAs: Control and loss of control in human physiology and disease. *World Journal of Surgery*, 33(4), 667–684. <https://doi.org/10.1007/s00268-008-9836-x>
32. Yan, H., & Bu, P. (2021). Non-coding RNA in cancer. *Essays in Biochemistry*, 65(4), 625–639. <https://doi.org/10.1042/EBC20200032>
33. Mattick, J. S., Amaral, P. P., Carninci, P., Carpenter, S., Chang, H. Y., Chen, L.-L., Chen, R., Dean, C., Dinger, M. E., & Fitzgerald, K. A. (2023). Long non-coding RNAs: definitions, functions, challenges and recommendations. *Nature Reviews Molecular Cell Biology*, 24(6), 430–447.
34. Statello, L., Guo, C. J., Chen, L. L., & Huarte, M. (2021). Gene regulation by long non-coding RNAs and its biological functions. *Nature Reviews Molecular Cell Biology*, 22(2), 96–118. <https://doi.org/10.1038/s41580-020-00315-9>
35. Fernandes, J. C. R., Acuña, S. M., Aoki, J. I., Floeter-Winter, L. M., & Muxel, S. M. (2019). Long non-coding RNAs in the regulation of gene expression: Physiology and disease. *Non-Coding RNA*, 5(1), 17. <https://doi.org/10.3390/ncrna5010017>
36. Déctor, M. A., Romero, P., López, S., & Arias, C. F. (2002). Rotavirus gene silencing by small interfering RNAs. *EMBO Reports*, 3(12), 1175–1180. <https://doi.org/10.1093/embo-reports/kvf234>
37. Rana, T. M. (2007). Illuminating the silence: Understanding the structure and function of small RNAs. *Nature Reviews Molecular Cell Biology*, 8(1), 23–36. <https://doi.org/10.1038/nrm2085>
38. Matera, A. G., Terns, R. M., & Terns, M. P. (2007). Non-coding RNAs: Lessons from the small nuclear and small nucleolar RNAs. *Nature Reviews Molecular Cell Biology*, 8(3), 209–220. <https://doi.org/10.1038/nrm2124>
39. Kiss, T. (2004). Biogenesis of small nuclear RNPs. *Journal of Cell Science*, 117(25), 5949–5951. <https://doi.org/10.1242/jcs.01487>
40. Xu, G., Xu, W. Y., Xiao, Y., Jin, B., Du, S. Da, Mao, Y. L., & Zhang, Z. T. (2020). The emerging roles of non-coding competing endogenous RNA in hepatocellular carcinoma. *Cancer Cell International*, 20(1), 496. <https://doi.org/10.1186/s12935-020-01581-5>

41. Thomson, D. W., & Dinger, M. E. (2016). Endogenous microRNA sponges: Evidence and controversy. *Nature Reviews Genetics*, 17(5), 272–283. <https://doi.org/10.1038/nrg.2016.20>
42. Anastasiadou, E., Jacob, L. S., & Slack, F. J. (2017). Non-coding RNA networks in cancer. *Nature Reviews Cancer*, 18(1), 5–18. <https://doi.org/10.1038/nrc.2017.99>
43. Wang, W., Min, L., Qiu, X., Wu, X., Liu, C., Ma, J., Zhang, D., & Zhu, L. (2021). Biological Function of Long Non-coding RNA (LncRNA) Xist. *Frontiers in Cell and Developmental Biology*, 9, 645647. <https://doi.org/10.3389/fcell.2021.645647>
44. Allis, C. D., & Jenuwein, T. (2016). The molecular hallmarks of epigenetic control. *Nature Reviews Genetics*, 17(8), 487–500. <https://doi.org/10.1038/nrg.2016.59>
45. O'Brien, J., Hayder, H., Zayed, Y., & Peng, C. (2018). Overview of microRNA biogenesis, mechanisms of actions, and circulation. *Frontiers in Endocrinology*, 9(AUG), 402. <https://doi.org/10.3389/fendo.2018.00402>
46. Saliminejad, K., Khorram Khorshid, H. R., Soleymani Fard, S., & Ghaffari, S. H. (2019). An overview of microRNAs: Biology, functions, therapeutics, and analysis methods. *Journal of Cellular Physiology*, 234(5), 5451–5465. <https://doi.org/10.1002/jcp.27486>
47. Qi, P., Zhou, X. yan, & Du, X. (2016). Circulating long non-coding RNAs in cancer: Current status and future perspectives. *Molecular Cancer*, 15(1), 39. <https://doi.org/10.1186/s12943-016-0524-4>
48. Peng, Y., & Croce, C. M. (2016). The role of microRNAs in human cancer. *Signal Transduction and Targeted Therapy*, 1(1), 15004. <https://doi.org/10.1038/sigtrans.2015.4>
49. Cai, Z., Liu, M., Zeng, L., Zhao, K., Wang, C., Sun, T., Li, Z., & Liu, R. (2023). Role of traditional Chinese medicine in ameliorating mitochondrial dysfunction via non-coding RNA signaling: Implication in the treatment of neurodegenerative diseases. *Frontiers in Pharmacology*, 14, 1123188. <https://doi.org/10.3389/fphar.2023.1123188>
50. Wang, R. C., & Wang, Z. (2023). Precision Medicine: Disease Subtyping and Tailored Treatment. *Cancers*, 15(15), 3837. <https://doi.org/10.3390/cancers15153837>
51. Van Roosbroeck, K., Pollet, J., & Calin, G. A. (2013). MiRNAs and long noncoding RNAs as biomarkers in human diseases. *Expert Review of Molecular Diagnostics*, 13(2), 183–204. <https://doi.org/10.1586/erm.12.134>
52. Setyati, R., Astuti, A., Putri Utami, T., Adiwijaya, S., Muhammad Hasyim, D., Tinggi Ilmu Kesehatan Kesosi, S., & Author, C. (2024). The Importance of Early Detection in Disease Management. *Journal of World Future Medicine*, 2(1), 51–63. <https://doi.org/10.55849/health.v2i1.692>
53. Zhou, S., Li, J., Yang, W., Xue, P., Yin, Y., Wang, Y., Tian, P., Peng, H., Jiang, H., Xu, W., Huang, S., Zhang, R., Wei, F., Sun, H. X., Zhang, J., & Zhao, L. (2023). Noninvasive preeclampsia prediction using plasma cell-free RNA signatures. *American Journal of Obstetrics and Gynecology*, 229(5), 553.e1-553.e16. <https://doi.org/10.1016/j.ajog.2023.05.015>
54. Hossam Abdelmonem, B., Kamal, L. T., Wardy, L. W., Ragheb, M., Hanna, M. M., Elsharkawy, M., & Abdelnaser, A. (2025). Non-coding RNAs: emerging biomarkers and therapeutic targets in cancer and inflammatory diseases. *Frontiers in Oncology*, 15, 1534862. <https://doi.org/10.3389/fonc.2025.1534862>
55. Chen, B. Q., Dragomir, M. P., Yang, C., Li, Q., Horst, D., & Calin, G. A. (2022). Targeting non-coding RNAs to overcome cancer therapy resistance. *Signal Transduction and Targeted Therapy*, 7(1), 121. <https://doi.org/10.1038/s41392-022-00975-3>
56. Liu, K., Gao, L., Ma, X., Huang, J. J., Chen, J., Zeng, L., Ashby, C. R., Zou, C., & Chen, Z. S. (2020). Long non-coding RNAs regulate drug resistance in cancer. *Molecular Cancer*, 19(1), 54. <https://doi.org/10.1186/s12943-020-01162-0>
57. Coan, M., Haefliger, S., Ounzain, S., & Johnson, R. (2024). Targeting and engineering long non-coding RNAs for cancer therapy. *Nature Reviews Genetics*, 25(8), 578–595. <https://doi.org/10.1038/s41576-024-00693-2>
58. Jamalnia, M., & Weiskirchen, R. (2025). Advances in personalized medicine: translating genomic insights into targeted therapies for cancer treatment. *Annals of Translational Medicine*, 13(2), 18–

18. <https://doi.org/10.21037/atm-25-34>
59. Jung, V., Vincent-Cuaz, C., Tumescheit, C., Fournier, L., Darsinou, M., Xu, Z. M., Saadat, A., Wang, Y., Tsantoulis, P., Michielin, O., Fellay, J., Patani, R., Ramos, A., Frossard, P., Hastings, J., Riccio, A., van der Plas, L., & Luisier, R. (2025). Decoding the interactions and functions of non-coding RNA with artificial intelligence. *Nature Reviews Molecular Cell Biology*, 26(10), 797–818. <https://doi.org/10.1038/s41580-025-00857-w>
60. Micheel, J., Safrastyan, A., & Wollny, D. (2021). Advances in non-coding RNA sequencing. *Non-Coding RNA*, 7(4), 70. <https://doi.org/10.3390/ncrna7040070>
61. Ho, P. T. B., Clark, I. M., & Le, L. T. T. (2022). MicroRNA-based diagnosis and therapy. *International Journal of Molecular Sciences*, 23(13), 7167.
62. Abd-Aziz, N., Kamaruzman, N. I., & Poh, C. L. (2020). Development of MicroRNAs as Potential Therapeutics against Cancer. *Journal of Oncology*, 2020(1), 8029721. <https://doi.org/10.1155/2020/8029721>
63. Hu, B., Zhong, L., Weng, Y., Peng, L., Huang, Y., Zhao, Y., & Liang, X.-J. (2020). Therapeutic siRNA: state of the art. *Signal Transduction and Targeted Therapy*, 5(1), 101.
64. Bobbin, M. L., & Rossi, J. J. (2016). RNA Interference (RNAi)-Based Therapeutics: Delivering on the Promise? *Annual Review of Pharmacology and Toxicology*, 56(1), 103–122. <https://doi.org/10.1146/annurev-pharmtox-010715-103633>
65. Yi, Q., Feng, J., Lan, W., Shi, H., Sun, W., & Sun, W. (2024). CircRNA and lncRNA-encoded peptide in diseases, an update review. *Molecular Cancer*, 23(1), 214. <https://doi.org/10.1186/s12943-024-02131-7>
66. Loganathan, T., & Doss, C. G. P. (2023). Non-coding RNAs in human health and disease: potential function as biomarkers and therapeutic targets. *Functional and Integrative Genomics*, 23(1), 33. <https://doi.org/10.1007/s10142-022-00947-4>
67. Pozdniakova, N., Generalov, E., Shevelev, A., & Tarasova, O. (2025). RNA Therapeutics: Delivery Problems and Solutions—A Review. *Pharmaceutics*, 17(10), 1305. <https://doi.org/10.3390/pharmaceutics17101305>
68. Eygeris, Y., Gupta, M., Kim, J., & Sahay, G. (2022). Chemistry of Lipid Nanoparticles for RNA Delivery. *Accounts of Chemical Research*, 55(1), 2–12. <https://doi.org/10.1021/acs.accounts.1c00544>
69. Jabbar, R. (2026). Association Between Age, Body Mass Index, and Hypertension Among Adults in Maysan Governorate, Iraq: A Cross-Sectional Study. *Libyan Journal of Applied and Contemporary Sciences*, 1(2), 50–58. <https://doi.org/10.64943/ljacs.2026.010205>
70. Samanta, S., Rajasingh, S., Drosos, N., Zhou, Z., Dawn, B., & Rajasingh, J. (2018). Exosomes: New molecular targets of diseases. *Acta Pharmacologica Sinica*, 39(4), 501–513. <https://doi.org/10.1038/aps.2017.162>
71. Muskan, M., Abeyasinghe, P., Cecchin, R., Branscome, H., Morris, K. V., & Kashanchi, F. (2024). Therapeutic potential of RNA-enriched extracellular vesicles: The next generation in RNA delivery via biogenic nanoparticles. *Molecular Therapy*, 32(9), 2939–2949. <https://doi.org/10.1016/j.ymthe.2024.02.025>
72. Winkle, M., El-Daly, S. M., Fabbri, M., & Calin, G. A. (2021). Noncoding RNA therapeutics — challenges and potential solutions. *Nature Reviews Drug Discovery*, 20(8), 629–651. <https://doi.org/10.1038/s41573-021-00219-z>
73. Bougea, A. (2026). Targeting Non-Coding RNAs as a Potential Therapeutic and Delivery Strategy Against Neurodegenerative Diseases. *International Journal of Molecular Sciences*, 27(7), 3260. <https://doi.org/10.3390/ijms27073260>
74. Kaikkonen, M. U., Lam, M. T. Y., & Glass, C. K. (2011). Non-coding RNAs as regulators of gene expression and epigenetics. *Cardiovascular Research*, 90(3), 430–440. <https://doi.org/10.1093/cvr/cvr097>
75. Altayli, E. (2020). Regulator non-coding RNAs: miRNA, siRNA, piRNA, lncRNA, circRNA. *Journal of Clinical Medicine of Kazakhstan*, 6 (60), 29–39.
76. Eldakhakhny, B., Sutaih, A. M., Siddiqui, M. A., Aqeeli, Y. M., Awan, A. Z., Alsayegh, M. Y.,

- Elsamanoudy, S. A., & Elsamanoudy, A. (2024). Exploring the role of noncoding RNAs in cancer diagnosis, prognosis, and precision medicine. *Non-Coding RNA Research*, 9(4), 1315–1323. <https://doi.org/10.1016/j.ncrna.2024.06.015>
77. Uppaluri, K. R., Challa, H. J., Gaur, A., Jain, R., Krishna Vardhani, K., Geddam, A., Natya, K., Aswini, K., Palasamudram, K., & K, S. M. (2023). Unlocking the potential of non-coding RNAs in cancer research and therapy. *Translational Oncology*, 35, 101730. <https://doi.org/10.1016/j.tranon.2023.101730>
78. Tingö, L., Ahlberg, E., Johansson, L., Pedersen, S. A., Chawla, K., Sætrum, P., Cione, E., & Simpson, M. R. (2021). Non-Coding RNAs in Human Breast Milk: A Systematic Review. *Frontiers in Immunology*, 12, 725323. <https://doi.org/10.3389/fimmu.2021.725323>
79. Piergentili, R., Basile, G., Nocella, C., Carnevale, R., Marinelli, E., Patrone, R., & Zaami, S. (2022). Using ncRNAs as Tools in Cancer Diagnosis and Treatment—The Way towards Personalized Medicine to Improve Patients' Health. *International Journal of Molecular Sciences*, 23(16), 9353. <https://doi.org/10.3390/ijms23169353>
80. Forterre, A., Komuro, H., Aminova, S., & Harada, M. (2020). A comprehensive review of cancer microRNA therapeutic delivery strategies. *Cancers*, 12(7), 1–21. <https://doi.org/10.3390/cancers12071852>
81. Yetgin, A. (2025). Revolutionizing multi-omics analysis with artificial intelligence and data processing. *Quantitative Biology*, 13(3), e70002. <https://doi.org/10.1002/qub2.70002>

الحمض النووي الريبي غير المشفر: من تنظيم التعبير الجيني إلى الطب الدقيق والتطبيقات العلاجية الحديثة – مراجعة علمية شاملة

الملخص

شهدت السنوات الأخيرة اهتمامًا متزايدًا بفهم تنظيم الجينات، وذلك بعد اكتشاف أن جزءًا كبيرًا من الجينوم البشري لا يُشفر البروتينات، بل يُنتج جزيئات من الحمض النووي الريبوزي غير المشفر (ncRNA) التي تؤدي وظائف تنظيمية معقدة وأساسية في مختلف العمليات الخلوية. وقد قلب هذا الاكتشاف الاعتقاد السابق بأن الحمض النووي الريبوزي غير المشفر (ncRNA) هو حمض نووي عديم الوظيفة. وأظهرت الدراسات الحديثة أن هذه الجزيئات تُعد من أهم منظمات التعبير الجيني على المستويات النسخية وما بعد النسخية والوراثية، وتشارك في التحكم في نمو الخلايا وتميزها وموتها المبرمج والاستجابة المناعية والحفاظ على التوازن الداخلي. وتتنوع هذه الجزيئات، وتشمل الحمض النووي الريبوزي الميكروي (microRNA)، والحمض النووي الريبوزي غير المشفر الطويل (lncRNA)، والحمض النووي الريبوزي الدائري (circular RNA)، والحمض النووي الريبوزي المتداخل الصغير (siRNA)، وأنواعًا أخرى تؤدي أدوارًا متخصصة في تنظيم الشبكات الجينية. وقد أظهرت الأبحاث الحديثة أن اضطرابات التعبير عن هذه الجزيئات ترتبط ارتباطًا وثيقًا بتطور العديد من الأمراض، بما في ذلك السرطان وأمراض القلب والأوعية الدموية والاضطرابات التنكسية العصبية وأمراض المناعة والأمراض الأيضية. في السنوات الأخيرة، أصبح الحمض النووي الريبوزي غير المشفر (ncRNA) محورًا رئيسيًا في الطب الدقيق نظرًا لإمكاناته الكبيرة كعلامة حيوية عالية الحساسية والنوعية للتشخيص المبكر، والتنبؤ بمسار المرض، وتقييم الاستجابة العلاجية، فضلًا عن دوره كهدف علاجي واعد في تطوير العلاجات الجزيئية الحديثة.

الكلمات المفتاحية: الحمض النووي الريبوزي غير المشفر، الطب الدقيق، العلاج الجيني، الحمض النووي الريبوزي الميكروي، الحمض النووي الريبوزي الدائري، العلاج بالحمض النووي الريبوزي المتداخل الصغير (siRNA)، توصيل الحمض النووي الريبوزي.