Development of modified siRNA for gene silencing

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Abstract

With the advent of RNA interference as a means to silence gene expression, small interfering RNA (siRNA) oligonucleotides have been recognized as powerful tools for targeting mRNAs and eliciting their gene inhibitory properties [1]. Small RNA duplexes are recognized by a protein complex called RISC provoking the specific degradation of messenger [2]. As a consequence of this discovery, siRNA oligonucleotides are now being intensively investigated as potential therapeutic agents for various biomedical indications [3]. siRNA are not readily taken up into tissues and are also susceptible to degradation by nucleases in the blood. For these reasons the interest in the design and preparation of modified RNA derivatives that are more stable, easier to produce at large scale and with a higher cellular uptake it is of vital importance to improve RNAi limitations [3].

Specifically we will show the development of siRNAs carrying conformationally restricted pseudonucleosides [4] as well as the synthesis and properties of siRNA conjugates with molecules that may enhance cellular uptake such as peptides, lipids and intercalating agents [5].

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