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USE OF MASS SPECTROMETRIC TECHNIQUE FOR IDENTIFICATION OF CANCER BIOMARKERS

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Article Info

Abstract

Mass spectrometry (MS) proves valuable as a diagnostic tool for cancer biomarker identification because it detects molecules linked to disease with robust sensitivity coupled to high specificity and good accuracy levels. The review analyses the use of MS-based techniques for cancer diagnostics through proteomics, metabolomics and lipidomics studies of biomarkers together with LC-MS, MALDI-MS and MS/MS methodologies for early disease detection and treatment monitoring and prognosis evaluation. Single-cell MS methods, multi-omics capabilities, and AI-powered analytical tools now boost biomarker detection accuracy while liquid biopsy integration enables non-invasive cancer testing through MS systems. The clinical adoption of MS remains obstructed by existing challenges that include difficulties with sample complexity as well as standardisation difficulties and interpretation challenges. The field of cancer biomarker research with MS-based approaches will progress through the creation of portable MS devices for patient testing as well as refined analytical methods alongside AI-supported examination techniques which demonstrate how MS can transform clinical cancer identification capabilities and help physicians make better care decisions and aid precision medicine programmes to boost survival rates.

Keywords:

Mass Spectrometry (MS), Cancer Biomarkers, Cancer Diagnostics, Proteomics, Liquid Biopsy, Precision Oncology, Early Detection.

1. Introduction

The disease cancer stands as one of the major contributors to worldwide deaths and illness because it killed 10 million people during 2020(1). Clinical manifestation of the disease remains absent during its beginning stages which leads to difficulty in diagnosing it on time. Biomarker discovery has garnered strong commitment because it provides essential features for cancer detection and therapeutic decision-making and disease prognosis assessment. Analyzed biomarkers within blood and urine and saliva fluids function as non-invasive measures to detect cancer early because these molecules show measurable biological indicators of normal or pathological processes (2). Cancer early detection at its earliest stages remains challenging because standard biomarker identification procedures like enzyme-linked immunosorbent assays (ELISA) and polymerase chain reaction (PCR) lack adequate sensitivity combined with precise identification capabilities.

The analytical revolution in cancer biomarker discovery comes through MS technology because this method provides sensitive identification and quantification of biomolecules with precise results (3). MS analyses biological sample molecular structures to detect preclinical carcinogenesis biomarkers, which helps physicians identify indicators earlier than symptom onset. MS stands apart from traditional methodologies because it examines biomarkers without specified predefined targets so scientists can detect biomarkers without presuppositions (4). MS has gained wide acceptance for proteomics, metabolomics, lipidomics and glycomics analysis, which supports advanced personalised cancer diagnostics.

Current mass spectrometry technologies, including high-resolution MS and MS/MS systems alongside machine learning analytical frameworks, have improved biomarker detection accuracy and operational speed (5). Medical research using these developments has resulted in major discoveries of cancer-detectable proteins and metabolites and lipids that function as effective diagnostic signals and therapeutic targets. MS-based proteomic profiling effectively detects serum-based biomarkers for lung and breast cancer, making these tests viable for clinical deployment (6). The biochemical changes in tumourigenesis become observable through metabolomic and lipidomic analysis, which creates new metabolic patterns for identifying various malignancies (7).

The wide range of benefits from mass spectrometry in cancer biomarker studies faces multiple research obstacles. The implementation of MS-based cancer diagnostics faces substantial obstacles as health professionals confront problems with sample complexity along with issues in reproducibility and data interpretation difficulties and high instrument expenses (8). The future accessibility along with the robustness of MS-based cancer diagnostics will improve due to continuous development in automation, miniaturisation and bioinformatics technologies.

This review performs a complete study of mass spectrometry applications for identifying cancer biomarkers. The article examines MS basics along with its proteomic and metabolomic applications, as well as presents current difficulties and shows recent developments in the field. Single-cell mass spectrometry and AI-driven MS data analysis show potential to transform cancer diagnostics as described in the discussed trends. Reviewing MS-based biomarker research both now and in upcoming terms enables this article to contribute to current initiatives for early cancer detection and precise medical approaches.

2. Principles of Mass Spectrometry in Biomarker Identification

Studies using MS for cancer biomarker detection and quantification have revolutionised molecular diagnostics research because this technique accurately analyses biomolecules in complex biological fluids (9). MS bases its operation on ionised molecule mass-to-charge ratio (m/z) measurements for identifying potential cancer biomarkers among proteins, peptides, metabolites and lipids (10). The quick development of MS technology together with sophisticated computational tools resulted in high-throughput biomarker discovery, which creates excellent conditions for early cancer detection and personalised medicine (11).

2.1 Fundamental Mechanism of Mass Spectrometry

The technological process of mass spectrometry first requires ionisation followed by mass analysis until it reaches the detection stage. The identification process along with biomarker characterisation depends upon these three sequential steps. Contemporary research into mass spectrometry mechanisms enables scientists to utilise its maximum capabilities and detect minimal molecular modifications for developing targeted therapeutic methods (12). The research on cancer uses the following three primary steps of mass spectrometry, which will be explained in detail below.

A. Ionization Methods and Their Role in Biomarker Identification

Protein-based separation in mass spectrometry happens following ionization that converts biomolecules into gas-phase ions. Cancer biomarker research makes widespread use of two primary ionization methods which involve:

MALDI-MS serves as an established technique for proteomic research to detect complete molecular ion structures without significant structural damage. Current cancer pathology depends significantly on MALDI imaging mass spectrometry (MALDI-MSI) for mapping biomolecular distributions throughout tissue samples (13). Scientific research demonstrates that tumour subtype identification achieves success by detecting distinctive protein patterns (14).

The ESI technique provides exceptional performance for LC-MS analysis because it assists researchers in studying metabolites as well as lipids and post-translational modifications. This technique serves as an essential tool for cancer cell metabolic reprogramming research since it reveals the changes in biochemical pathways (15).

B. Mass Analyzers and Their Significance in Cancer Research

Biomolecules move through various mass analysers following ionisation because these devices possess specific advantages that help identify cancer biomarkers (16).

The Time-of-Flight (TOF) Mass Spectrometry operates with high detection resolution, making it suitable for proteomic research. MALDI-TOF-MS has achieved successful discrimination of malignant and benign tumours through identification of unique protein signatures (17). Mass spectrometry by using a quadrupole to choose precursor ions and a quadrupole time-of-flight (Q-TOF) unit produces high-resolution detection and better-targeted biomarker quantification (18).

The high-resolution Orbitrap and FT-ICR mass spectrometers allow for precise biomolecular profiling specifically used to identify minor cancer-associated modification patterns.

2.2 Advantages of Mass Spectrometry in Biomarker Research

MS provides the best possible features for identifying cancer biomarkers. The technology provides high-speed operation together with absolute marker asymmetry and non-biased biomolecule assessment, which exceeds traditional immunoassay techniques (19). MS succeeds antibody-based techniques by finding new biomarkers through simplified sample preparation protocols.

Medical science serves as a fundamental tool for personalised medicine because it develops individualised care approaches through unique biomarker patterns (20). Metabolic profiling through MS has discovered vital metabolites that predict resistance to drugs in breast cancer patients (21).

2.3 Challenges and Limitations of Mass Spectrometry-Based Biomarker Discovery

Multiple obstacles prevent the practical application of MS-based biomarker discovery techniques (22). The lack of reproducibility in laboratories stems from variations in sample preparation methods alongside instrument sensitivities during analysis. The researchers state that solving this issue requires standardised workflows in combination with data normalisation methods (23).

MS instruments with Orbitrap and FT-ICR capabilities operate at elevated prices and need expert technicians to run them effectively. Artificial intelligence systems are now enhancing machine learning capabilities for MS data analysis, thus expanding laboratory automation capabilities (24).

3. Mass Spectrometry-Based Approaches for Cancer Biomarker Identification

The clinical practice of cancer biomarker discovery changed drastically because mass spectrometry (MS) enables quick and accurate measurements of molecular changes linked to cancers. The extensive research applying MS-based proteomics, metabolomics and lipidomics approaches revealed different cancer type biomarkers useful for diagnosis and prognosis and predicting disease outcomes (25). The detection of delicate tissue-composition differences between healthy and cancerous tissues depends on advanced ionisation methods and mass analysers and bioinformatics software (26).

3.1 Proteomic Approaches in Cancer Biomarker Identification

MS's large-scale protein study has become a fundamental proteomic application of oncology research. Cancer cells possess specific protein expression signatures and post-translational modifications as well as proteolytic cleavage activities, thus making proteomic profiling essential for biomarker investigation (27). The analysis of protein sequences through MS-based proteomics can be achieved by using two primary approaches.

A. Bottom-Up Proteomics

By applying enzymatic protein digestion, scientists convert proteins into peptides before their analysis through liquid chromatography coupled mass spectrometry (LC-MS/MS). The combined assessment of protein expression levels and modifications with interactions takes place effectively in cancer and non-

cancer tissues through this technique (28). High-end MS instrumentation, including Orbitrap and Q-TOF MS systems, has improved peptide identification capabilities, thus facilitating the discovery of new cancer biomarkers like alpha-fetoprotein (AFP) for hepatocellular carcinoma and HER2 for breast cancer (29).

B. Top-Down Proteomics

On its own, top-down proteomics differs from bottom-up by maintaining intact proteins while identifying their isoform variations as well as specific PTMs like phosphorylation, glycosylation and ubiquitination that affect cancer advancement (30). The identification of histone epigenetic regulations in tumours and leukaemia-related oncogenic fusion proteins proves particularly successful by using this analytical method (31). The dedication of handling massive intact proteins faces difficulties mainly due to the requirement of advanced MS methodologies, including FT-ICR MS, for achieving high-resolution outcomes (32).

3.2 Metabolomic Approaches in Cancer Biomarker Discovery

The field of metabolomics helps scientists examine modified metabolic routes that happen in cancer cells by analysing their small metabolite composition. The MS-based metabolomics method detects cancer-related metabolic reprogramming events effectively by monitoring both cancer cell glycolytic changes, known as the Warburg effect, as well as lipidosomic transformations (33). The detection and evaluation of cancer evolution now hinges on the analysis of particular metabolites called oncometabolites, according to recent research (34).

A. Targeted vs. Untargeted Metabolomics

The quantification of targeted metabolites through commonly used methods includes triple quadrupole mass spectrometry (QQQ-MS) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) (35). The levels of 2-hydroxyglutarate (2-HG) show potential as an IDH-mutant glioma biomarker. By performing targeted metabolomics, researchers gain precise measurements of recognised cancer-related metabolites because this technique permits them to validate biomarker candidates and check drug treatment effectiveness (36).

The analysis of all detectable metabolites throughout the sample makes up untargeted metabolomics. Q-TOF and Orbitrap MS help researchers discover new cancer-linked metabolites, including polyamine elevation in patients with prostate cancer. Through this unbiased technique, researchers detect new information about cancer-related changes to the metabolome (37).

3.3 Lipidomic Approaches for Cancer Biomarker Identification

Metabolomics specificity called lipidomics studies lipid composition together with lipid metabolic pathways that show considerable alterations during cancer development. Through MS-based lipidomics, scientists gain information about tumour membranes and their signalling lipids as well as their drug resistance mechanisms caused by lipids (38). The development of modern lipidomic methods enables scientists to detect distinct lipid changes which become effective cancer diagnostic indicators. Various cancers show aggressive behaviour together with poor prognoses because their lipid metabolism becomes altered (39).

Research shows that phosphatidylcholines together with sphingolipids function as biomarkers for diagnosing lung and ovarian cancers (40). The major membrane components known as phosphatidylcholines enable both cell membrane maintenance and signalling pathway operation, while sphingolipids regulate cellular development and apoptosis and differentiation processes. The levels of these lipids shift when cancer develops or advances, which makes them beneficial targets to discover biomarkers (41).

The tumour tissue lipid analysis through DESI-MS and MALDI-MS enables spatial identification of biomolecules that provide essential diagnostic information (42). Through DESI-MS combined with the MALDI-MS imaging technique, researchers can perform direct analysis on tissue sections to establish both lipid distribution patterns and composition throughout the sample space. The spatial lipidomics method enables researchers to separate cancer cells from normal tissues along with separating tumour margins, which facilitates accurate surgical interventions (43).

3.4 Integration of Multi-Omic Approaches with Mass Spectrometry

The combination of proteomic, metabolomic and lipidomic techniques produces more dependable biomarker results when analysing complex cancer biology. A combination of multi-omic techniques gives complete molecular insights that enable more reliable diagnoses between benign and malignant conditions (44). Modern artificial intelligence (AI) technology enhances biomarker identification through its ability to merge extensive databases that combine different omic information layers (45).

The integration of multiple omic techniques allows researchers to analyse all molecular events within cancer development, thus creating new methods to understand disease mechanisms and detect powerful diagnostic signatures. This method allows the discovery of both individual biomarkers and better understanding of the molecular interactions, which leads to improved biomarker panels for diagnostic purposes. Researchers use proteomic together with metabolomic data to detect cancer cell metabolism modifications that result from changes in protein expression patterns The combination of various omic strategies could lead to new therapeutic target discovery and improved methods for patient-specific treatment (46).

The development of biomarker research in modern medicine became possible after AI combined with machine learning technology was applied to multi-omic data analysis. The detection of advanced connections within extensive heterogeneous datasets remains a strength of AI algorithms due to their superior analytical abilities. AI systems enable researchers to develop better multi-omic data integration models that lead to precise and repeatable biomarker discoveries (47).

4. Applications of Mass Spectrometry in Identifying Cancer Biomarkers

Because mass spectrometry (MS) offers extremely sensitive and precise molecular insights, it has greatly improved cancer diagnoses, prognostics, and therapy monitoring (48). Given its capacity to perform proteome, metabolomic, and lipidomic analyses of complex biological material, MS has been included into a number of clinical workflows to improve disease monitoring, individualized treatment, and early

detection (9). Recent developments like single-cell proteomics and liquid biopsy-based MS analysis have improved the clinical usefulness of MS in oncology (49).

4.1 Mass Spectrometry in Early Cancer Detection

A. Proteomic Biomarkers for Early Diagnosis

The identification of tumour-specific proteins in serum plasma and urine by MS-based proteomics has become essential to early cancer detection because it improves patient survival statistics (8). Two proteomic MS techniques known as iTRAQ and TMT proteomics combined with isobaric tag for relative and absolute quantification have allowed scientists to identify early-stage cancer biomarkers (50).

The cancer screening tools include alpha-fetoprotein (AFP) for hepatocellular carcinoma (HCC) detection along with prostate-specific antigen (PSA) screening for prostate cancer diagnosis (51). The improved accuracy of biomarker detection at minimal concentrations can be achieved through advanced high-resolution mass spectrometers, including Orbitrap and time-of-flight (TOF) MS (52).

B. Metabolomic Profiling for Cancer Screening

The changes that occur within metabolic processes create dependable markers of tumourigenic developments. The metabolic signatures of cancer show enhancements in glycolysis activity known as the Warburg effect while demonstrating increased amino acid consumption and dysregulated lipid metabolism (53).

IDH-mutant glioma diagnosis relies on MS detection of 2-hydroxyglutarate (2-HG) accumulation to improve glioma classification and treatment strategy selection (54). Mass spectrometric lipidomics has established a method to detect abnormal phospholipid levels in ovarian cancer, which enables doctors to obtain diagnostic outcomes without invasive procedures (55).

4.2 Mass Spectrometry in Personalized Cancer Therapy

A. Drug Target Identification and Pharmacokinetics

Through mass spectrometry oncologists succeed in finding practical molecular targets while tracking cancer drug metabolism patterns within patients' systems (56). Quantitative proteomics by LC-MS/MS serves as a key component for profiling kinase inhibitors along with monoclonal antibodies and immune checkpoint inhibitors in different cancer type (57).

MS-based testing methods track how TKIs such as imatinib (Gleevec) are absorbed into the body and processed through metabolism (58). Mass Spectrometry Imaging (MSI) allows scientists to create spatial drug distribution maps inside tumours while reducing systemic drug toxicity (59).

B. Proteomic and Metabolomic Biomarkers for Therapy Response

MS-based proteomics and metabolomics systems allow healthcare providers to track patient reactions to chemotherapy treatments and immunotherapy and targeted therapy (60). Chemo-resistance monitoring in

patients receiving target-based treatments becomes possible through MS examination of circulating tumour DNA (ctDNA) and circulating tumour cells (CTCs) found in liquid biopsies (61).

The analysis of tumour metabolite changes during radiotherapy resistance enabled researchers to develop improved adaptive strategies through their profiling work (62).

4.3 Mass Spectrometry in Cancer Prognostics and Disease Monitoring

A. Prognostic Biomarkers for Patient Stratification

MS-based multi-omic profiling through prognostic biomarkers helped discover vital molecular signatures linked to tumour aggressiveness and both metastasis and recurrence risk probabilities (63). High S100 protein levels and heat shock protein expressions serve as indicators for unfavourable outcomes in patients with breast or lung cancer (64).

SRM, together with PRM, serves as quantitative MS techniques for validating prognostic protein panels in clinical settings to ensure precise risk assessment (65).

B. Longitudinal Monitoring of Cancer Progression

The analysis capabilities of MS have established a system for continuous active monitoring of cancer development and recurrence through liquid biopsy applications. The analysis of plasma proteomes together with plasma metabolomes allows healthcare professionals to detect leukaemia and solid tumour MRD (minimal residual disease) so they can intervene early in case of relapse (66).

Research analysts utilise MALDI-MS imaging (MALDI-MSI) to study treatment-induced changes in tumour microenvironments, as this method explores resistance mechanisms while generating insight into combination therapy approaches (67).

4.4 Future Prospects and Challenges of MS in Clinical Oncology

The clinical implementation of mass spectrometry (MS) encounters multiple barriers because it demands expensive equipment and complex systems in addition to requiring standardised operational methods (48). Obviously, clinical adoption depends on resolving these major obstacles. High-throughput MS as well as artificial intelligence-driven MS data analysis along with single-cell MS methods demonstrate substantial capabilities for transforming precision oncology (68). Such innovative techniques will boost cancer identification as well as treatment options and surveillance methods to enable innovative therapeutic strategies. MS clinical oncology will succeed in the future through applying modern technical developments to overcome current obstacles and create better healthcare outcomes and quality.

5. Challenges and Limitations of Mass Spectrometry in Cancer Biomarker

MS currently transforms cancer biomarker discovery through its technology, which allows fast and sensitive analysis of multiple biomolecules existing in different biological samples. The development of modern MS technology has produced breakthroughs that enhance both equipment features and data

processing methods along with omics methodologies integration (12). Recent advances in MS technology enable more precise and repeatable along with individualised detection and treatment methods for cancer diseases (69). The present section investigates modern developments in cancer biomarker research using MS techniques and elaborates on potential implementation methods for clinical fields.

5.1 Advances in Mass Spectrometry Technologies

A. High-Resolution and High-Throughput MS Techniques

Enhancements in high-resolution mass spectrometry (HRMS) equipment now enable better identification of scarce cancer biomarkers, which makes detecting diseases at early stages possible. The instruments Orbitrap MS and Fourier-transform ion cyclotron resonance (FT-ICR) MS have achieved sub-parts-per-million (ppm) mass accuracy through advanced design, which enables precise measurement of cancer biomarkers (70).

Time-of-flight (TOF) MS joined with matrix-assisted laser desorption/ionisation (MALDI-MS) has advanced tissue imaging spatial resolution to visualise cancer biomarker distribution at a cellular resolution. The technological developments in MS now enhance MS's capabilities for tumour identification together with biomarker confirmation and therapy outcome assessment (71).

B. Single-Cell Mass Spectrometry for Cancer Research

Researchers now use single-cell MS as an innovative research tool to study tumour cellular heterogeneity while detecting unique tumour cells (72). Shallow bulk analytical techniques cannot detect important cancer cell groups, including circulating tumour cells (CTCs) and cancer stem cells (CSCs), which determine tumour development and metastasis (73).

The single-cell metabolic and proteomic profiling has improved significantly due to nanoelectrospray ionisation (nESI-MS) and microfluidic-MS platforms (74). New technological developments create the foundation for treating cancer patients based on their individual situations.

5.2 Integration of Mass Spectrometry with Multi-Omics Approaches

A. Proteogenomics for Precision Oncology

The association of mass spectrometry-based proteomics and next-generation sequencing (NGS) techniques has facilitated the proteogenomics approach as a powerful tool for unraveling the DNA mutations and post-translational modifications (PTMs) in cancer cells. The integrated approach enhances the understanding of tumor biology, as it maps genetic alteration insights back to the actual functioning of proteins (75).

Breast, ovarian, and lung cancers with successful biomarker approvals and target selection are used to detect protein biomarkers for treatment targets using MS-based proteogenomics by the Clinical Proteomic Tumor Analysis Consortium (CPTAC) (76).

B. Metabolomics and Lipidomics in Cancer Research

Effective applications of mass spectrometry-based metabolomics and lipidomics now show how tumours develop distinct metabolic weaknesses (77). Research shows that MS demonstrates its ability to find cancer-specific metabolic changes, which include:

1. Scientific studies have found that excessive lipid accumulation within prostate cancer cells enables researchers to detect targetable metabolic processes (78).
2. The metabolic changes in glioblastoma amino acid pathways led researchers to discover fresh biomarkers for disease evolution (79).

MS-based multi-omics strategies have proven powerful for developing metabolic cancer therapies through these recent discoveries.

5.3 Artificial Intelligence and Computational Advancements in MS-Based Biomarker Discovery

A. Machine Learning for Biomarker Identification

AI and ML technology advancements during the current era enhance the ability to interpret MS-based cancer biomarkers. ML algorithms process extensive proteomic and metabolomic datasets to recognise previously impossible-to-detect patterns and correlations (68).

The application of deep learning models using MS spectra led to better cancer subtype identification with superior performance than conventional medical diagnosis techniques (80). Medical systems now employ AI technologies to merge into decision support tools that boost the predictive analytic capabilities of biomarker assays based on MS analysis.

B. Cloud-Based Platforms for MS Data Sharing

The sharing of mass spectrometry data has become a key focus in cancer biomarker research globally, supporting collaborative discovery. Cloud-based formats (for example, ProteomeXchange or MetaboLights) enable experimentalists to retrieve, analyze, and verify biomarker data in real time, speeding up the conversion of mass-spectrometry (MS)-based findings to clinical usage (81).

5.4 Challenges and Future Directions in MS-Based Cancer Biomarker Research

Although notable advances for MS-based biomarker research have been made, significant challenges that must be taken into account for clinical implementation are still relevant (9).

A. Standardization and Reproducibility Issues

A significant challenge in MS-based cancer biomarker discovery is the absence of standardized protocols in the areas of sample preparation, data acquisition, and analysis. This variability in mass spectrometry (MS) instruments, ionization techniques, and bioinformatics workflows can create inconsistencies in biomarker identification and validation (82). MS-based clinical assays urgently need to be harmonized so they can be reproduced, as well as approved by regulatory bodies.

B. Cost and Accessibility Barriers

Mass spectrometry is still a high-cost and technologically demanding technology that severely hampers its widespread use in resource-limited settings. The expense of instrumentation, upkeep, and expert personnel hinders the integration of MS into routine clinical diagnostics (9). Developing low-cost, compact MS platforms could make cancer diagnostics more accessible at the point of care and on a larger scale.

C. Future Innovations in MS-Based Cancer Research

In this regard, several innovations hold promise for advancing MS-based cancer biomarker research:

1. Portable and handheld MS devices for on-site cancer diagnostics.
2. MS-based liquid biopsy assays for real-time disease monitoring.
3. Ultra-fast biomarker discovery through the integration of MS data analysis with quantum computing.

These innovations will further amplify the clinical impact of mass spectrometry in oncology, making cancer diagnostics more precise, accessible, and affordable.

6. Recent Advances and Future Perspectives in MS-Based Cancer Biomarker

The advancements in mass spectrometry (MS) technology have fueled new methods in cancer biomarker discovery, enabling the detection of low-abundance proteins, metabolites, and lipids with exceptional sensitivity and specificity. Recent developments in MS-based methodologies, improvements in data analysis, and integration with other omics technologies are opening new opportunities for accurate and personalized cancer diagnostics (83). These innovations have also enhanced the clinical translation of biomarker research, bridging the gap between laboratory findings and real-world applications.

6.1 Cutting-Edge Innovations in MS-Based Cancer Biomarker Research

A. High-Resolution and Hybrid MS Technologies

High-resolution MS instruments, such as Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS) and Orbitrap MS, have significantly improved the detection of post-translational modifications (PTMs), metabolic profiles, and rare biomolecules in complex biological samples (84). The integration of tandem mass spectrometry (MS/MS) with hybrid platforms, such as quadrupole time-of-flight (Q-TOF) and ion mobility spectrometry-mass spectrometry (IMS-MS), has further enhanced biomarker specificity, particularly in distinguishing isobaric molecules (25).

B. Single-Cell Mass Spectrometry for Cancer Biomarkers

A major breakthrough in MS-based oncology research is the emergence of single-cell MS, which enables the analysis of cellular heterogeneity within tumors. Traditional bulk MS analyses often miss critical variations in cancer cell subpopulations, leading to incomplete biomarker profiling (85). Advances in laser ablation electrospray ionization (LAESI-MS) and matrix-assisted laser desorption/ionization (MALDI-

MS) imaging now allow researchers to map biomarker distributions at a single-cell level, offering new insights into tumor microenvironment dynamics and drug resistance mechanisms (86).

C. Multi-Omics Integration and Systems Biology Approaches

The integration of MS with other high-throughput technologies, such as genomics, transcriptomics, proteomics, and metabolomics, has opened new frontiers for multi-omics biomarker discovery. By leveraging artificial intelligence (AI)-driven analytical tools and deep learning algorithms, researchers can now correlate MS-based biomarker data with genetic and epigenetic changes, leading to a more comprehensive understanding of cancer biology. This approach is especially valuable in personalized medicine, where MS-driven insights help tailor therapeutic interventions based on an individual's molecular profile (87).

D. Advancements in Liquid Biopsy for Non-Invasive Cancer Detection

Recent innovations in MS-based liquid biopsy technologies have expanded the potential for early cancer detection and monitoring through the analysis of circulating tumor cells (CTCs), exosomes, and cell-free nucleic acids. These non-invasive techniques are transforming cancer diagnostics, enabling real-time tracking of tumor evolution, treatment response, and minimal residual disease (88). The application of surface-enhanced laser desorption/ionization (SELDI-MS) and nanoparticle-assisted MS has further improved biomarker detection sensitivity in various biofluids, including blood, urine, and cerebrospinal fluid (89).

6.2 Future Directions in MS-Based Cancer Biomarker Research

Despite these advancements, several challenges remain that require future research and technological improvements to enhance the clinical utility of MS-based cancer biomarker discovery.

A. Enhancing Sensitivity and Specificity in Complex Biological Samples

The complexity of body fluids and tissue extracts poses difficulty in detecting biomarkers of high specificity that have low abundance. Sample preparation protocols must be created or optimized by future studies through pre-fractionation of high efficiency combined with microfluidic separations technology to advance biomarker identification (68).

B. AI and Machine Learning for Automated Biomarker Analysis

The integration of AI-based and machine learning-based algorithms into MS data analysis has demonstrated remarkable increases in biomarker discovery and validation to date. Nevertheless, there is a requirement for continuing research to set up AI-based standardized platforms that can handle big data analytics, suppress false positives, and ensure the clinical reliability of MS-based biomarkers (Bergman et al., 2022).

C. Development of Portable MS Devices for Point-of-Care Testing

One of the biggest challenges of MS-based biomarker discovery is that MS is extremely costly and complex instrumentation. The use of hand-carried, miniaturized MS devices can make point-of-care diagnostics of cancer feasible within developing regions. Ambient ionization processes, paper spray ionization (PSI), and microchip-based MS have tremendous potential for point-of-care diagnostics of cancer in the future (90).

D. Regulatory Standardization and Clinical Translation

A significant obstacle to implementing MS-based biomarkers is that there is no regulation of biomarkers. The next generation of research will have to focus on harmonizing global MS databases, facilitating reproducibility of biomarker validation experiments, and establishing clear pathways of regulation for MS-based diagnostic tests (91).

6.3 Final Reflections

The recent technological leaps in MS-based discovery of cancer biomarkers have significantly advanced the sensitivity, specificity, and clinico-translational usefulness of mass spectrometry in oncology. From multi-omics integration through AI-based interpretation to single-cell MS, MS has developed into a key part of precision medicine. Nevertheless, to realize its full promise, ongoing investments in technological innovation, cross-disciplinary collaboration, and regulation will remain key. Portable MS devices, advanced AI-based analytical tools, and universal protocols for biomarker validation will, within a matter of years, continue to shake up cancer diagnostics, leading to earlier diagnosis, improved therapy outcomes, and better patient survival rates.

7. Conclusion

MS technology revolutionized cancer biomarker identification through its ability to perform quick and accurate disease-specific molecular signature detection at high volumes and at maximum precision levels. Various advancements in mass spectrometry technology have brought about improved precision in biomarker discovery capabilities, which enables healthcare professionals to detect the biomarkers early for better arrival to patients and better determination of their developmental track and medication response status. Scientists in this field advanced from conventional mass spectrometry instruments to complex hybrid systems and single-cell tools and multi-omics research methods, which resulted in superior biomarkers for medical use.

Multiple issues need resolution before biomarker detection research based on MS protocols can be adequately translated for clinical purposes. Development directions in this field depend on three main aspects: biological sample complexity and sensitivity specifications plus artificial intelligence in analytical tools. The widespread usage of MS in clinical practice requires advancements in three areas: sample preparation methods, computation-based data analysis, and standardized regulatory procedures. The path of MS-based cancer biomarker research will concentrate on dynamic biomarker surveillance and non-tissue intrusive blood tests along with scaled-down clinical testing tools and individualized treatment

methods. AI and machine learning applications with biomarker identification systems will enhance diagnostic accuracy so medical treatments reinforce better patient outcomes.

With the potential to completely transform disease detection and treatment, multiple sclerosis has shown to be an essential tool in cancer research overall. Realizing MS's full potential will require interdisciplinary cooperation, streamlined regulatory frameworks, and ongoing technological developments. The future of oncology could be greatly influenced by MS-based techniques as they develop further, resulting to better treatment interventions, earlier identification, and higher survival rates for cancer patients all around the world.

8. Reference

1. Trifonova OP, Maslov DL, Balashova EE, Lokhov PG. Mass spectrometry-based metabolomics diagnostics–myth or reality? Expert Review of Proteomics. 2021;18(1):7-12.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2021;71(3):209-49.
3. Wenk D, Zuo C, Kislinger T, Sepiashvili L. Recent developments in mass-spectrometry-based targeted proteomics of clinical cancer biomarkers. Clinical Proteomics. 2024;21(1):6.
4. Akhoundova D, Rubin MA. Clinical application of advanced multi-omics tumor profiling: Shaping precision oncology of the future. Cancer Cell. 2022;40(9):920-38.
5. Beck AG, Muhoberac M, Randolph CE, Beveridge CH, Wijewardhane PR, Kenttamaa HI, et al. Recent developments in machine learning for mass spectrometry. ACS Measurement Science Au. 2024;4(3):233-46.
6. Honoré B, Rice GE, Vorum H. Proteomics and nucleotide profiling as tools for biomarker and drug target discovery. MDPI; 2021. p. 11031.
7. Carmona A, Mitri S, James TA, Ubellacker JM. Lipidomics and metabolomics as potential biomarkers for breast cancer progression. npj Metabolic Health and Disease. 2024;2(1):24.
8. Haga Y, Minegishi Y, Ueda K. Frontiers in mass spectrometry–based clinical proteomics for cancer diagnosis and treatment. Cancer Science. 2023;114(5):1783-91.
9. Son A, Kim W, Park J, Park Y, Lee W, Lee S, et al. Mass Spectrometry Advancements and Applications for Biomarker Discovery, Diagnostic Innovations, and Personalized Medicine. International Journal of Molecular Sciences. 2024;25(18):9880.
10. Mechref Y, Hu Y, Garcia A, Hussein A. Identifying cancer biomarkers by mass spectrometry-based glycomics. Electrophoresis. 2012;33(12):1755-67.
11. Varahalarao V. Technological Advances in Detection and Diagnosis of Cancer. EURASIAN JOURNAL OF MEDICAL ADVANCES. 2024;4(2):74-9.
12. Wang P, Whiteaker JR, Paulovich AG. The evolving role of mass spectrometry in cancer biomarker discovery. Cancer biology & therapy. 2009;8(12):1083-94.
13. Drake RR, Powers TW, Jones EE, Bruner E, Mehta AS, Angel PM. MALDI mass spectrometry imaging of N-linked glycans in cancer tissues. Advances in cancer research. 2017;134:85-116.

14. Junker K, Gneist J, Melle C, Driesch D, Schubert J, Claussen U, et al. Identification of protein pattern in kidney cancer using ProteinChip® arrays and bioinformatics. International journal of molecular medicine. 2005;15(2):285-90.

15. Higashi T, Ogawa S. Isotope-coded ESI-enhancing derivatization reagents for differential analysis, quantification and profiling of metabolites in biological samples by LC/MS: A review. Journal of pharmaceutical and biomedical analysis. 2016;130:181-93.

16. Crutchfield CA, Thomas SN, Sokoll LJ, Chan DW. Advances in mass spectrometry-based clinical biomarker discovery. Clinical proteomics. 2016;13:1-12.

17. Li D, Yi J, Han G, Qiao L. MALDI-TOF mass spectrometry in clinical analysis and research. ACS Measurement Science Au. 2022;2(5):385-404.

18. Dasí-Navarro N, Lozano M, Llop S, Esplugues A, Cimbalo A, Font G, et al. Development and validation of LC-Q-TOF-MS methodology to determine mycotoxin biomarkers in human urine. Toxins. 2022;14(10):651.

19. Dakal TC, Dhakar R, Beura A, Moar K, Maurya PK, Sharma NK, et al. Emerging methods and techniques for cancer biomarker discovery. Pathology-Research and Practice. 2024:155567.

20. Su M, Zhang Z, Zhou L, Han C, Huang C, Nice EC. Proteomics, personalized medicine and cancer. Cancers. 2021;13(11):2512.

21. Lanning NJ, Castle JP, Singh SJ, Leon AN, Tovar EA, Sanghera A, et al. Metabolic profiling of triple-negative breast cancer cells reveals metabolic vulnerabilities. Cancer & metabolism. 2017;5:1-14.

22. Sallam RM. Proteomics in cancer biomarkers discovery: challenges and applications. Disease markers. 2015;2015(1):321370.

23. Safari F, Kehelpannala C, Safarchi A, Batarseh AM, Vafaee F. Biomarker Reproducibility Challenge: A Review of Non-Nucleotide Biomarker Discovery Protocols from Body Fluids in Breast Cancer Diagnosis. Cancers. 2023;15(10):2780.

24. Ain QU, Nazir R, Nawaz A, Shahbaz H, Dilshad A, Mufti IU, et al. Machine Learning Approach towards Quality Assurance, Challenges and Possible Strategies in Laboratory Medicine. Journal of Clinical and Translational Pathology. 2024;4(2):76-87.

25. Chen CJ, Lee DY, Yu J, Lin YN, Lin TM. Recent advances in LC-MS-based metabolomics for clinical biomarker discovery. Mass spectrometry reviews. 2023;42(6):2349-78.

26. Ifa DR, Eberlin LS. Ambient ionization mass spectrometry for cancer diagnosis and surgical margin evaluation. Clinical chemistry. 2016;62(1):111-23.

27. Zhou Y, Lih TM, Pan J, Höti N, Dong M, Cao L, et al. Proteomic signatures of 16 major types of human cancer reveal universal and cancer-type-specific proteins for the identification of potential therapeutic targets. Journal of Hematology & Oncology. 2020;13:1-15.

28. Ahmed H, Ajat M, Mahmood RI, Mansor R, Razak ISA, Al-Obaidi JR, et al. LC-MS/MS proteomic study of MCF-7 cell treated with dox and dox-loaded calcium carbonate nanoparticles revealed changes in proteins related to glycolysis, actin signalling, and energy metabolism. Biology. 2021;10(9):909.

29. Hu L, Zhu Y, Zhang H, Zhang X, Li Y, Yao Q, et al. Differentiation of three commercial tuna species through GC-Q-TOF and UPLC-Q/Orbitrap mass spectrometry-based metabolomics and chemometrics. Food Chemistry. 2024;452:139603.

30. Xu T, Wang Q, Wang Q, Sun L. Mass spectrometry-intensive top-down proteomics: an update on technology advancements and biomedical applications. Analytical Methods. 2024.

31. Pejkovska A. Epigenetic Deregulation by BCOR Oncogenic Fusions in Sarcomas 2025.

32. Smits AH, Vermeulen M. Characterizing protein–protein interactions using mass spectrometry: challenges and opportunities. Trends in biotechnology. 2016;34(10):825-34.

33. Domenick TM, Gill EL, Vedam-Mai V, Yost RA. Mass spectrometry-based cellular metabolomics: current approaches, applications, and future directions. Analytical Chemistry. 2020;93(1):546-66.

34. Cai Y, Wang Z, Guo S, Lin C, Yao H, Yang Q, et al. Detection, mechanisms, and therapeutic implications of oncometabolites. Trends in Endocrinology & Metabolism. 2023.

35. Zhang Y-F, Wang Y, Zhang K-R, Lei H-M, Tang Y-B, Zhu L. Development and validation of a rapid, robust and sensitive UPLC-QQQ-MS/MS method for simultaneous quantification of GSH metabolism in lung cancer cells. Journal of chromatography B. 2020;1148:122145.

36. Riviere-Cazaux C, Lacey JM, Carlstrom LP, Laxen WJ, Munoz-Casabella A, Hoplin MD, et al. Cerebrospinal fluid 2-hydroxyglutarate as a monitoring biomarker for IDH-mutant gliomas. Neuro-Oncology Advances. 2023;5(1):vdad061.

37. Pan S, Yin L, Liu J, Tong J, Wang Z, Zhao J, et al. Metabolomics-driven approaches for identifying therapeutic targets in drug discovery. MedComm. 2024;5(11):e792.

38. Pan M, Qin C, Han X. Lipid metabolism and lipidomics applications in cancer research. Lipid Metabolism in Tumor Immunity. 2021:1-24.

39. Buszewska-Forajta M, Pomastowski P, Monedeiro F, Walczak-Skierska J, Markuszewski M, Matuszewski M, et al. Lipidomics as a diagnostic tool for prostate cancer. Cancers. 2021;13(9):2000.

40. Yu B, Wang J. Lipidomics identified lyso-phosphatidylcholine and phosphatidylethanolamine as potential biomarkers for diagnosis of laryngeal cancer. Frontiers in Oncology. 2021;11:646779.

41. Farooqui AA, Farooqui T. Phospholipids, Sphingolipids, and Cholesterol-Derived Lipid Mediators and Their Role in Neurological Disorders. International Journal of Molecular Sciences. 2024;25(19):10672.

42. Ellertsson H. Profiling metabolites in breast cancer tissue using DESI-MSI.

43. Wheeler K, Gosmanov C, Sandoval MJ, Yang Z, McCall L-I. Frontiers in Mass Spectrometry-Based Spatial Metabolomics: Current Applications and Challenges in the Context of Biomedical Research. TrAC Trends in Analytical Chemistry. 2024:117713.

44. Ullah I, Yang L, Yin F-T, Sun Y, Li X-H, Li J, et al. Multi-omics approaches in colorectal cancer screening and diagnosis, recent updates and future perspectives. Cancers. 2022;14(22):5545.

45. Wu Y, Xie L. AI-driven multi-omics integration for multi-scale predictive modeling of causal genotype-environment-phenotype relationships. arXiv preprint arXiv:240706405. 2024.

46. Nalbantoglu S, Karadag A. Metabolomics bridging proteomics along metabolites/oncometabolites and protein modifications: paving the way toward integrative multiomics. Journal of Pharmaceutical and Biomedical Analysis. 2021;199:114031.

47. DeGroat W, Abdelhalim H, Peker E, Sheth N, Narayanan R, Zeeshan S, et al. Multimodal AI/ML for discovering novel biomarkers and predicting disease using multi-omics profiles of patients with cardiovascular diseases. Scientific Reports. 2024;14(1):26503.

48. Macklin A, Khan S, Kislinger T. Recent advances in mass spectrometry based clinical proteomics: applications to cancer research. Clinical proteomics. 2020;17(1):17.

49. Ding Z, Wang N, Ji N, Chen Z-S. Proteomics technologies for cancer liquid biopsies. Molecular Cancer. 2022;21(1):53.

50. Rao R, Gulfishan M, Kim M-S, Kashyap MK. Deciphering Cancer Complexity: Integrative Proteogenomics and Proteomics Approaches for Biomarker Discovery. Proteogenomics: Methods and Protocols. 2024:211-37.

51. Desai S, Guddati AK. Carcinoembryonic antigen, carbohydrate antigen 19-9, cancer antigen 125, prostate-specific antigen and other cancer markers: a primer on commonly used cancer markers. World Journal of Oncology. 2023;14(1):4.

52. Wallace MAG, McCord JP. High-resolution mass spectrometry. Breathborne Biomarkers and the Human Volatilome: Elsevier; 2020. p. 253-70.

53. Mathew M, Nguyen NT, Bhutia YD, Sivaprakasam S, Ganapathy V. Metabolic signature of Warburg effect in cancer: An effective and obligatory interplay between nutrient transporters and catabolic/anabolic pathways to promote tumor growth. Cancers. 2024;16(3):504.

54. Autry AW, Lafontaine M, Jalbert L, Phillips E, Phillips JJ, Villanueva-Meyer J, et al. Spectroscopic imaging of D-2-hydroxyglutarate and other metabolites in pre-surgical patients with IDH-mutant lower-grade gliomas. Journal of neuro-oncology. 2022;159(1):43-52.

55. Yu J, Hu D, Cheng Y, Guo J, Wang Y, Tan Z, et al. Lipidomics and transcriptomics analyses of altered lipid species and pathways in oxaliplatin-treated colorectal cancer cells. Journal of Pharmaceutical and Biomedical Analysis. 2021;200:114077.

56. Kowalczyk T, Ciborowski M, Kisluk J, Kretowski A, Barbas C. Mass spectrometry based proteomics and metabolomics in personalized oncology. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease. 2020;1866(5):165690.

57. Babačić H, Lehtiö J, de Coaña YP, Pernemalm M, Eriksson H. In-depth plasma proteomics reveals increase in circulating PD-1 during anti-PD-1 immunotherapy in patients with metastatic cutaneous melanoma. Journal for immunotherapy of cancer. 2020;8(1).

58. Liang L, Sun F, Wang H, Hu Z. Metabolomics, metabolic flux analysis and cancer pharmacology. Pharmacology & Therapeutics. 2021;224:107827.

59. Davoli E, Zucchetti M, Matteo C, Ubezio P, D'Incalci M, Morosi L. The space dimension at the micro level: mass spectrometry imaging of drugs in tissues. Mass spectrometry reviews. 2021;40(3):201-14.

60. Metwali E, Pennington S. Mass Spectrometry-Based Proteomics for Classification and Treatment Optimisation of Triple Negative Breast Cancer. Journal of Personalized Medicine. 2024;14(9):944.

61. Asante D-B, Calapre L, Ziman M, Meniawy TM, Gray ES. Liquid biopsy in ovarian cancer using circulating tumor DNA and cells: Ready for prime time? Cancer letters. 2020;468:59-71.

62. Kery M, Papandreou I. Emerging strategies to target cancer metabolism and improve radiation therapy outcomes. The British Journal of Radiology. 2020;93(1115):20200067.

63. Nevedomskaya E, Haendler B. From omics to multi-omics approaches for in-depth analysis of the molecular mechanisms of prostate cancer. International Journal of Molecular Sciences. 2022;23(11):6281.

64. Gonzalez LL, Garrie K, Turner MD. Role of S100 proteins in health and disease. Biochimica et Biophysica Acta (BBA)-Molecular Cell Research. 2020;1867(6):118677.

65. Hossain M, Hossain M. SRM-MS applications in proteomics. Selected Reaction Monitoring Mass Spectrometry (SRM-MS) in Proteomics: A Comprehensive View. 2020:173-96.

66. Zhang C, Li T, Zhao Q, Ma R, Hong Z, Huang X, et al. Advances and prospects in liquid biopsy techniques for malignant tumor diagnosis and surveillance. Small. 2024;20(44):2404709.

67. He Q, Sun C, Liu J, Pan Y. MALDI-MSI analysis of cancer drugs: Significance, advances, and applications. TrAC Trends in Analytical Chemistry. 2021;136:116183.

68. Liu J, Bao C, Zhang J, Han Z, Fang H, Lu H. Artificial intelligence with mass spectrometry-based multimodal molecular profiling methods for advancing therapeutic discovery of infectious diseases. Pharmacology & Therapeutics. 2024:108712.

69. Du R, Zhu L, Gan J, Wang Y, Qiao L, Liu B. Ultrasensitive detection of low-abundance protein biomarkers by mass spectrometry signal amplification assay. Analytical chemistry. 2016;88(13):6767-72.

70. Cochran D, Powers R. Fourier Transform Ion Cyclotron Resonance Mass Spectrometry Applications for Metabolomics. Biomedicines 2024, 12, 1786. 2024.

71. Rodrigo MAM, Zitka O, Krizkova S, Moulick A, Adam V, Kizek R. MALDI-TOF MS as evolving cancer diagnostic tool: a review. Journal of pharmaceutical and biomedical analysis. 2014;95:245-55.

72. Liang A, Kong Y, Chen Z, Qiu Y, Wu Y, Zhu X, et al. Advancements and applications of single-cell multi-omics techniques in cancer research: Unveiling heterogeneity and paving the way for precision therapeutics. Biochemistry and Biophysics Reports. 2024;37:101589.

73. Kravchenko-Balasha N. Translating cancer molecular variability into personalized information using bulk and single cell approaches. Proteomics. 2020;20(13):1900227.

74. Zhang D, Qiao L. Microfluidics coupled mass spectrometry for single cell multi-omics. Small Methods. 2024;8(1):2301179.

75. Ang MY, Low TY, Lee PY, Nazarie WFWM, Guryev V, Jamal R. Proteogenomics: from next-generation sequencing (NGS) and mass spectrometry-based proteomics to precision medicine. Clinica chimica acta. 2019;498:38-46.

76. Suo Y, Song Y, Wang Y, Liu Q, Rodriguez H, Zhou H. Advancements in proteogenomics for preclinical targeted cancer therapy research. Biophysics Reports. 2025.

77. Gaca-Tabaszewska M, Bogusiewicz J, Bojko B. Metabolomic and lipidomic profiling of gliomas—a new direction in personalized therapies. Cancers. 2022;14(20):5041.

78. Chen L, Xu Y-X, Wang Y-S, Zhou J-L. Lipid metabolism, amino acid metabolism, and prostate cancer: a crucial metabolic journey. Asian Journal of Andrology. 2024;26(2):123-34.

79. Fontanilles M, Heisbourg J-D, Daban A, Di Fiore F, Pépin L-F, Marguet F, et al. Metabolic remodeling in glioblastoma: a longitudinal multi-omics study. Acta Neuropathologica Communications. 2024;12(1):1-13.

80. Cobanaj M, Corti C, Dee EC, McCullum L, Celi LA, Curigliano G, et al. Artificial intelligence in the oncology workflow: Applications, limitations, and future perspectives. Artificial Intelligence for Medicine: Elsevier; 2024. p. 91-111.

81. Xu B, Zhou F. The roles of cloud-based systems on the cancer-related studies: a systematic literature review. IEEE Access. 2022;10:64126-45.

82. Percy AJ, Byrns S, Pennington SR, Holmes DT, Anderson NL, Agreste TM, et al. Clinical translation of MS-based, quantitative plasma proteomics: status, challenges, requirements, and potential. Expert review of proteomics. 2016;13(7):673-84.

83. Banerjee S. Empowering clinical diagnostics with mass spectrometry. ACS Omega 5 (5): 2041–2048. 2020.

84. Lai Y, Koelmel JP, Walker DI, Price EJ, Papazian S, Manz KE, et al. High-resolution mass spectrometry for human exposomics: Expanding chemical space coverage. Environmental Science & Technology. 2024;58(29):12784-822.

85. Nalla LV, Kanukolanu A, Yeduvaka M, Gajula SNR. Advancements in Single-Cell Proteomics and Mass Spectrometry-Based Techniques for Unmasking Cellular Diversity in Triple Negative Breast Cancer. PROTEOMICS–Clinical Applications. 2025;19(1):e202400101.

86. Samarah LZ. Single-Cell Metabolic Analysis and Molecular Imaging of Biological Tissues by Mass Spectrometry: The George Washington University; 2021.

87. He X, Liu X, Zuo F, Shi H, Jing J, editors. Artificial intelligence-based multi-omics analysis fuels cancer precision medicine. Seminars in Cancer Biology; 2023: Elsevier.

88. Li S, Xin K, Pan S, Wang Y, Zheng J, Li Z, et al. Blood-based liquid biopsy: Insights into early detection, prediction, and treatment monitoring of bladder cancer. Cellular & Molecular Biology Letters. 2023;28(1):28.

89. Suwanvecho C, Krčmová LK, Švec F. Centrifugal-assisted sample preparation techniques: Innovations and applications in bioanalysis. TrAC Trends in Analytical Chemistry. 2024:117909.

90. Zhou Z, Xu T, Zhang X. Empowerment of AI algorithms in biochemical sensors. TrAC Trends in Analytical Chemistry. 2024:117613.

91. Fernández-Metzler C, Ackermann B, Garofolo F, Arnold ME, DeSilva B, Gu H, et al. Biomarker assay validation by mass spectrometry. The AAPS Journal. 2022;24(3):66