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Review

The Vital Role of Non-Coding RNA Regions in Hemoglobin Gene Regulation

Mohammad Ahmad Ahmad Odah

Prince Sattam Bin Abdulaziz University, Preparatory Year Deanship, Basic Science Department, 151 Alkharj 11942, KSA; corresponding m.odah@psau.edu.sa ; Tel: +966-55 820 2366. ORCID: 0000-0003-1883-6992

Abstract: Non-coding RNA regions have long been considered the "dark matter" of the genome, with their significance in gene regulation remaining enigmatic. However, recent advances in genomics and molecular biology have illuminated the pivotal role that non-coding RNA regions play in the fine-tuned orchestration of hemoglobin expression. Hemoglobin, the oxygen-carrying protein vital for life, is tightly regulated, and any disruption in its production can lead to severe medical conditions, such as hemoglobinopathies. This review delves into the intricate world of non-coding RNA regions, exploring how they act as master conductors in controlling hemoglobin gene expression. We will discuss various classes of non-coding RNAs, including long non-coding RNAs, microRNAs, and circular RNAs, and their specific mechanisms in fine-tuning hemoglobin levels. Additionally, we will highlight emerging therapeutic approaches that target non-coding RNA regions to ameliorate hemoglobin-related disorders. Understanding the critical role of non-coding RNA regions in hemoglobin regulation opens new avenues for precision medicine and gene therapies, offering hope for those affected by hemoglobinopathies and related conditions. This comprehensive review sheds light on the significance of these non-coding RNA regions, demonstrating that the "silent" players in the genome are, in fact, the conductors of harmony in the symphony of hemoglobin regulation.

Keywords: non-coding RNA regions; hemoglobin regulation; hemoglobinopathies; MicroRNAs (miRNAs); long non-coding RNAs (lncRNAs); circular RNAs (circRNAs); RNA-based therapeutics

1. Introduction

Hemoglobin, the intricate iron-rich protein primarily found within red blood cells, is the linchpin of oxygen transport throughout the human body. This oxygen-carrying protein is indispensable for human survival and the overall maintenance of physiological functions. Given its crucial role, the precise regulation of hemoglobin expression is paramount in sustaining the delicate balance of oxygen supply to tissues and organs. However, dysregulation in hemoglobin production can give rise to a group of genetic disorders collectively known as hemoglobinopathies. These disorders encompass a broad spectrum of conditions, most notably including sickle cell anemia and thalassemia, which affect millions of individuals worldwide. The morbidity and mortality associated with hemoglobinopathies, coupled with the economic burden they pose on healthcare systems globally, underscore the urgent need for a deeper understanding of hemoglobin regulation [1,2]. Traditionally, research in the field of hemoglobinopathies has predominantly focused on elucidating the role of coding sequences (the DNA segments that directly code for proteins) and the resultant protein products. However, a paradigm shift has occurred in recent years, revealing a previously underappreciated facet of gene regulation: the pivotal role of non-coding RNA regions [3].

Non-coding RNAs (ncRNAs), once dismissed as "genomic dark matter," comprise a diverse array of RNA molecules that, unlike messenger RNAs (mRNAs), do not serve as blueprints for protein synthesis. The family of non-coding RNAs includes long non-coding RNAs (lncRNAs), microRNAs (miRNAs), circular RNAs (circRNAs), and other emerging classes, each with its unique characteristics and functions. While previously relegated to the periphery of genetic research, non-

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coding RNA regions are increasingly being recognized as integral components of the intricate machinery that orchestrates gene expression. The transition from considering non-coding RNAs as genomic "noise" to recognizing their active participation in the regulation of vital genes, such as hemoglobin genes, has been facilitated by a surge in genetic studies. These studies have unveiled the role of non-coding RNAs in the modulation of various aspects of hemoglobin production. They regulate the fine-tuned expression of hemoglobin genes at the transcriptional and post-transcriptional levels, revealing their capacity to act as master conductors in the complex symphony of hemoglobin regulation [4–6].

In this comprehensive review, we aim to delve deeper into the emerging understanding of how non-coding RNA regions drive the precise control of hemoglobin expression. We will explore the intricate molecular mechanisms through which non-coding RNAs interact with hemoglobin genes, influencing their expression levels and, by extension, the regulation of oxygen-carrying capacity. Furthermore, we will critically examine the potential clinical implications arising from this newfound knowledge, including the development of innovative therapeutic strategies that target non-coding RNA regions for the treatment of hemoglobinopathies. Understanding the multifaceted role of non-coding RNA regions in hemoglobin regulation holds promise for advancing precision medicine, diagnostic strategies, and innovative therapeutic interventions for hemoglobin-related disorders. These findings highlight that what was once considered the "silent" genome is, in reality, the conductor orchestrating the harmonious and precise expression of hemoglobin.

2. Literature Review

2.1. Harmony in Hemoglobin: The Fundamental Role of Non-Coding RNA Regions

Non-coding RNA regions, previously overlooked in the realm of genomics, have emerged as instrumental conductors in the intricate symphony of hemoglobin gene expression. In this section, we will delve into their fundamental role and unravel the profound significance of non-coding RNA regions in maintaining the balance of hemoglobin levels.

2.1.1. MicroRNAs as Precision Conductors

MicroRNAs (miRNAs), a class of small non-coding RNAs, have emerged as precision conductors orchestrating the fine-tuned regulation of hemoglobin gene expression with remarkable precision [7]. These petite RNA molecules, typically composed of approximately 22 nucleotides, play a critical role in controlling hemoglobin levels by interacting with the 3' untranslated regions (3' UTR) of messenger RNA (mRNA) molecules encoding hemoglobin [8]. In doing so, miRNAs exert meticulous control over the synthesis of hemoglobin at the post-transcriptional level. The interaction between miRNAs and the 3' UTR of hemoglobin-encoding mRNAs is a highly intricate and specific process. MiRNAs bind to these target mRNA regions with great specificity, initiating a sequence of events that lead to the modulation of hemoglobin production. These actions enable miRNAs to act as master regulators of hemoglobin gene expression, contributing to the overall balance of oxygen transport and ensuring that oxygen-carrying capacity aligns with the body's requirements.

Within the realm of hemoglobin regulation, a trio of miRNAs stands out for their pivotal roles: miR-144, miR-150, and miR-451 [9]. These miRNAs have demonstrated their significance in the orchestration of precise hemoglobin expression. They engage in a complex interplay of molecular interactions, delicately adjusting hemoglobin levels to meet the body's oxygen demands. Any disruption in the activity of these miRNAs can lead to aberrations in hemoglobin production, with potential consequences ranging from anemia to other hematological disorders. MiR-144, for instance, has been found to directly target and modulate the expression of erythroid-specific genes, including those related to hemoglobin synthesis. Its influence on erythropoiesis, the process of red blood cell formation, highlights the intricate web of regulation in which miRNAs are entangled.

MiR-150 contributes to hematopoiesis, the formation of blood cells, and has been associated with the balance of erythroid and myeloid cell differentiation. Its role in the hematopoietic stem cell population underscores the far-reaching influence of miRNAs beyond the erythroid lineage.

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MiR-451 is notable for its involvement in erythrocyte maturation and regulation. It has been linked to erythrocyte maturation, highlighting its role in ensuring the proper development of red blood cells and, consequently, hemoglobin levels. These examples serve as a testament to the complexity and precision of miRNA-based regulation in hemoglobin synthesis. The collective actions of miR-144, miR-150, and miR-451, among other miRNAs, contribute to the exquisite control of hemoglobin production, fine-tuning it to meet the ever-changing demands of oxygen transport in the body. miRNAs, particularly miR-144, miR-150, and miR-451, form an integral part of the non-coding RNA orchestra that regulates hemoglobin expression. Their ability to target and modulate hemoglobin-encoding mRNAs with remarkable specificity highlights their significance in maintaining the delicate balance of hemoglobin levels, a task essential for human survival.

2.1.2. Long Non-Coding RNAs: The Maestros of Hemoglobin Control

Long non-coding RNAs (lncRNAs) have garnered recognition as the maestros of hemoglobin control, orchestrating the intricate symphony of gene expression [10]. These lncRNAs, often spanning hundreds to thousands of nucleotides, have been unveiled as central figures in the complex regulatory landscape of hemoglobin production, donning the roles of both enhancers and suppressors.

H19, a standout among lncRNAs, takes a leading role in the control of hemoglobin expression. Its influence is particularly pronounced during crucial stages of development, such as embryogenesis and the transition from fetal to adult hemoglobin. H19 exerts its control by engaging in a multifaceted dance with proteins and other RNA molecules, forming part of a complex network of gene regulation that governs the fine-tuned expression of hemoglobin genes [11]. This lncRNA's significance is underscored by its participation in processes that dictate the fate of hemoglobin genes, influencing whether they are activated or silenced. These actions are pivotal in ensuring that hemoglobin synthesis aligns with the body's specific needs, such as the shift from fetal to adult hemoglobin during development. H19 and its network of interactions are vital players in safeguarding the harmony and precision of hemoglobin production.

As researchers delve deeper into the world of lncRNAs, more conductors of hemoglobin regulation are likely to emerge, each contributing their unique notes to the symphony of gene expression. Together, these lncRNAs fine-tune the balance of hemoglobin, ensuring the body's oxygen-carrying capacity remains finely attuned to its dynamic requirements.

2.1.3. Circular RNAs (circRNAs): The Unconventional Conductors

Circular RNAs (circRNAs) have emerged as unconventional conductors, adding their unique notes to the complex symphony of hemoglobin regulation [12]. Although circRNAs are relatively recent discoveries, their roles in gene regulation, particularly in the context of hemoglobin expression, have garnered increasing attention. These circRNAs contribute to the harmonious control of hemoglobin production by engaging in a unique mode of interaction with microRNAs, thereby indirectly influencing the expression of hemoglobin genes. One exemplar of a circRNA that participates in the regulation of hemoglobin is ciRS-7, which stands for "circular RNA sponge for miR-7." It functions as a sponge for miR-7, preventing miR-7 from inhibiting the production of hemoglobin [13]. This intricate interplay between ciRS-7 and miR-7 highlights the complexity of the interactions between different classes of non-coding RNA regions in orchestrating the precise control of hemoglobin gene expression.

The role of non-coding RNA regions in regulating hemoglobin expression has transitioned from being the enigmatic "dark matter" of the genome to becoming fundamental conductors in the symphony of hemoglobin gene regulation. MicroRNAs, long non-coding RNAs (lncRNAs), and circRNAs each play unique and vital roles in this complex orchestration. Their ability to exert precise control over hemoglobin levels ensures the harmonious balance required for the essential function of oxygen transport within the human body. This understanding opens new avenues for research, diagnostic approaches, and therapeutic interventions in the realm of hemoglobinopathies, promising hope for individuals affected by these conditions.

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2.2. Dancing with the Genome: Molecular Mechanisms of Non-Coding RNA-Hemoglobin Interactions

This section delves into the intricate molecular mechanisms through which non-coding RNA regions, including microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), interact with the hemoglobin genes, orchestrating their expression with remarkable precision.

2.2.1. MicroRNAs (miRNAs) in Gene Regulation

MicroRNAs (miRNAs) have emerged as pivotal conductors orchestrating the regulation of hemoglobin gene expression [14]. These small non-coding RNA molecules, typically composed of around 22 nucleotides, exercise exquisite control over hemoglobin levels by engaging with the 3' untranslated regions (3' UTRs) of messenger RNA (mRNA) molecules responsible for encoding hemoglobin. Their involvement in this regulatory ballet allows them to either suppress mRNA translation or initiate its degradation, thereby precisely fine-tuning the production of hemoglobin [15]. This intricate and highly coordinated dance guarantees that hemoglobin levels are meticulously maintained within the narrow range essential for effective oxygen transport. A trio of miRNAs, comprising miR-144, miR-150, and miR-451, holds a prominent position within this symphony of regulation [16]. These miRNAs are fundamental precision conductors, playing pivotal roles in the nuanced regulation of hemoglobin expression. Any perturbation in the activity of these miRNAs can disrupt the harmonious balance of hemoglobin production, potentially leading to hematological disorders. This underscores their critical role in ensuring the fine-tuned control of hemoglobin levels in the bloodstream.

Moreover, the involvement of miRNAs in gene regulation extends beyond their interactions with hemoglobin genes. Recent research has unveiled their broader influence on various biological pathways, implicating them in diverse cellular processes and the development of diseases [17,18]. This expanded understanding highlights the multifaceted roles of miRNAs in maintaining the equilibrium of physiological processes and underscores their potential as targets for therapeutic interventions. miRNAs have emerged as precision conductors in the finely tuned regulation of hemoglobin expression. Their involvement in the orchestration of hemoglobin levels ensures the seamless functioning of oxygen transport throughout the body. The interplay of miRNAs within the symphony of gene regulation extends to broader biological pathways and holds great promise for future research and therapeutic strategies aimed at addressing various disorders.

2.2.2. Long Non-Coding RNAs (lncRNAs): The Architects of Regulation

Long non-coding RNAs (lncRNAs) have risen to prominence as the architects of regulation, wielding significant influence over the intricate control of hemoglobin gene expression [19]. These lncRNAs, which can span thousands of nucleotides, are versatile in their functions, acting both as enhancers and suppressors, enabling them to play pivotal roles in shaping the landscape of hemoglobin regulation. H19, a standout example among these lncRNAs, holds a key position as a master conductor in the symphony of hemoglobin gene regulation [20]. Its orchestration is particularly vital during crucial developmental transitions, such as hemoglobin switching. H19 achieves this by engaging in intricate interactions with a cast of characters, including proteins and other RNA molecules, to carefully mold the expression of hemoglobin genes.

This architectural role of lncRNAs, like H19, is not limited to a single gene or a specific pathway. They have been implicated in orchestrating a myriad of cellular processes and gene networks, often extending their influence to various biological pathways. Their broad-reaching impact underscores their importance as central figures in the intricate world of gene regulation, with potential implications for the development of novel therapeutic interventions [21,22].

Long non-coding RNAs (lncRNAs) function as the architects of regulation, intricately shaping the control of hemoglobin gene expression and beyond. With their roles extending into diverse biological processes, these lncRNAs stand as vital conductors in the grand symphony of gene regulation.

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2.2.3. Circular RNAs (circRNAs)

Circular RNAs (circRNAs) are emerging as skillful intermediaries in the intricate orchestration of hemoglobin gene expression. While the precise roles of circRNAs in gene regulation are still being elucidated, they have been implicated in controlling the delicate balance of hemoglobin levels, adding another layer of complexity to this genomic dance. CircRNAs are unique among non-coding RNAs for their covalently closed-loop structures. This circular configuration makes them resistant to exonucleases, increasing their stability within the cell [23]. In the realm of hemoglobin regulation, circRNAs have been recognized for their ability to "sponge" microRNAs (miRNAs), a class of small non-coding RNAs that are known precision conductors in the fine-tuned control of hemoglobin expression [24].

One circRNA, in particular, stands out as a prime example of this miRNA "sponging" phenomenon – ciRS-7 (circular RNA sponge for miR-7). This circRNA effectively acts as a sponge for miR-7, preventing it from inhibiting the production of hemoglobin [25]. This intricate interaction forms part of a web of complex cross-talk between different classes of non-coding RNA regions, including miRNAs and circRNAs, in the regulation of hemoglobin. The existence of circRNAs as intermediaries in the regulation of hemoglobin implies a multifaceted network of regulatory mechanisms. They indirectly impact hemoglobin gene expression by influencing the activity of miRNAs, which act as precision conductors in this symphony. The intricate interplay between circRNAs and miRNAs adds depth and nuance to our understanding of hemoglobin regulation.

The circRNAs serve as skillful intermediaries in the dance with the genome, ensuring that hemoglobin levels are harmoniously balanced to fulfill their crucial role in oxygen transport. This newly discovered layer of complexity underscores the precision required to maintain the delicate balance of hemoglobin expression. These findings not only advance our understanding of hemoglobin regulation but also open new avenues for research, diagnostics, and therapeutic strategies in the context of hemoglobinopathies.

2.3. Clinical Crescendo: Non-Coding RNA-Based Therapeutic Strategies for Hemoglobinopathies

This section examines the clinical applications of our understanding of non-coding RNA regions in the context of hemoglobinopathies. It delves into the emerging therapeutic strategies that leverage non-coding RNAs to ameliorate these conditions.

2.3.1. RNA-Based Therapeutics for Hemoglobinopathies

RNA-based therapeutics represent a promising avenue for addressing the complex challenges presented by hemoglobinopathies. Among the numerous non-coding RNAs, microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) have emerged as potential therapeutic targets, offering hope for individuals affected by these conditions. In the context of hemoglobinopathies, researchers have gained insights into how specific non-coding RNAs intricately regulate the expression of hemoglobin genes. These discoveries have paved the way for the development of RNA-based therapies designed to restore the delicate balance of hemoglobin production, thereby ameliorating the symptoms associated with these disorders.

One illustrative example is in the case of sickle cell anemia, a hereditary condition characterized by the production of abnormal hemoglobin, specifically hemoglobin S (HbS). In recent years, researchers have turned their attention to miRNAs as precision tools for inhibiting the expression of HbS. These synthetic miRNA molecules are custom-designed to target the problematic HbS genes. By doing so, they hold the potential to reduce the levels of HbS in affected individuals, offering a ray of hope for those battling the symptoms of sickle cell anemia [26]. Moreover, the delivery of therapeutic miRNAs or other RNA-based molecules is being explored through innovative methods. Viral vectors, for example, have shown promise as vehicles for introducing specific miRNAs into target cells. This approach aims to precisely modulate hemoglobin gene expression, restoring the balance required for healthy hemoglobin production.

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The field of RNA-based therapeutics for hemoglobinopathies continues to evolve rapidly. While challenges remain, the progress made in understanding the roles of non-coding RNAs in hemoglobin regulation offers the potential for novel, more effective, and less invasive treatment options. These advancements bring renewed hope to individuals and families affected by hemoglobin disorders, offering the promise of improved quality of life and a brighter, healthier future.

2.3.2. Genome Editing and Non-Coding RNAs

The integration of genome editing technologies, most notably CRISPR-Cas9, into the realm of non-coding RNA-based therapeutics has ushered in a new era of promising interventions for hemoglobinopathies. Scientists are diligently exploring the remarkable synergy between non-coding RNAs and CRISPR-Cas9, revealing a pathway towards more precise and effective treatments for these disorders. The core concept behind this innovative approach is the use of non-coding RNAs to guide CRISPR-Cas9 to specific target sites within the genome. CRISPR-Cas9 acts as a molecular scissor, capable of making highly precise cuts or edits to DNA. However, its remarkable precision relies on its ability to be directed to the correct genomic location. This is where non-coding RNAs, with their intrinsic ability to interact with specific gene sequences, come into play [27]. In the context of hemoglobinopathies, these RNA-guided genome editing strategies can be directed towards the hemoglobin genes themselves. By pairing non-coding RNAs with CRISPR-Cas9, researchers can selectively target and modify the genetic elements responsible for hemoglobin production. For instance, in cases where an overproduction of abnormal hemoglobin is the problem, this approach offers the potential to reduce its levels to normal, alleviating the associated symptoms [28].

While this field of research is still in its early stages, the promise it holds is immense. The ability to precisely modulate hemoglobin gene expression through RNA-guided genome editing offers hope to countless individuals affected by hemoglobinopathies. As technology and understanding progress, these innovative therapies may emerge as transformative treatments, ultimately improving the quality of life for patients and their families.

2.3.3. Circular RNAs (circRNAs) as Therapeutic Agents

The emerging field of circular RNAs (circRNAs) in the context of therapeutic interventions for hemoglobin disorders represents a fascinating avenue of research and innovation. Scientists are exploring the potential of circRNAs, both natural and engineered, as therapeutic agents with the capacity to restore the balance in hemoglobin gene expression, ultimately offering hope for individuals affected by hemoglobinopathies. One of the key strategies involves the design and engineering of circRNAs to act as molecular sponges or miRNA sequestering agents. These custom-designed circRNAs are engineered to selectively bind to and inhibit specific miRNAs associated with hemoglobin disorders. By sequestering these miRNAs, engineered circRNAs aim to alleviate the inhibitory effect they have on hemoglobin gene expression [29].

This innovative approach seeks to rectify imbalances in hemoglobin production. For instance, in cases where certain miRNAs contribute to the overproduction of abnormal hemoglobin, engineered circRNAs could act as precision conductors in restoring normal hemoglobin gene expression. This would have the potential to alleviate the symptoms and complications of hemoglobinopathies such as sickle cell anemia or thalassemia [30]. While the field of circRNAs as therapeutic agents is still in its infancy, the promise it holds for treating hemoglobin disorders is noteworthy. The ability to engineer circRNAs tailored to specific miRNAs offers a level of precision and control in gene regulation that was previously elusive. As research in this area progresses and our understanding deepens, engineered circRNAs may pave the way for groundbreaking treatments that significantly enhance the quality of life for individuals living with hemoglobinopathies.

2.4. Clinical Trials and Future Directions

The journey towards non-coding RNA-based therapies for hemoglobinopathies has reached an exciting phase marked by ongoing clinical trials. These trials represent a pivotal step in translating

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promising preclinical research findings into real-world applications and bringing innovative treatments for hemoglobin disorders closer to clinical practice [31]. In these clinical trials, researchers are rigorously assessing the safety and efficacy of various non-coding RNA-based therapeutic approaches. The ultimate goal is to provide robust scientific evidence that supports the use of these interventions as viable treatment options for individuals living with hemoglobinopathies. These trials involve carefully designed protocols, patient recruitment, and meticulous monitoring to ensure both safety and effectiveness [32]. As we move into this clinical crescendo of non-coding RNA-based therapies, it is essential to underscore the profound potential of these interventions. They offer a level of precision and specificity previously unattainable in the realm of hemoglobinopathies. These therapies hold the promise of providing more effective, potentially curative treatments by addressing the root causes of these conditions at the genetic and molecular level. Such an approach represents a paradigm shift in the treatment of hemoglobin disorders, potentially transforming the lives of affected individuals [33]. However, it's important to acknowledge that while we stand at the precipice of remarkable advancements, challenges remain. Ethical considerations, regulatory approvals, and broader accessibility to these innovative treatments are all facets that need careful attention. The ethical dimensions include issues surrounding patient consent, equitable access to cutting-edge therapies, and the long-term monitoring of patients who undergo these novel treatments. The medical community, policymakers, and ethical bodies must work collaboratively to address these concerns [33].

Nonetheless, this field is at the forefront of advancing the prospects for those suffering from hemoglobinopathies. With each clinical trial, we inch closer to realizing the full potential of non-coding RNA-based therapies. The combined efforts of scientists, healthcare providers, and patients participating in these trials promise to bring us closer to a future where hemoglobin disorders are managed with greater precision, less invasiveness, and potentially with curative outcomes.

3. Conclusion

The journey to unravel the enigma of non-coding RNA regions and their pivotal role in hemoglobin regulation has transformed our understanding of gene orchestration. These once-dismissed non-coding RNA regions have emerged as the master conductors in the complex symphony of hemoglobin gene expression. As we reflect on the significance of this discovery, it is evident that these "silent" players in the genome are, in reality, the conductors of harmony, ensuring the precise and delicate balance of hemoglobin production. This newfound knowledge not only enhances our understanding of hemoglobin regulation but also offers promising avenues for clinical applications and therapeutic strategies. The integration of non-coding RNAs, including microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), has ushered in a new era of precision medicine and therapeutic interventions for hemoglobinopathies. These non-coding RNAs, each with its unique functions and roles, contribute to the fine-tuned control of hemoglobin levels, essential for effective oxygen transport throughout the body. miRNAs, such as miR-144, miR-150, and miR-451, serve as precision conductors, exerting meticulous control over hemoglobin expression at the post-transcriptional level. LncRNAs, like H19, act as maestros of hemoglobin control, orchestrating gene expression during crucial developmental transitions. CircRNAs add their unique notes to the symphony, indirectly influencing hemoglobin gene expression by interacting with miRNAs.

The clinical application of this understanding is exemplified in RNA-based therapeutics, genome editing guided by non-coding RNAs, and the engineering of circRNAs. These innovative approaches hold the potential to restore the balance in hemoglobin gene expression and offer hope for individuals affected by hemoglobinopathies. Ongoing clinical trials are a testament to the transformative power of these therapies, bringing us closer to a future where these genetic disorders are managed with unprecedented precision and effectiveness. As we embark on this exciting phase of research and clinical trials, it is important to remain mindful of the ethical, regulatory, and accessibility challenges that lie ahead. Collaboration between the scientific community, policymakers,

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and ethical bodies is paramount in ensuring the responsible and equitable advancement of non-coding RNA-based therapies for hemoglobinopathies.

The revelation of non-coding RNA regions as the conductors of hemoglobin regulation signifies a paradigm shift in our approach to addressing hemoglobin disorders. It offers a glimpse of a future where precision medicine and gene therapies provide new hope and improved quality of life for individuals and families affected by these conditions. This comprehensive review shines a light on the significance of non-coding RNA regions, highlighting their transformative potential in the symphony of hemoglobin gene regulation.

Use of AI Tools Declaration

No Artificial Intelligence (AI) tools are used in the creation of this work or part of it.

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