Introduction

Biomarkers and their impact on precision medicine

William Slikker Jr.

National Center for Toxicological Research, US-Food and Drug Administration, Jefferson, AR 72079, USA
Corresponding author: William Slikker Jr. Email: william.slikker@fda.hhs.gov

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Both the definition and the use of biomarkers have evolved over the years. In 1987, the US National Academy of Sciences/National Research Council's Committee on Biological Markers[1] defined biological markers as indicators signaling events in biological systems or samples and classified them into three types including those of exposure, effect, and susceptibility. In an effort to enhance development of novel therapies the FDA's Center for Drug Evaluation and Research initiated a process to qualifying biomarkers for regulatory decision-making. The focus of this biomarker qualification process was to provide a framework to aid in overcoming drug develop challenges while providing increased certainty about drug efficacy and safety.[2] As part of this process, the definition of biomarker was focused to fit for purpose: A characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.[3]

More recently, the US National Institutes (NIH) and the FDA Joint Leadership Council[4] sanctioned an effort to define the many types of biomarkers used in therapeutic development and safety assessment. The goal was to reduce obstacles to medical product development by providing consistency and clarity of terms related to study endpoints and biomarker programs. Working together, the NIH and FDA developed the BEST (Biomarkers, EndpointS, and other Tools) Resource: a living glossary designed to enhance medical product development and aid in the advancement of precision or personalized to improve human health. Although these landmark publications have extolled the definitions, virtues, and possible uses of biomarkers, researchers and clinical practitioners have been enlisting the use of biomarkers for a much longer time.

One could argue that the clinical use of biomarkers dates back to when body temperature and blood pressure were introduced as traditional indicators of health by physicians. Taking one's temperature or blood pressure remains a common feature of most annual physicals or check-ups today but was first made possible by technology advances to provide quantitative measures. Although the routine clinical assessment of blood pressure did not occur until the 1900s, it was first described as measured in animals in 1733 by Stephen Hales.[5] The clinical thermometer came to routine clinical use over 130 years ago following its development by Carl Wunderlich in 1868.[6] However, Galileo devised a crude temperature-measuring instrument in 1592.[7] So from the very beginning, the acceptance and routine use of biomarkers have been a ponderous process.

The development and use of biomarkers have impacted many biological, disease and target organ segments of environmental and human health. The definition of biomarker may be as broad as that defined by the WHO: "almost any measurement reflecting an interaction between a biological system and a potential hazard, which may be chemical, physical, or biological. The measured response may be functional and physiological, biochemical at the cellular level, or a molecular interaction".[8] It is not surprising therefore that over 850,000 citations are associated with a PubMed search on biomarkers. However, despite this enormous effort in the biomarker research field, only around 100 biomarkers have been validated for the routine clinical use as of 2011.[9] This clearly indicates the great complexity of the field and crucial need for the development of novel comprehensive approaches in biomarker discovery and validation studies.

The role of biomarkers in the development of precision medicine provides a strategic opportunity for technological developments to improve human health and reduce healthcare cost. Precision medicine as a concept concerns the adjustment of treatments to individual or subgroups of patients based on the use of disease-specific biomarkers. There continues a great debate as to the overall success of this personalized process to identify actionable molecular targets to pinpoint therapies.[10,11] There is no doubt that the analytical tools are currently abundant including molecular imaging, genomics, proteomics, metabolomics, and next generation sequencing. These and other approaches have resulted in the development and use of over a dozen specific biomarkers and therapies for cancer treatment that have FDA approval.[11] The jury is still out but the search for acceptable biomarkers to drive precision medicine is at an all-time high. In addition, there are many applications of disease-specific biomarkers to promote precision medicine in addition to cancer diagnostics and therapies.

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In this thematic issue the development and application of biomarkers will be illustrated for both preclinical and clinical use. Although the application of biomarkers and precision medicine has seen greatest use in oncology, application to a variety of target organs including the heart, liver, kidney, and brain and all of these will be addressed in this thematic issue. I gratefully thank the many authors who have contributed to this issue and hope by summarizing the field in this manner the development and use of biomarkers will enhance the application of precision medicine and improve public health.

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