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Foreword

Translating complex genomic discoveries into molecular diagnostic tests

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Changes in the structure, regulation and function of the human genome define diseases' pathogenesis. Inherited and, more frequently, somatic acquired mutations in conjunction with deregulation of gene expression and signaling transduction pathways transform normal cells to disease cells. If complex intracellular signaling networks and cell–cell interactions fail to restore normal cells' function and tissue and organ homeostasis through biochemical signals, disease becomes evident with clinical symptoms [1–4].

Next-generation sequencing (NGS) technologies coupled with advanced microarrays referred together as high-throughput technologies (HTs) enable new identification of mutations and deeper exploration of the functional principles orchestrating the function of genes, genomes and cells. This low-cost power for fast and accurate DNA sequencing at a genome-wide scale has revolutionized life science and research. Application of HT with integrated advanced bioinformatics using systems computational biology approaches can transform raw data into biochemical pathways. The field of genome sciences is rapidly evolving into clinical genomics aiming to improve healthcare. The current HT-based deeper insight into the clinical genome now provides the potential of molecular characterization of the genome in healthy and disease states and raises exciting opportunities for medical applications, such as molecular diagnostics and therapeutic target discoveries for most major diseases [5–12]. Translating these complex genomic discoveries into clinical medicine, substantial benefits for the population can emerge as we are moving to clinical personalized health management [2].

This book explores the power and challenges for the integration of NGS into the clinic. Deep sequencing with whole-genome sequencing allows for the identification of all classes of mutations, including translocations that may impact disease initiation and progression in some patients. RNA sequencing and chromatin immunoprecipitation sequencing at a genome-wide scale provide the capacity for transcription factor identification and transcriptome analysis. In addition NGS, in conjunction with modern microarrays can expand the analysis of epigenome modifications, such as DNA methylation and histones as well as noncoding RNAs, providing a big picture of biology underlying health and disease.

In Chapter 1, Ziogas and colleagues describe the sequencing technological advances from NGS or second-generation sequencing technologies to third- and fourth-generation nanopore sequencing platforms. In Chapter 2, Ku and colleagues discuss the opportunities and challenges in translating NGS-based raw data into biological meaningful signals for cancer diagnostic applications. In Chapter 3, Ng and colleagues describe how gene expression profiling measurements of mRNA and miRNAs in cancer could be used for developing multigene assays with prognostic and predictive value for cancer patients in the clinic. Silva and colleagues then describe the opportunities for microbiome analysis using NGS and microarrays for identifying bacteria pathogenic mechanisms underlying drugs resistance and develop new more effective drugs against bacteria in Chapter 4. Pareek in Chapter 5 focuses on functional genomics and complex functional elements of human genome. The author describes the advantages and challenges in understanding DNA protein binding events by using chromatin immunoprecipitation sequencing. The field of transcriptome analysis now attracts major biomedical research interest because of exciting medical applications. However, understanding genome regulation and function represents one of the bigger challenges in biology. The recent reports of the Encyclopedia of DNA Elements (ENCODE) project reveal that despite advances, only approximately 10% of the work towards understanding the genome function has been completed [13–15]. In the last chapter, Xu and colleagues describe how deeper insights into the genome landscape could be translated into clinical molecular diagnostics.

We have entered into the NGS-based and network-biology-based era [16] of genomic network medicine [1–4]. Exciting perspectives are now being created. However, to reach clinical success, innovation will be required [17]. The reason is that long-term and extensive research work is needed to understand the principles of genome regulation and functioning. Despite this lack of a comprehensive genome landscape view, innovation in clinical genomics and dynamic network biology [17] can result in novel molecular

diagnostics and robust molecular subtypes in various diseases for personalizing treatment decisions.

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