



RNA interference (RNAi): Harnessing molecular mechanisms for therapeutic applications

Elli Toivonen*

Department of Genetics, University of Navarra, Pamplona, Spain

Corresponding author: Elli Toivonen

E-mail: Ellitoivonen@mssm.edu

Genet. Mol. Res. 21 (1): gmr34036

Received January 17, 2022

Accepted January 19, 2022

Published February 16, 2022

Copyright © 2022 Toivonen E. This is an open-access article distributed under the terms of the

Creative Commons Attribution Share A like (CC BY-SA) 4.0 License.

INTRODUCTION

RNA interference (RNAi) represents a powerful molecular mechanism for regulating gene expression and has emerged as a promising therapeutic approach for a wide range of diseases. RNAi is a natural biological process that involves the silencing of gene expression through the sequence-specific degradation of messenger RNA (mRNA) molecules. This process is mediated by small RNA molecules, such as Small interfering RNAs (siRNAs) and microRNAs (miRNAs), which guide the RNA-Induced Silencing Complex (RISC) to target mRNAs, leading to their degradation or translational repression.

The discovery of RNAi has revolutionized our understanding of gene regulation and provided a powerful tool for manipulating gene expression in a precise and targeted manner. RNAi-based therapies hold great promise for treating a variety of diseases, including cancer, infectious diseases, genetic disorders, and neurodegenerative diseases. By harnessing the natural mechanisms of RNAi, researchers can develop therapeutic agents that specifically target disease-causing genes or pathways, offering the potential for highly selective and effective treatments with minimal off-target effects.

DESCRIPTION

One of the key advantages of RNAi-based therapies is their ability to target genes that are difficult to modulate using traditional small molecule drugs or protein-based therapies. Many disease-causing genes are considered "undruggable" due to their complex structure or lack of suitable binding sites for small molecules. RNAi offers a complementary approach for targeting these genes by directly interfering with their expression at the mRNA level. Moreover, RNAi-based therapies can be designed to target specific isoforms or splice variants of a gene, allowing for precise control over gene expression and function.

In the context of cancer therapy, RNAi holds promise for selectively targeting oncogenes or genes involved in tumor progression, metastasis, and drug resistance. By delivering siRNAs or miRNAs that target key signaling pathways or regulatory molecules in cancer cells, researchers can inhibit tumor growth, induce apoptosis, and enhance the sensitivity of cancer cells to chemotherapy or immunotherapy. RNAi-based therapies may also be used to overcome resistance mechanisms that limit the effectiveness of existing cancer treatments, providing new avenues for combination therapies and personalized medicine approaches.

In addition to cancer, RNAi-based therapies are being investigated for the treatment of infectious diseases, including viral infections, bacterial infections, and parasitic diseases. RNAi offers a promising approach for inhibiting the replication of pathogenic viruses, such as Hepatitis B Virus (HBV), Human Immunodeficiency Virus (HIV), and Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), by targeting essential viral genes or host factors required for viral replication. Similarly, RNAi-based strategies may be used to suppress the expression of virulence factors in bacterial pathogens or disrupt essential metabolic pathways in parasites, leading to the clearance of infections and improved patient outcomes.

In the field of genetic disorders, RNAi holds potential for correcting or modulating the expression of disease-causing genes associated with inherited genetic diseases, such as Huntington's disease, Amyotrophic Lateral Sclerosis (ALS), and Duchenne Muscular Dystrophy (DMD). By delivering siRNAs or Antisense Oligonucleotides (ASOs) that target mutant alleles or aberrant transcripts, researchers can reduce the production of toxic proteins, restore normal gene expression patterns, and alleviate disease symptoms. RNAi-based therapies may also be used to modulate the expression of disease-modifying genes or pathways, offering new therapeutic strategies for treating a wide range of genetic disorders.

Furthermore, RNAi-based therapies hold promise for treating neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, and ALS, which are characterized by progressive loss of neurons and accumulation of toxic protein aggregates. RNAi offers a means of selectively targeting disease-associated genes or pathways implicated in neurodegeneration, such as genes encoding amyloid-beta peptides, tau proteins, or Superoxide Dismutase 1 (SOD1). By delivering siRNAs or miRNAs that inhibit the expression of these genes, researchers can reduce the accumulation of toxic protein aggregates, mitigate neuroinflammation, and preserve neuronal function, offering the potential for disease-modifying treatments that slow or halt disease progression.

Despite the tremendous potential of RNAi-based therapies, several challenges remain to be addressed for their clinical translation and widespread adoption. These include issues related to delivery, stability, specificity, and immunogenicity of RNAi molecules, as well as concerns about off-target effects, dose-dependent toxicity, and long-term safety. Developing effective delivery systems that can target RNAi molecules to specific tissues or cell types while minimizing systemic exposure and immune activation is critical for the success of RNAi-based therapies. Moreover, optimizing the design and chemical modification of RNAi molecules to enhance their stability, specificity, and potency is essential for maximizing therapeutic efficacy and minimizing adverse effects.

CONCLUSION

RNA interference (RNAi) represents a powerful molecular mechanism for regulating gene expression and has emerged as a promising therapeutic approach for a wide range of diseases. By harnessing the natural mechanisms of RNAi, researchers can develop targeted therapies that specifically inhibit the expression of disease-causing genes or pathways, offering the potential for highly selective and effective treatments with minimal off-target effects. Despite the challenges that remain to be addressed, RNAi-based therapies hold great promise for transforming the treatment of cancer, infectious diseases, genetic disorders, and neurodegenerative diseases, and may ultimately lead to the development of new therapies that improve patient outcomes and quality of life.