

Chapter 4

Current Omics Technologies in Biomarker Discovery

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ABSTRACT

Biomarkers are playing an increasingly important role in drug discovery and development and can be applied for many purposes, including disease mechanism study, diagnosis, prognosis, staging, and treatment selection. Advances in high-throughput “omics” technologies, including genomics, transcriptomics, proteomics and metabolomics, significantly accelerate the pace of biomarker discovery. Comprehensive molecular profiling using these “omics” technology has become a field of intensive research aiming at identifying biomarkers relevant for improved diagnostics and therapeutics. Although each “omics” technology plays important roles in biomarker research, different “omics” platforms have different strengths and limitations. This chapter aims to give an overview of these “omics” technologies and their current application in the biomarker discovery.

INTRODUCTION

Biomarker research is an interdisciplinary field that bridges basic scientific research and drug discovery with clinical development. Offering great potential to stratify patient populations, quantify

drug benefits, improve risk assessment and evaluate the impact of regulatory actions, biomarker fits perfectly with the vision of personalized medicine. Biomarker research has been a central focus in many research labs across academia, government agencies, and the pharmaceutical industry and is evolving at a fast pace.

DOI: 10.4018/978-1-60960-491-2.ch004

There are many different ways to define biomarkers based on their applications and molecular properties. The U.S. Food and Drug Administration (FDA) defines a biomarker as “a characteristic that is objectively measured and evaluated as an indicator of normal biological or pathogenic processes or pharmacological responses to a therapeutic intervention”. A biomarker can be genetic variations in DNA, gene expression profiles in tissue biopsies, proteins, metabolites or lipids in blood, etc. Hence, the discovery, analytical validation and qualification of biomarkers require multidisciplinary skills and a proper application of technologies available at present.

There are four types of biomarker application, *target engagement biomarkers, efficacy biomarkers, Safety biomarkers and Surrogate endpoint biomarker*.

- *Target engagement biomarkers*: occur early in the pathophysiological cascade and inform on physical or biological interactions with the drug target. used to establish pharmacological response in the pre-clinical animal model;
- *Efficacy biomarkers*: used to estimate the efficacy of drug;
- *Safety biomarkers*: used to assess predict or anticipate toxicity or adverse events;
- *Surrogate endpoint biomarkers*: used in therapeutic trials as a substitute for a clinically meaningful endpoint that is a direct measure of how a patient feels, functions, or survives and is expected to predict the effect of the therapy.

While many existing biological and analytical technologies have been directly applied to biomarker research, many novel high-throughput technologies, especially in the fields of genomics, transcriptomics, proteomics, and metabolomics, have been developed and made it easier to interrogate hundreds, or even thousands of potential biomarkers simultaneously, without prior knowledge

of the underlying biology or pathophysiology of system being studied. These “omics” technologies have been used for identifying potential biomarkers at different molecular levels and revolutionized the methods of biomarker discovery. The goal of the chapter is to provide a review of these “omics” technologies and their application in the biomarker discovery. The issues on the analysis, validation, and qualification of biomarkers based on these technologies are also discussed.

GENETIC BIOMARKER

A genetic biomarker is a gene or DNA sequence with a known location on a chromosome and associated with a particular gene or trait. A genetic biomarker may be a short DNA sequence, such as a sequence surrounding a single base-pair change (single nucleotide polymorphism, SNP), or a long one, like microsatellites.

The history of human genetics has focused on mapping regions of the genome that can explain part or all of a disease or human trait. With the completion of the Human Genome Project in 2003, researchers began to pinpoint areas of the genome that varied between individuals. Shortly thereafter, they discovered that the most common type of DNA sequence variation found in the genome is the single nucleotide polymorphism (International HapMap Consortium, 2005; Sachidanandam et al., 2001; Chanock, 2001). A worldwide effort known as the HapMap Project seeks to identify and localize these and other genetic variants, and to learn how the variants are distributed within and among populations from different parts of the world. To date, the project has identified over 10 million SNPs across the human genome.

In the early days, linkage study and candidate gene approach are popular ways to identify genetic biomarkers.

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