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BIOMARKERS
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The cover art is called “Biofluid” and represents biological fluid with visible signs of biomarkers. Created by Dr. Ina Schuppe-Koistinen using watercolors, Dr. Schuppe-Koistinen is a senior principal scientist and molecular toxicologist at AstraZeneca, Sweden. Additional science watercolors by Dr. Schuppe-Koistinen can be found at http://www.inasakvareller.se

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Printed in the United States of America.
To:
My parents, Sudhakar and Suhasini; my wife, Alka; and my sons, Ariv and Rian.

Vishal Vaidya

To:
My wife, Kristie; my daughter, Joanna; my son, Andrew; my son-in-law, Brian; and my grandson, Daniel.

Joseph Bonventre
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PREFACE

A biomarker is defined as a characteristic that can be objectively measured and evaluated as an indicator of normal biologic or pathogenic processes of pharmacological responses to a therapeutic intervention. Examples of biomarkers are proteins; lipids; genomic, metabolomic, or proteomic patterns; imaging patterns; electrical signals; and cells present on a urinalysis.

In medicine, disease processes are heterogeneous in their pathophysiology and clinical presentation, making diagnosis and prognosis challenging. In drug development, biomarkers are critical at a variety of stages of the process, with the need for informative determination of efficacy and toxicity that spans the preclinical-clinical spectrum. In commenting on a major initiative of the FDA that focuses on biomarkers, Janet Woodcock, MD, deputy commissioner for operations and head of FDA's Critical Path Initiative, said, "Most researchers agree that a new generation of predictive biomarkers would dramatically improve the efficiency of product development, help identify safety problems before a product is on the market (and even before it is tested in humans), and facilitate the development of new types of clinical trials that will produce better data faster." The FDA has provided guidance that a biomarker can be considered "valid" if 1) it is measured in an analytical test system with well-established performance characteristics, and 2) there is an established scientific framework or body of evidence that elucidates the physiologic, pharmacologic, toxicologic, or clinical significance of the test result.

We need better biomarkers to predict clinical efficacy and toxicity in preclinical studies, diagnose disease earlier, predict outcome in a patient with disease, and identify who will respond to an intervention and whether the intervention is working. In addition, better biomarkers will permit better stratification of patients for clinical trials and potentially lead to definition of new therapeutic targets. A good predictive biomarker will have a significant effect on evaluation of potential therapies because it will enable the identification of subgroups of patients who will have a high incidence of injury and hence reduce the number of patients needed to study in order to test potential therapeutic strategies. A clinically useful new biomarker will improve the sensitivity and specificity for the detection of and characterization of disease. It is also likely that some of these biomarkers will be useful to monitor severity and progression of disease.
Translational biomarkers that can be measured in blood or urine in both experimental animals and man are of particular interest. Biomarkers that have been well studied and characterized as very sensitive biomarkers of injury in animals, if they function similarly in man, may make it possible to monitor safety and efficacy in clinical trials when the ability to obtain kidney tissue is severely constrained and when the severity of the injury early on is insufficient to result in obvious alterations in clinical state.

Given the importance to the clinical, pharmaceutical, and regulatory communities motivated by more specific and timely diagnoses, early intervention, and safer therapies, there has been a great deal of activity devoted to discovery and "fit for purpose" qualification of various potential biomarkers in a number of diseases that affect many different organs.

In this book we have tried to capture the excitement and potential of biomarkers over a wide variety of applications spanning medical diagnostics to safety monitoring in therapeutic and environmental exposures. The early chapters are devoted to individual treatments of applicability of genomics, proteomics, glycomics, and metabolomics to this rapidly evolving field of biomarker discovery. The next set of chapters takes specific organs or disease processes and considers in depth the state of the biomarker art in this specific area. Individual chapters are devoted to Alzheimer's and Parkinson's disease, cardiac injury, lung injury, drug-induced liver injury, acute kidney injury, drug-induced vascular injury, immunotoxicity, and obstetric medicine. These are followed by chapters discussing biomarkers in cancer, HIV, and drug-induced mitochondrial dysfunction. The book then moves to a more technical perspective incorporating chapters on immunoassay-based technologies, nanoscale techniques, and lateral flow immunodiagnostics at point of care. Chapters on environmental exposure, clinical trial design, and statistical issues in biomarker analysis then follow. The last two chapters deal with the regulatory perspectives of the FDA and the European Medicines Agency.

The chapters are written by leaders in their respective fields and we are very grateful to them for their comprehensive chapters. We hope that the readers will agree with us that the material in this book is timely and will go far to advance the field of biomarker research and facilitate the development of new drugs that are safe, add new biological targets to our therapeutic armamentarium, and ensure environmental safety.

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