Oligonucleotide therapeutics: Is the promise ready to be fulfilled?

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The promise of RNA-targeting therapeutics (antisense, siRNA and RNA-splice modulation) is that it is possible to design therapeutic entities based solely on the sequence of the RNA target, taking advantage of Watson-Crick base-pairing rules for rational drug design. The concept is simple, however full realization of the potential has not yet been achieved. Recent advancements are turning the promise into reality. Since the first description of antisense activity and the subsequent discovery of siRNA, significant progress has been made in the understanding of mechanisms of action and how these processes exploit naturally occurring phenomena. In addition to a better understanding of the enzymologic basis for these technologies, there have been remarkable advancements in understanding of mechanisms associated with the adverse effects of RNA-targeted therapies. How administering oligonucleotides produces adverse effects and how to avoid adverse effects has been the subject of intensive research in bioinformatics, innate immunity, pharmacokinetics and pharmaceutics. Delivery of oligonucleotide-based therapeutics remains a challenge. Nature has solved the delivery problem using exosomes and self-assembling oligonucleotide containing nanoparticles (viruses). To solve the delivery problem it might be useful to learn from nature. We are in an important time for oligonucleotide technology and there are many new advancements and new clinical results each week. This talk will highlight some of the key activities ongoing in the field.