Preface

Advancing cancer research through genomics technology evolution

Cancer is a disease of the genome, each cancer is the result of a unique combination of germline and somatic mutations, as well as epigenetic aberrations. A comprehensive catalog of all types of variants in a cancer opens new and unrivaled opportunities for understanding the mechanism of cancer onset and progression, predicting the response to therapeutics, and providing new biomarkers for diagnosis and prognosis. Over the past 20-30 years, genomics technology evolutions have drastically transformed cancer researches. Powerful genomics platforms and tools have enabled whole-genome gene expression analysis, mutation analysis of millions of genetic markers in hundreds and thousands individuals, and ultimately the complete cancer genome sequencing in large clinical cohorts as exampled by The Cancer Genome Atlas Project (TCGA; http://cancergenome. nih.gov) and the International Cancer Genome Consortium initiatives (ICGC; http://www.icgc.org).

In this special edition of the *Translational Cancer Research* Journal, we try to document some examples to show how the genomics technologies have driven both the basic and translational cancer researches. Dr. Liu and her colleagues from Illumina provide a brief overview of genomics technologies, both microarray and next-gen sequencing (NGS), and their applications in cancer research.

In 2001, the Human Genome Project delivered the first draft of the human genome at a cost of $3 billion. In 2014, a human genome can be sequenced for less than $1,000. The dramatic increase in throughput and the drop in the cost of sequencing offer an unprecedented opportunity to comprehensively understand a cancer by determining all genomic, epigenomic, and transcriptomic changes to reveal the repertoire of oncogenic mutations, define clinically relevant subtypes for prognosis and therapeutic management, and enable the development of new cancer therapies. Dr. Chuang and colleagues at National Taiwan University, Taiwan, describe their work on using a gene-set approach to analyze copy number alterations (CNA) in cancer, identifying CNA-affected, as well as CNA-driven, biological functions and pathways in breast cancer. Dr. Heng and colleagues at Wayne State University take a genome-wide view to characterize cancer evolution. Their work also suggests that understanding cancer evolution holds the key to understanding other complex diseases and evolutionary theory in general. Dr. Weisenberger and Dr. Liang at USC/Norris Comprehensive Cancer Center review the contributions of DNA methylation aberrancies to the cancer epigenome; it highlights DNA methylation changes and their significance in human cancers from mechanistic, biomarker and treatment perspectives. Dr. Sieber and colleagues at Walter and Eliza Hall Institute of Medical Research, Australia, review results of recent translational studies of the colorectal cancer genome, transcriptome, methylome and miRNAome, with a focus on tumor classification, diagnostic, prognostic and predictive findings.

The ability to analyze cancer genomes at low cost provides an unrivalled and previously inaccessible opportunity to characterize individual cancers with high specificity and sensitivity. This has led to a new understanding of oncogenic mechanisms and identification of potent diagnostic and prognostic markers, which are used to classify a tumor and accurately predict the response to treatments. Two important questions can now be posed: (I) what are the primary mutational events that trigger carcinogenesis? And (II) what are the cascades of genomic changes that lead to metastasis and to resistance to therapeutics? Studies based on microarray analyses and second-generation sequencing technology has already revealed many unexpected etiologies for a number of cancers. In their review, Dr. Hoshida and colleagues from Icahn School of Medicine at Mount Sinai summarize the steps of biomarker development, highlight key issues in successful validation and implementation, and overview representative examples in the oncology field. They also discuss regulatory issues and future perspectives in the era of big data analysis and precision medicine. Dr. Wang at Ventana Medical Systems, Inc., a member of the Roche group, provides a comprehensive review on cancer biomarkers. It focus on the development of (I) molecular and cellular diagnostic assays that have the potential to aid clinical decision-making and patient management in oncology; (II) the steps to translate and develop novel biomarkers into quality diagnostic tests that can be readily deployed into clinical laboratories; and (III) some examples illustrating how tissue- and cancer-specific biomarkers, coupled with new molecular technologies, can add value to conventional diagnostic methods by providing standardized, objective and highly informative diagnostic tests.

To fully enable personalized precision healthcare it is desirable for clinicians to have a more easily accessible way to screen patients, stratify for treatment decision and monitor treatment response in real-time without the need for repeat biopsy. Dr. Skog and colleagues at Exosome Diagnostics review three approaches in the liquid biopsy field that try to address this need, circulating tumor cells (CTCs), cell free-DNA (cfDNA) and exosomes. They also outline some of the analytical challenges encountered using liquid biopsy techniques to detect rare mutations in a background of wild-type sequences.

In summary, we predict an even broader application of whole-genome technologies to analyze large numbers of archived tumor tissue samples as well as samples that can be accessed non-invasively, such as cfDNA. In the near future we anticipate a revolution in healthcare and personalized cancer treatment, including early cancer detection and real-time cancer monitoring, with accurate, high-throughput, low-cost sequencing at the heart of clinical practice.

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Jian-Bing Fan, PhD. *CEO, AnchorDx Corp., Professor, Cancer Research Institute, Southern Medical University, Guangzhou 510300, China. (Email: jianbing_fan@anchordx.com.)*

Jian-Bing Fan, PhD

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