The RNA drug revolution -- a new approach to gene therapy

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RNA interference (RNAi) represents an innovative new strategy for using small RNA molecules to silence specific genes associated with disease processes, and a series of review articles describing the state-of-the-art and potential therapeutic applications of RNAi and microRNAs will begin with two review papers in the January 2008 issue (Volume 19, Number 1) of *Human Gene Therapy*, a peer-reviewed journal published by Mary Ann Liebert, Inc. The papers are available free online.

At least six clinical trials using RNA interference (RNAi) have been approved, “with many more coming down the pipeline,” according to the Editorial by Mark A. Kay, MD, PhD, an Associate Editor of Human Gene Therapy and the Dennis Farrey Family Professor in Pediatrics and Professor of Genetics at Stanford University School of Medicine. “One thing is clear,” adds Kay, “small RNAs as a therapeutic platform are here to stay.”

The excitement surrounding RNAi and the two main approaches to delivering RNA-based therapeutics—as mature siRNA molecules or as short hairpin RNAs (shRNAs)—relates to the discovery of native microRNA molecules in human cells and their intrinsic ability to block the expression of a target gene. siRNA therapeutic strategies in development aim to harness the cells’ natural RNAi pathway and specifically silence a mutant or dysregulated gene.

Traditionally, gene therapy has focused on supplying a normal copy of a faulty gene, whereas RNAi turns off a problematic gene. These

contrasting approaches share some of the same techniques and challenges, including delivery of a therapeutic gene or siRNA into cells.

Human Gene Therapy will publish a series of review papers in four consecutive issues focusing on a range of topics related to therapeutic applications of small RNAs. The series begins in the January issue with a paper entitled, “Behind the Scenes of a Small RNA Gene-Silencing Pathway,” by Gregory Ku, MD, PhD, and Michael McManus, PhD, from the University of California, San Francisco, which presents the current understanding of microRNA mechanisms of action and the potential for applying this knowledge to the development of RNAi-based treatments.

In the review by Anton McCaffrey, PhD, and Rebecca Marquez, MA, entitled, “Advances in Micro-RNAs: Implications for Gene Therapists,” the authors discuss the likelihood that microRNAs, which are believed to regulate as many as one-third of all human gene transcripts (or messenger RNAs), are implicated in many human diseases. Using gene therapy to manipulate microRNA levels represents an attractive new approach for controlling gene expression and identifying targeted and effective therapeutics.

"The concept of using RNA as a therapeutic product is quite attractive and adds an important new dimension to the field of nucleic acid based therapeutics including gene therapy. Mark Kay, Associate Editor of Human Gene Therapy, has organized an exciting series of reviews summarizing the state of the art of this emerging field," says James M. Wilson, MD, PhD, Editor-in-Chief, and Head of the Gene Therapy Program, Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, in Philadelphia.

Source: Mary Ann Liebert, Inc.