The use of animal models in development of novel therapeutic strategies is the main emphasis of this report. Creation of new animal models is an important part of this research. Discussed in this publication:

- Case studies of the use of established animal models in developing novel therapeutic strategies
- Emerging animal models for use in drug discovery and the development of new therapeutic strategies
- Development of animal models that are more predictive of drug efficacy
- Technological developments in progress
- Use of computer models and translational biomarkers to move more effectively from preclinical animal studies to the clinic

Thought leader interviews and a user survey are also included.
**OVERVIEW**

**ANIMAL MODELS for Therapeutic Strategies**

Author: Allan B. Haberman, Ph.D.

Although animal models based on mammalian species have been long employed, more recently the pharmaceutical/biotechnology industry has also adopted several invertebrate and lower vertebrate animal models. The aim of using animal models to develop novel therapeutic strategies is to achieve knowledge of pathways and targets that leads to new paradigms for drug discovery and development.

Chapters 2, 3, 4, and 6 focus on the nematode *Caenorhabditis elegans*, the fruit fly Drosophila, the zebrafish, and the mouse, respectively. Each chapter includes cases studies of the use of each of these established animal models in developing novel therapeutic strategies for human disease. Chapters 5 and 7 focus on emerging animal models, the African clawed toad *Xenopus tropicalis* and emerging mammalian animal models. Each of these chapters focuses on technological developments in progress to develop tractable animal models based on these organisms. Chapter 7 also includes a discussion of the rat as an animal model, which is “reemerging” as the result of new technologies and collaborations.

Chapter 8 discusses the use of computer models and translational biomarkers in helping researchers move more effectively from preclinical animal studies to human clinical trials. Pharmaceutical and biotechnology company researchers have been increasingly applying pharmacokinetic/pharmacodynamic modeling to all stages of drug development. These models, as well as biophysical models such as those developed by Novartis and physiological models such as those developed by Entelos, can help researchers more effectively use animal model data in the design of clinical trials. In particular, they can help researchers reduce drug attrition in clinical trials due to suboptimal dosing.

Chapter 6, which focuses on the mouse, concludes with a discussion of the issue of developing more predictive animal models of drug efficacy, specifically more predictive mammalian models. One main reason for researchers’ difficulties in producing predictive mouse models is major unknown factors in disease biology. Although these factors make developing predictive animal models difficult, researchers can use animal models to learn about unknown or poorly understood areas of disease biology. This is expected to lead to the development of improved animal models as well as the development of new therapeutic strategies and drugs.

Developing animal models that are more predictive of efficacy is an iterative process. But progress is being made, as researchers apply new knowledge and experimental approaches in elucidating the biology of particular diseases to creation of animal models.

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INSIGHT PHARMA REPORTS’ ANIMAL MODELS SURVEY: JANUARY 2010

Question 1. Please classify your organization.
Question 2. What aspect(s) of the drug development process do you work in?
Question 3. What class(es) of drugs do you work on?
Question 4. Do you work directly with animal models?
Question 5. If you answered yes to question 4, in what aspect of drug development do you work with animal models?
Question 6. What types of animal models does your company use in-house?
Question 7. What types of animal models are used in studies that your company outsources to CROs?
Question 8. Do you agree that poorly predictive animal models have been a major reason for the low productivity of drug development?
Question 9. Has there been any improvement in the predictiveness of animal models for use in discovery research and preclinical studies since the initiation of the FDA’s Critical Path Initiative in 2004?
Question 10. Do you expect any improvements in the predictiveness of animal models for use in discovery research and preclinical studies in the next five years?
Question 11. Do you expect human cellular models that are based on induced pluripotent stem cells or similar technology to replace some uses of animals in pharmaceutical/biotechnology research over the next five years?
Question 12. Does your company use modeling/simulation to move from animal studies in the discovery and preclinical stages into human trials?
Question 13. Do you expect computer models (“virtual animal models,” “virtual human models,” “virtual physiological systems,” “virtual tumors,” etc.) to replace some uses of animal models over the next five years?
Question 14. Is development of computer-based animal or human models severely limited by researchers’ limited knowledge of biological systems and disease biology?
Question 15. How do regulations that are designed to promote animal welfare (e.g., the Animal Welfare Act, the Public Health Services’ Guide for the Care and Use of Laboratory Animals, local regulations, the 3Rs) affect your operations?
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