

Preface

This is the second edition of *Antisense Therapeutics*. The first edition was edited by Sudhir Agrawal and published in 1996. At that time there was no therapy based on antisense, but plenty of promise for the highly specific targeting of genes that cause disease. Antisense oligonucleotides were first reported as viral replication inhibitors by Paul Zamecnik and Mary Stephenson in 1978. Although this was excellent work, nothing much happened until new procedures for synthesizing DNA sequences were developed. Once oligonucleotides were easy to make, more and more studies were published in the 1980s, most of which were directed to cells in culture. In the early 1990s antisense oligonucleotides were increasingly tested in vivo. There were many controversies and a great deal of concern about backbone modification of the phosphodiester bridges that link the DNA bases. To protect against breakdown by nucleases in cells or blood, phosphorothioate oligonucleotides were adopted. In 1998 a phosphorothioated antisense agent was the first FDA-approved antisense therapy. Vitravene™, developed by Isis Pharmaceuticals, made antisense therapeutics a reality.

Since then, the complete sequencing of the human genome in April, 2003 has demonstrated the presence of a vast number of targets for antisense oligonucleotides. So we now have thousands of targets, hundreds of preclinical animal studies, and some 20 clinical trials ongoing. Any successful trial with an antisense compound will open a floodgate of new therapies for a panoply of diseases.

This second edition of *Antisense Therapeutics* deals less with the basic science of antisense and more with the actual therapeutic applications. For that reason it is organized into disease states.

I thank the authors for their patience and their strong contributions. Since this book was being edited at a time when I moved from the University of Florida to the University of South Florida, I ended up with two secretaries. I would like to thank Ms. Gayle Butters at the University of Florida and Mr. Eric J. Wheeler at the University of South Florida for their essential help. I am also grateful to Craig Adams at Humana Press for his patience.

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