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Tracing the voyage of SELDI-TOF MS in cancer biomarker discovery and its current depreciation trend – need for resurrection?

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ABSTRACT

Surface-enhanced laser desorption/ionization time of flight mass spectrometry (SELDI-TOF MS) has been established as a powerful analytical tool for biomarker discovery in oncology. This review visits the milestones achieved by this technique and scans the advantages and limitation of the technique as well. The need for expanding this technique for biomarker discovery with respect to diseases other than cancer has been emphasized. The future of this technique and its application to clinical research has been highlighted to have hit a dead-end. This review is an eye opener to break the silence, amidst the analytical chemists for revival of this technique, breaking barriers in its application to clinical research.

Contents

1. Introduction

Human beings are often being forced to encounter a particular abnormal condition that impairs normal homeostasis which is revealed by specific symptoms and signs. Such a condition, is referred to as 'diseased' which can be identified more promptly and accurately, by the altered molecular profiles in the cellular milieu. Therefore, recently much attention is being paid to elucidate such molecules (biomarkers) associated, with each and every disease. This will enable better disease diagnosis and lead to effective prognostication and treatment of diseases. For the first time, the term "biomarker" was introduced by medics as "measurable and quantifiable biological parameters" (eg, specific enzyme concentration, specific hormone concentration, specific gene phenotype distribution in a population, and presence of biological substances). These serve as indices of health- and physiology-related assessments. Disease risk, psychiatric disorders, environmental exposure and its effects, disease diagnosis, metabolic processes, substance abuse, pregnancy, cell line development, epidemiologic studies, etc. include few such assesments. The term biomarker was further defined by an NIH working group as, "a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacologic responses to a therapeutic intervention" [1].

Through the biomarkers, considerable wealth of clinical or health related information can be harnessed that would be extremely useful alert patients at the risk zone of disease development. It would also be helpful in disease treatment in accordance with (preclinical or clinical biomakers and to monitor biomarkers for disease progression [2]. Further, biomarkers are also helpful in exhibiting the clinical therapeutic end points and thereby cut down further medication costs [3]. The ideal biomarkers are being chosen with the following desirable characteristics such as: (i) can be detected at the earliest stage of the disease, (ii) higher reproducibility and quantitative

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correlation with disease state, (iii) appear and disappear over the course of disease progression, (iv) should ensure maximum safety and minimum discomfort to the patient upon collection, (v) should be fairly consistent across individuals irrespective of genders and ethnic groups and (vi) should involve less cost for performing the tests [4]. Based on the purpose of disease diagnosis process, the biomarker working group has classified biomarkers into the following categories: antecedent biomarkers – identifying the risk of developing disease, screening biomarkers – screening for subclinical disease, diagnostic biomarkers – recognizing overt disease, staging biomarkers – categorizing disease severity or prognostic biomarkers – predicting future disease course, including recurrence and response to therapy and monitoring efficacy of therapy [4]. Biomarkers from different parts of the body, are being detected employing techniques which includes, genomic technologies, proteomic technologies, glycomic technologies, lipomic technologies and molecular imaging technologies. This review focuses on the use of SELDI MS technique towards cancer biomarker discovery.

2. SELDI-TOF-MS

Techniques such as two-dimensional gel electrophoresis (2-DE), one- or two-dimensional liquid chromatographic (LC-MS), or surface-enhanced laser desorption/ionization time of flight mass spectrometry (SELDI TOF-MS), are regarded as powerful analytical tools [5–8]. However, of these techniques, SELDI-MS, which is also known as ProteinChip® technology, is a high-throughput proteomics technique that facilitates multiple biomarker discovery, purification and identification. Hutchens and Yip [9] in 1993 first described SELDI-TOF/MS, this technique combines chip-based solid-phase chromatography with TOF-MS. Fig. 1 presents the working scheme of the SELDI-MS technique. The working principle involves binding of a crude sample to a ProteinChip array followed by protein separation and protein analysis. This is performed within the same system, facilitating simultaneous sensitive detection of a multitude of distinct proteins in biological samples. The sample to be analyzed is spotted onto a “protein-chip array” [10]. Each spot on

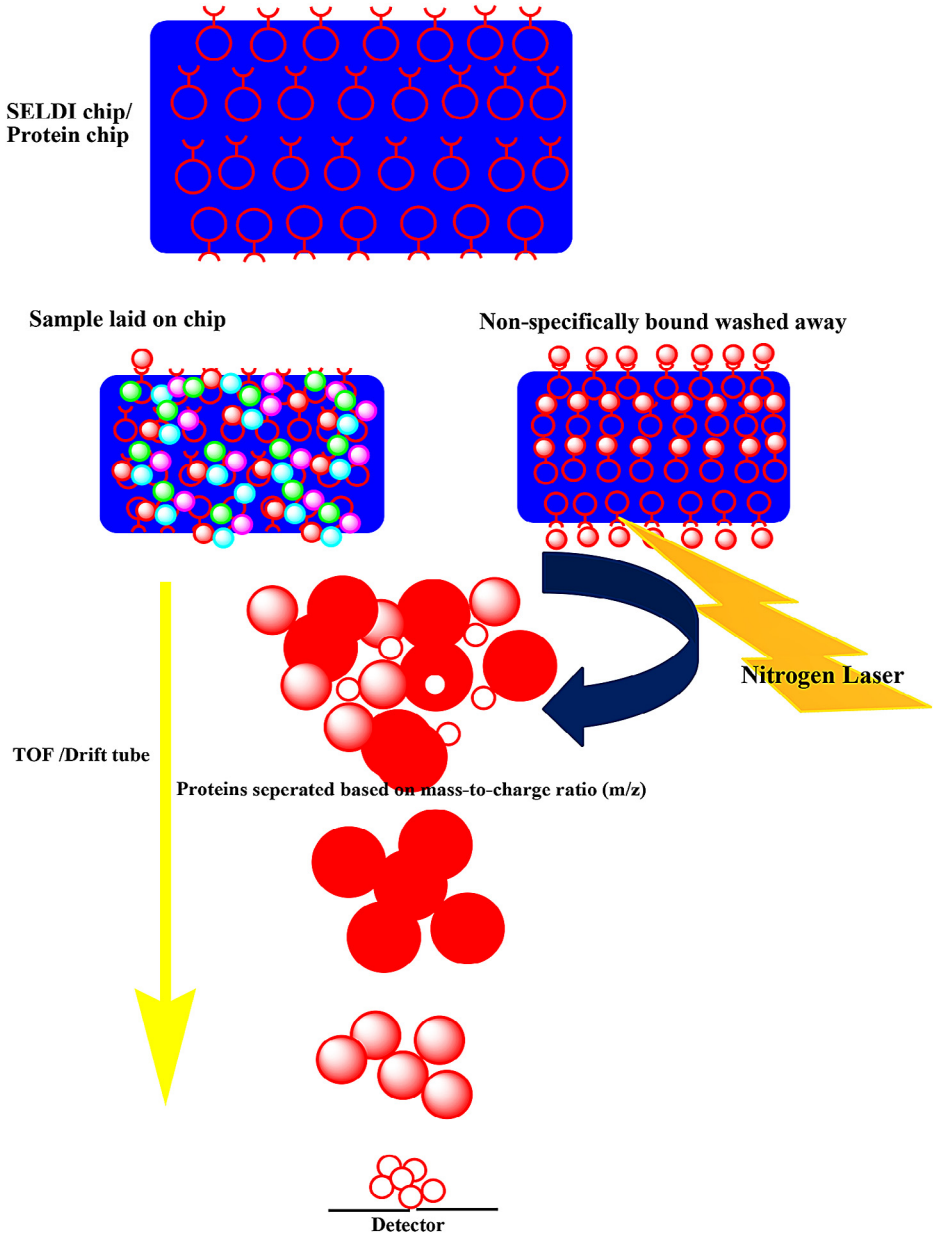

Fig. 1. Schematic showing the working principle behind SELDI-TOF MS.