# siRNAs based therapies: a recent overview





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#### siRNAs based therapies: a recent overview

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Dedicated to My family

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### Abstract

Gene therapy, through the introduction of genes in human cells to restore normal cellular function, is a powerful tool for the innovative treatments of different diseases such as solid tumors, viral infections and genetic diseases.

RNA interference (RNAi) is a potent and specific mechanism for regulating gene expression. Harnessing RNAi to silence genes involved in disease holds promise for the development of a new class of therapeutics. One powerful class of RNAi-based therapeutics is represented by short interfering RNA structures (siRNAs), i.e. small pieces of double-stranded RNA which are involved in gene silencing mechanism. The therapeutic application of siRNAs is extremely promising due to their efficient and specific gene silencing ability, however, to be generally applicable, a number of issues linked to their delivery in living systems must be overcome. Indeed, one of the major problems in siRNA administration is that the cell plasma membrane represents an impermeable barrier to large and polar macromolecules such as siRNA, thus the diffusion of these poly-anions into the cells is particularly difficult. The most widespread strategy to overcome this problem consists in the encapsulation of siRNA molecules into "drug carriers" structures, in order to ensure a controlled drug delivery, also reducing siRNA toxicity, and above all improving their pharmacokinetics properties, stability and efficiency.

In this work, a detailed presentation of the different methods for siRNAs delivery into target tissues and the main carriers used in their administration has been performed. In particular, the attention is focused on the main and more recent research activities that involve new siRNA drugs emphasizing kind of delivery system used and diseases target. For each research activity the disease to treat, the target, the siRNAs delivery system used, the sponsor, the status and Pag. X

the phase of clinical trial and publications, if available, are presented and explained in detail. The thesis, thus, provides an overview of siRNA therapeutics in clinical trials, including the clinical progress, challenges and the future perspectives in siRNA therapy for the treatments of several diseases.

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I conclude with a part of the most famous Steve Jobs discussion, addressed to the graduates at Stanford University in June 12, 2005:

"...Your time is limited, so don't waste it living someone else's life. Don't be trapped by dogma — which is living with the results of other people's thinking. Don't let the noise of others' opinions drown out your own inner voice. And most important, have the courage to follow your heart and intuition. They somehow already know what you truly want to become. Everything else is secondary...Stay Hungry. Stay Foolish".