Preface

In recent years we have witnessed a fast evolution of diagnostic technologies and their applications. The latest breakthroughs include a paradigm shift in sequencing and advances in mass spectrometry.

In 2012 we celebrated the 50th anniversary of the Nobel Prize in Physiology or Medicine for the discovery of the structure of DNA by Francis Crick, James Watson and Maurice Wilkins. This anniversary coincided with the complete decoding of the three billion base pair genome of James Watson, an effort which represented an unprecedented display of genomic diagnostics that just a few years ago was only possible in science fiction. This early success of complete genome sequencing of a few individuals was followed by the "1000 Genome Project" which aimed to decode comprehensively the base pairs of 1,000 individuals sampled around the world. The decoding of a significant percentage of the genome of an individual marks the new era of Personalized Genomic Medicine. Today's technology of massive parallel sequencing (also known as next generation sequencing and high throughput sequencing) has been made possible by using at least three Nobel Prize winning technologies, namely (1) sequencing of nucleic acids (Walter Gilbert and Frederick Sanger, 1980 Chemistry), (2) polymerase chain reactions (Kary Mullis, 1993 Chemistry), and (3) imaging semiconductor circuits (Willard Boyle and George Smith, 2009 Physics). More state-of-the-art technology is being incorporated into forthcoming generations of equipment in order to achieve a further increase in sequencing throughput and precision.

In this volume, a review of the existing and emerging massive parallel sequencing platforms sets the stage for a subsequent discussion of the application of genomic diagnosis (see chapter "Next Generation Sequencing: Chemistry, Technology and Applications"). This rapidly evolving and powerful technology moves quickly from the explorative stage to clinical application, despite ongoing discussions of various ethical, social, and regulation issues. The innovative utility of simultaneously analyzing a group of genes for making genetic diagnoses is reviewed in the chapter "Application of Next Generation Sequencing to Molecular Diagnosis of Inherited Diseases." One of the many applauded applications is the non-invasive prenatal diagnosis for genomic abnormality of the fetus. Screening for Down syndrome is now possible using a sample of peripheral blood collected from the pregnant mother. This is covered comprehensively in the chapter "Clinical Applications of the Latest Molecular Diagnostics in Noninvasive Prenatal Diagnosis." However, new analytic

and bioinformatic algorithms are required to handle the vast amount of data or genetic variants generated by massive parallel sequencing. The chapter "The Role of Protein Structural Analysis in the Next Generation Sequencing Era" provides a review on how the current knowledge of protein structure and sequencing information help in the data processing.

The chapter "Emerging Applications of Single-Cell Diagnostics" introduces the emerging diagnostic area of single cell analysis. While all current diagnostic techniques sample hundreds or thousands of cells for analysis and return either a summative or average readout of an analyte in these hundreds or thousands of cells, no information is known about the concentrations or their variation in an individual cell. Therefore, there is a need to carry out analysis at the single cell level and it is hoped that this will lead to further development in the future.

Mass spectrometry has played a key role in metabolomics diagnostics in the clinics, allowing unambiguous identification of metabolites and their isoforms. Quantification at high precision can be achieved through various approaches. The application of multiple reaction monitoring in simultaneous assays of multiple analytes is covered in the chapter "Mass Spectrometry in High-Throughput Clinical Biomarker Assays: Multiple Reaction Monitoring." It is followed by a critical appraisal of the use of matrix-assisted laser desorption (MALDI) time-of-flight mass spectrometry (TOF-MS), especially surface-enhanced laser desorption/ionization (SELDI) TOF-MS, which possesses both the ability to discover novel biomarkers and quantification of known proteins and biomolecules (see the chapter "Advances in MALDI Mass Spectrometry in Clinical Diagnostic Applications"). The volume is concluded with the case of successful applications in the medical field. By using few drops of blood, newborn screening can identify babies with various genetic diseases soon after birth. These developments in tandem mass spectrometry methods in newborn screening are reviewed in the chapter "Application of Mass Spectrometry in Newborn Screening: About Both Small Molecular Diseases and Lysosomal Storage Diseases."

Hong Kong SAR, People's Republic of China Nelson L.S. Tang

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