

S014 Gene Silencing Therapeutics: Lessons from the Past,
Prospects for the Future

Alan M. Gewirtz

University of Pennsylvania School of Medicine

The promise of gene silencing therapeutics began with the pioneering anti-viral work of Zamecnick and Stephenson in 1978. Some 18,000 manuscripts, and more than 15 clinical trials later, DNA and RNA based gene silencing medicines remain a promise unfulfilled. The reasons for this are numerous and will be discussed in detail. Progress on the critical issues of molecule chemical composition, delivery, and mRNA target sequence selection will be reviewed, along with the problems of target validation and design of clinical trials. While RNA interference (RNAi) has rejuvenated the field, this approach to therapeutics will be subject to many of the same considerations as traditional antisense strategies including drug delivery, molecule stability, and off target effects. In the course of discussing where the field has been, it is hoped that a useful map detailing the location of old minefields, and a clearer path to the goal of efficient, specific and cost effective therapeutics, can be constructed.