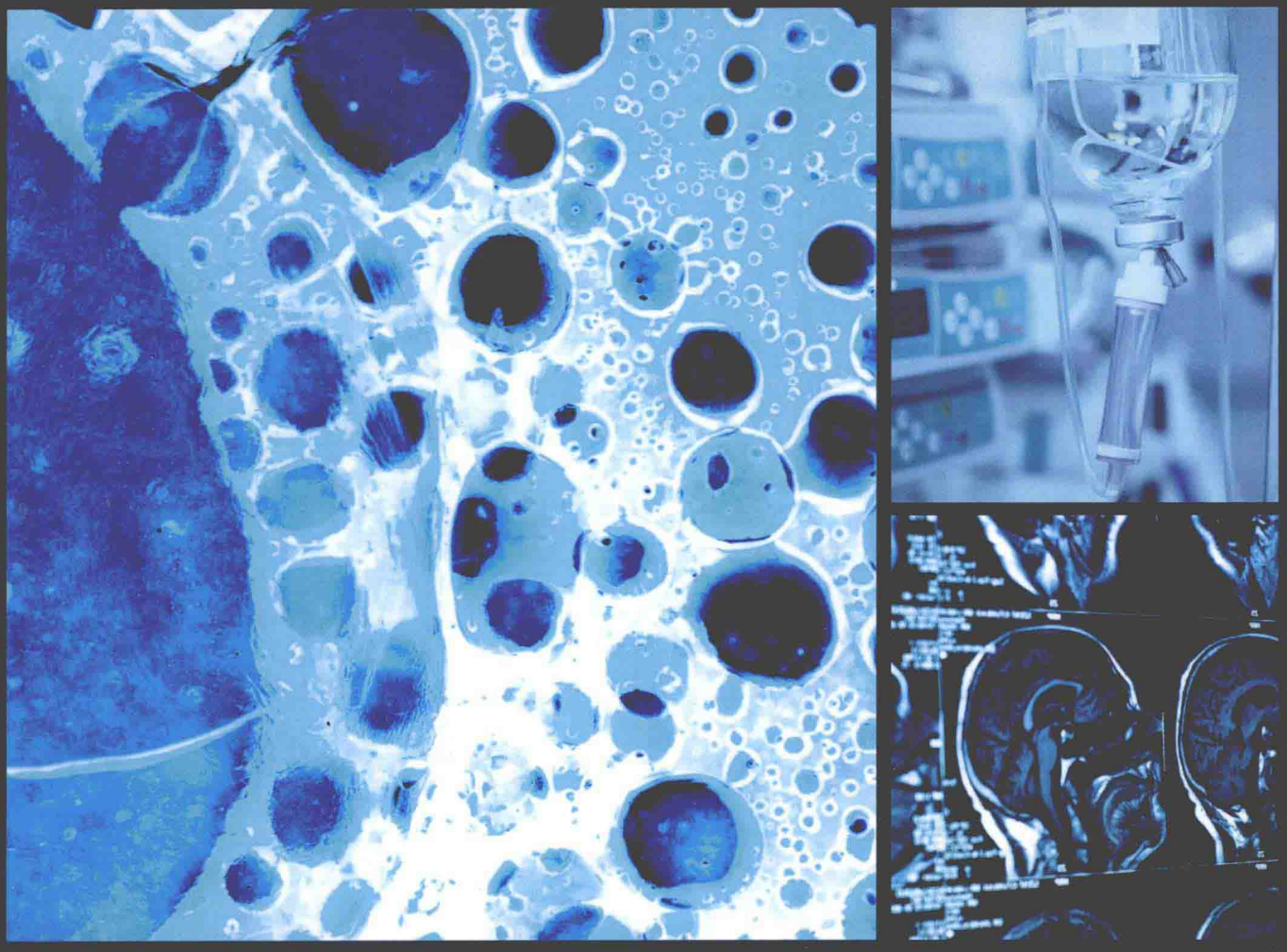
CANCER THERANOSTICS



EDITED BY

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Preface

The term "theranostics" has been used by many different people in a variety of contexts. Over the past decade, the field of theranostics has evolved considerably and has seen spectacular advances in biomarker identification, new molecular imaging probes and techniques, imaging guided molecular therapy, and novel nanotheranostics. The field is ripe to transform medicine as a whole and a greater dissemination of this knowledge can only speed its rate of acceptance and improvement. New physicians, researchers, and students working in this multidisciplinary field often ask how to blend *in vitro* diagnostics, *in vivo* imaging and therapy together for personalized medicine, and express the desire to have an authoritative textbook. This textbook, the first of its kind, is designed specifically to meet that demand, and is published in time to meet the needs of medical researchers in a comprehensive manner encompassing diagnostics, *in vivo* imaging and its use for image-guided therapy, and a variety of other miscellaneous subjects. To accomplish this daunting task we had the good fortune to recruit nearly 60 leaders in the field worldwide contributing to the twenty-six chapters.

Given the multidisciplinary nature of the field, the book is broken into five different sections. Part I (*In vitro* Diagnostics) consists of three chapters. Many theranostic approaches for cancer are based on analysis of tumor biopsy samples removed from the patient and analyzed in a laboratory setting. Chapter 1 defines the term "theranostics" and provides an overview of the specific aspects of cancer theranostics. Chapter 2 reviews the advanced biotechnology and computational biology efforts necessary to identify novel genomic biomarkers needed for developing targeted imaging probes and therapeutics. Chapter 3 describes the application of bioinformatics methods to discover proteomic biomarkers that are helpful for early tumor diagnosis, prognosis, and treatment.

Part II (Molecular Imaging) consists of Chapters 4–9. Numerous advances have been made in recent years in exogenous probes that allow precise and specific imaging of cancer *in situ* as well as label-free clinical imaging approaches. Chapter 4 summarizes the major radionuclide imaging procedures employed in assessing treatment response in patients with cancer. Chapter 5 focuses on the design of near-infrared fluorescent probes for optical imaging-guided cancer diagnosis and treatment. Chapter 6 provides a concise review of optical bioluminescence imaging in the preclinical evaluation of tumors in response to various cancer therapies. Chapter 7 highlights the role of magnetic resonance imaging (MRI) in clinical and experimental oncology to characterize tumor structure, cell density, blood volume/flow, vessel permeability, viable/necrotic components, and metabolic changes. Chapter 8 exploits the potential of ultrasound imaging at morphological, functional and molecular levels for cancer treatment response assessment. Chapter 9 discusses the recent development of photoacoustic imaging (PAI) to provide functional and molecular information about tumor tissue and the applications of PAI in cancer therapies.

Part III (Imaging-Guided Therapy) is composed of Chapters 10–13 and describes how advanced imaging techniques now make highly precise surgical intervention possible. Chapter 10 reveals how the recent advancement of image-guided intervention techniques allows real-time visualization of the device and patient anatomy for efficient, accurate, and safe intervention procedures. Chapter 11 describes the emerging coherent anti-Stokes Raman scattering (CARS) imaging technique that combines label-free molecular vibrational imaging and automated image quantitation for intraoperative characterization of cancer lesions. Chapter 12 reviews oncologic application of multimodality image-guided treatment (MIGT) in theory and in practice. Chapter 13 introduces medical robotics for cellular and molecular imaging of cancer.

Part IV (Theranostic Platforms) consists of Chapters 14–22. The ultimate application of theranostics is to diagnose, treat, and monitor a local disorder using a single platform. Chapter 14 discusses the application of light in medicine and the role of porphyrins in photonic diagnostics and interventions, as well as applications beyond photonics and strategies for improving their utilization in oncology. Chapter 15 addresses the fundamental design and characteristics of magnetic nanoparticles and their attributes in magnetic resonance imaging and alternating magnetic fields. Chapter 16 emphasizes the potential of ultrasound-mediated drug and gene delivery strategies as a means of controlled release of therapeutic cargos by either acoustic cavitation or hyperthermia. Chapter 17

introduces imaging and therapeutic radionuclides as well as respective radiopharmaceutical agents used internally in nuclear medicine. Chapter 18 summarizes the basic properties of gold-based nanoparticles and highlights their recent advances as multifunctional platforms in cancer theranostics. Chapter 19 summarizes the unique physical, chemical, and mechanical characteristics of carbon nanomaterials for multimodality imaging, photothermal therapy and drug/gene delivery. Chapter 20 presents some of the recent advances in the development of silica nanoparticle based co-delivery of therapeutic and imaging contrast agents. Chapter 21 explores the design, synthesis, and application of photoluminescent semiconductor nanocrystals, or quantum dots (QDs) for traceable therapeutic delivery using optical imaging. Chapter 22 reviews the development of polymer- and protein-based nanoparticle platforms for theranostic applications and discusses the opportunities and challenges that the clinical translation of such nanoparticle platforms may encounter.

Part V (Other) consists of Chapter 23–26 and covers a number of informative topics that were too important to be left out. Chapter 23 is an overview of the regulatory aspects of cancer theranostics and discusses the ethics of human subject protection and FDA review of investigational drugs and devices as they relate to theranostics. Chapter 24 summarizes the current preparation processes of various theranostic nanoparticles at a lab scale, the scaling-up methods, and corresponding pilot plants of nanoparticle production. Chapter 25 provides an overview of commercialization of nanotechnology, nanomedicine, and theranostic nanomedicine (nanotheranostics) as a foundation for understanding the challenges of bringing theranostics to market. Chapter 26 introduces the origins of cell heterogeneity in cancer and discusses how this emerging knowledge has shed light on the difficulties encountered in the management of neoplasias over the past few decades.

It is impossible to describe all the areas that theranostics has had, or will have, an impact on the science and practice of personalized medicine. It is not our aim to offer up a complete solution to combined cancer diagnosis and therapy, but to give readers a sense of the opportunities and challenges in this relatively new field. It has been a great pleasure working with the authors of this book. Without their enthusiasm, encouragement and professional delivery of their contributions in a timely manner, it would not have been possible to make this book a reality. Although this book focuses on cancer theranostics, many of the concepts and principles described are applicable to other disease types. We hope that this book may form a foundation for further advances in the field of theranostics.

Xiaoyuan (Shawn) Chen, PhD
Stephen T.C. Wong, PhD, PE

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Organizing and editing this book volume was primarily done out of our normal working hours, which had an enormous impact on family time. Both editors are indebted to their wives and children and thank them for their support, constant encouragement, and patience.

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Dr. Xiaoyuan (Shawn) Chen is a Senior Investigator and Chief of the Laboratory of Molecular Imaging and Nanomedicine (LOMIN) at the National Institute of Biomedical Imaging and Bioengineering (NIBIB), National Institutes of Health (NIH). His current research interests include development of molecular imaging toolbox for better understanding of biology, early diagnosis of disease, monitoring therapy response, and guiding drug discovery/development. His lab puts special emphasis on high-sensitivity nanosensors for biomarker detection and theranostic nanomedicine for imaging, gene and drug delivery, and monitoring of treatment. He received his BS (1993) and MS (1996) in chemistry from Nanjing University and PhD (1999) in chemistry from the University of Idaho. Dr. Chen has published over 400 peer-reviewed papers (H-index = 74, total citations > 20,000, over 50 papers with IF ≥ 10) and numerous books and book chapters. He is the founding editor of journal *Theranostics* (2012 IF = 7.8).

Dr. Stephen Wong is the Founding Chair for Department of Systems Medicine and Bioengineering, Houston Methodist Research Institute (HRMI). He holds the John S. Dunn Distinguished Endowed Chair in Biomedical Engineering. He is a Professor of Radiology, Neurosciences, Pathology and Laboratory Medicine at Weill Cornell Medical College; Director of Translational Research at Methodist Cancer Center, Chief of Medical Physics and Chief Research Information Officer at Houston Methodist Hospital. He also serves as the Director of the Chao Center for BRAIN and of the NCI Center for Modeling Cancer Development at HMRI. Dr. Wong has over 25 years of experience in academia and industry, including Hewlett Packard, AT&T Bell Labs, Philips Medical Systems, Charles Schwab, UCSF, Harvard Medical School and made original contributions in medical imaging, biomedical informatics, drug repositioning, and electronics. He has published over 400 peer-reviewed papers. He received his BEng in Electrical Engineering with honors from the University of Western Australia, MSc and PhD in Computer Science from Lehigh University, and senior executive education from Stanford University, Columbia University, and MIT. He is a licensed professional engineer.

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