sequence-specific, selective knockdown of tumor-causing mutants has tremendous therapeutic potential.

Concluding remarks

This was an excellent conference that included important contributions from several experts over two days. The advantages and limitations of RNAi approaches to the important topic of target validation were discussed. More importantly, measures were suggested to remedy some of the drawbacks of the new technologies.

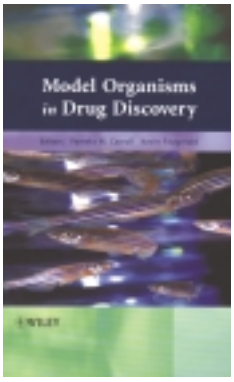
References

1 Jain, K.K. (2004) *RNAi: technologies, markets and companies*. Jain PharmaBiotech Publications, Basel

2 Ntambi, J.M. et al. (2002) Loss of stearoyl-CoA desaturase-1 function protects mice against adiposity. *Proc. Natl. Acad. Sci. U. S. A.* 99, 11482–11486

3 Shinagawa, T. and Ishii, S. (2003) Generation of Ski-knockdown mice by expressing a long double-strand RNA from an RNA polymerase II promoter. *Genes Dev.*17, 1340–1345

4 Lu, P.Y. et al. (2003) siRNA-mediated antitumorigenesis for drug target validation and therapeutics. *Curr. Opin. Mol. Ther.* 5, 225–234



Model organisms in drug discovery

Edited by Pamela M. Carroll and Kevin Fitzgerald, Wiley Europe, 2003, 302 pages in hardback, ISBN: 0-470-84893-6

Over the past decade, huge advances in science have been made in areas such as genomics and proteomics, including, most significantly, the completion of the draft human genome sequence. Additionally, there has been an increase in spending in the pharmaceutical industry. However, these monumental steps forward have to date had little impact on our ability to combat and cure many human diseases and over the last ten years the number of marketable drugs has not significantly increased.

The process of getting a drug to market is long and arduous. Many promising targets and drugs fail along the way, costing time and millions of dollars. The process involves identifying and then validating a target, ultimately in human clinical trials, which still take the same amount of time as they did in years past. However, many inroads have been made in trying to shorten the time taken to identify targets and the use of model organisms has helped in this regard. These systems provide several advantages, including available genetic and molecular tools, cost, and short reproductive and generation times. Additionally, experiments in model systems are conducted in an intact organism.

Model systems have been used for decades for scientific study. Often, they provide an advantage for processes that seem too complex for study in more complex eukaryotes. Additionally, many of these studies have been groundbreaking (for example, the discovery of cell death genes in *Caenorhabditis elegans*), opening up new areas of study in mammals, including humans. Recently, many drug companies have begun to use model organisms as a faster, cheaper method to identify new drug targets. In the new book edited by Carroll and Fitzgerald, the use of model organisms in drug discovery is reviewed.

The book begins with a brief overview and comparison of each model system discussed in the book. The chapters are then organized in such a way as to start from the simplest to the most complex organism when compared with humans, including budding yeast (*Saccharomyces cerevisiae*), nematodes (*C. elegans*), flies (*Drosophila melanogaster*), zebrafish (*Danio rerio*) and mice (*Mus musculus*). Chapters are written by a researcher from the pharmaceutical field who has worked or works with that organism and provides details on almost all of the methods that have been or can be used for that organism in the pursuit of drug discovery. Moreover, both the advantages and disadvantages of the organism in this effort are discussed. Chapter 3 is particularly enlightening because the authors discuss in great detail how one goes from model system to target identification and validation using *C. elegans* as a model for unipolar depression.

This book is an invaluable resource for any researcher in the academic or private sector looking to expand into a model organism work because it reviews all available techniques for each model system. This is both an advantage as well as a limitation because, at times, chapters provide too little detail and are more like a good survey of available experimental techniques. However, this book should also be essential for any graduate level course on drug discovery or any researcher wanting to understand how model systems can be used in the laboratory.

The availability and understanding of model organisms might provide new tools for both academic researchers and drug companies. One watches the next few years with interest to see if this impacts on our ability to combat the complex diseases that ail our society.

Heidi A. Tissenbaum
Program in Gene Function and Expression
Program in Molecular Medicine
University of Massachusetts Medical School
Aaron Lazare Research Building Suite 615
364 Plantation Street
Worcester, MA 01605, USA
email: heidi.tissenbaum@umassmed.edu

  PII: S1359-6446(04)03049-1