

Interfering With RNA as a Therapeutic Tool

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Description

RNA interference is a technique in which a dsRNA sequence is introduced into cells and the function of endogenous genes that are complementary to the injected RNA is disrupted. The first instance of RNA-induced silencing was discovered in petunia plants, where the introduction of a transgene to boost purple colour expression resulted in the silencing of both the endogenous gene and the transgene [1].

Plants have been shown to be able to generate virus specific resistance as a result of this RNA silencing approach. In *C. elegans*, RNA silencing has been shown to regulate gene expression. Fungi and human cells both have similar processes that aid in the regulation of biological functioning [2]. RNA interference is a revolutionary strategy for regulating a variety of diseases by targeting specific critical genes that are important for disease progression. MicroRNA (miRNA), small interfering RNA (siRNA), and short hairpin RNA can all cause RNA interference (shRNA). MiRNA is a type of non-coding RNA that plays a role in gene control during normal cellular processes, whereas siRNA and shRNA are delivered into the cell to aid gene expression [3].

MicroRNA (miRNA) and siRNA production have slightly different biogenesis, although their functionality is identical in many ways. Dicer, an ATP-dependent ribonuclease from the RNase III family, attaches to dsRNA with two nucleotide 3' overhangs and cuts it to create siRNA. siRNAs are dsRNA duplexes with 2 or 3 nucleotide 3' overhangs that are 21-23 nucleotides long. These siRNAs bind to RNA-induced silencing complexes (RISC), which unwind the siRNA duplex. The guide strand directs the RISC to the complementary site on the target mRNA, while the passenger strand is cut and escapes the complex. The argonaute protein catalyses the cleavage of target mRNA, which is then released while the active strand containing RISC directs the cleavage of further target mRNAs. The technology of RNA interference has emerged as a promising therapeutic option [4].

The cell's interferon response is bypassed by the short length synthetically

created siRNA. The following factors may contribute to the increased interest in siRNA as a therapeutic: Targeting various locations of the same gene, low quantities of siRNA required to produce the response, capacity of silencing similar mRNA in different species, and minimal effect on other cell control mechanisms are all advantages of siRNA. Around a thousand patents have been submitted for siRNA as an antiviral agent, second only to siRNA as an anticancer agent. Several clinical trials including siRNA therapy have also been started, with promising outcomes [5]. The transport of siRNA to the cells is the most difficult part of this approach. Several oligonucleotide modification technologies as well as polymeric nanocarriers can be used to tackle this challenge.

Conflict of Interest

None.

References

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