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Biochemical Markers for Early Cancer Detection

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Abstract

Early detection of cancer significantly enhances treatment outcomes and patient survival. Biochemical markers represent a pivotal tool in identifying malignancies at an early stage. These markers include proteins, nucleic acids, and metabolites that reflect physiological and pathological processes in the body. This article explores the major types of biochemical cancer biomarkers, their mechanisms, current clinical applications, and emerging technologies in biomarker discovery.

Keywords: cancer, biochemical markers, tumours, pathological processes

Introduction

Cancer is a multifactorial disease characterized by uncontrolled cell proliferation, genomic instability, and metastasis. According to the World Health Organization, cancer was responsible for approximately 10 million deaths in 2020, with early detection remaining a cornerstone of successful management [1]. Biochemical markers have emerged as valuable tools for early diagnosis, prognosis, and therapy monitoring.

Early diagnosis of cancer significantly improves treatment outcomes and patient survival. Among the various tools available for early detection, biochemical markers—molecules measurable in biological samples such as blood, urine, and tissue—play a pivotal role. These markers reflect the molecular and cellular changes associated with oncogenesis and are broadly categorised into protein biomarkers, nucleic acid biomarkers, and metabolite biomarkers.

Protein biomarkers represent one of the most extensively studied categories due to their relative ease of detection in bodily fluids and their correlation with disease progression. Prostate-specific antigen (PSA) is a well-established marker used in screening for prostate cancer, often elevated in the early stages of the disease [2]. Another important protein marker, carcinoembryonic antigen (CEA), has shown increased levels in cancers of the colon, stomach, and pancreas, serving as both a diagnostic and prognostic tool [3]. Cancer antigen 125 (CA-125), though

Vol.9, No. 04; 2025

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widely used in monitoring ovarian cancer, suffers from limited specificity as its levels may also rise in benign conditions such as endometriosis or pelvic inflammatory disease [4].
In recent years, nucleic acid biomarkers have gained considerable attention due to their ability to provide molecular-level insights into tumour biology. Circulating tumour DNA (ctDNA) consists of fragmented DNA molecules released into the bloodstream by tumour cells. These fragments can reveal crucial genomic alterations, including point mutations, methylation patterns, and gene copy number variations, thus offering a non-invasive means for early cancer detection and monitoring [5]. Similarly, microRNAs (miRNAs), a class of small non-coding RNAs involved in post-transcriptional gene regulation, have emerged as stable and specific biomarkers in multiple cancer types. Their expression profiles are often altered in malignancy, reflecting tumour type and stage [6].

Additionally, metabolite biomarkers—small molecules resulting from cellular metabolic processes—have demonstrated potential in early cancer detection. Metabolic reprogramming is a hallmark of cancer, and altered levels of metabolites such as choline-containing compounds, lactate, and certain amino acids can be detected before any visible morphological changes occur in tissues. Techniques like metabolomics allow for the comprehensive profiling of these metabolites, revealing cancer-specific metabolic fingerprints that could facilitate earlier diagnosis [7].

Collectively, the integration of protein, nucleic acid, and metabolite biomarkers into clinical practice could revolutionize early cancer detection strategies, enabling personalised treatment and improved prognosis. Future research should aim to validate these markers across large, diverse patient cohorts and develop robust, cost-effective platforms for their routine use in clinical settings.

Clinical Applications

Biochemical markers play a central role in modern oncology by enabling early detection, risk assessment, prognostication, therapeutic monitoring, and the implementation of personalized treatment strategies. These biomarkers, measurable in blood, urine, and tissues, reflect molecular alterations associated with tumour development and progression and are instrumental in improving patient outcomes through timely and targeted interventions.

Protein-based biomarkers are among the most extensively studied due to their accessibility and detectability in biological fluids. Prostate-specific antigen (PSA) is one of the earliest and most widely used protein markers, particularly valuable for the early detection and monitoring of prostate cancer therapy [2]. Carcinoembryonic antigen (CEA) is another important protein marker, elevated in colorectal, gastric, and pancreatic cancers, and often used in conjunction with imaging and clinical assessments for disease staging and recurrence monitoring [3]. Cancer antigen 125 (CA-125), although commonly associated with ovarian cancer, suffers from low specificity as elevated levels can also occur in benign conditions such as endometriosis or liver disease, limiting its utility as a sole diagnostic tool [4].

Vol.9, No. 04; 2025

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In addition to proteins, nucleic acid biomarkers such as circulating tumour DNA (ctDNA) and microRNAs (miRNAs) offer high specificity and insight at the molecular level. ctDNA consists of small fragments of DNA released into the bloodstream by tumour cells. These fragments can harbor specific genetic alterations, including mutations, methylation changes, and copy number variations, making them powerful tools for non-invasive cancer detection and molecular profiling [5]. Similarly, miRNAs—short non-coding RNAs that regulate gene expression—are stable in circulation and have emerged as promising biomarkers for cancer diagnosis, prognosis, and even prediction of therapeutic responses due to their tumour-specific expression patterns [6]. Metabolite biomarkers also offer valuable information for early cancer detection. Cancer cells undergo metabolic reprogramming to support uncontrolled proliferation, which leads to measurable changes in metabolite levels before morphological abnormalities become apparent. Elevated concentrations of choline-containing compounds, lactate, and specific amino acids have been reported in various cancers, and metabolomics has enabled the identification of cancer-specific metabolic signatures in body fluids [7]. Such biomarkers not only provide diagnostic insight but also help distinguish between benign and malignant conditions based on metabolic profiles.

Beyond early detection, biochemical markers are increasingly applied in population-level cancer screening, prognosis, and monitoring. For example, the fecal immunochemical test (FIT), when used alongside CEA, has demonstrated improved sensitivity for colorectal cancer detection in asymptomatic individuals [8]. Liquid biopsy techniques that detect ctDNA have shown promise in identifying lung and breast cancers at early stages, especially when traditional tissue biopsies are not feasible [8]. In risk stratification, BRCA1 and BRCA2 mutations have been instrumental in predicting the likelihood of developing breast and ovarian cancers, guiding decisions on prophylactic interventions and enhanced surveillance [9]. Moreover, somatic mutations such as those affecting the tumour suppressor gene p53 or HER2 overexpression significantly impact cancer prognosis and inform the selection of targeted therapies in multiple tumor types [9].

Biomarkers also play a crucial role in monitoring therapeutic efficacy. A decline in PSA levels during treatment is an established indicator of response in prostate cancer management. Similarly, the presence and dynamics of tyrosine kinase mutations in the epidermal growth factor receptor (EGFR) gene are routinely monitored in non-small cell lung cancer to guide the administration or adjustment of tyrosine kinase inhibitors [10].

Despite their advantages, several challenges limit the widespread clinical application of biomarkers. A primary issue is sensitivity and specificity; many biomarkers fail to provide sufficient accuracy for reliable early-stage detection, leading to false positives or false negatives. Tumour heterogeneity further complicates this by introducing genetic and epigenetic variability both within and between tumors, which can affect biomarker expression and interpretation. Variability in pre-analytical and analytical procedures—such as differences in sample handling, processing, and assay standardisation—reduces reproducibility across laboratories. Furthermore,

Vol.9, No. 04; 2025

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the high cost of high-throughput screening technologies remains a significant barrier to routine implementation in clinical settings, particularly in low-resource environments.

To overcome these limitations, several advanced technologies have emerged in biomarker discovery and application. High-throughput omics platforms, including proteomics and metabolomics, allow for the comprehensive profiling of biomolecules in biological samples. Next-generation sequencing (NGS) facilitates the sensitive detection of low-abundance nucleic acid biomarkers, including point mutations, insertions, deletions, and epigenetic alterations [11]. Artificial intelligence (AI) and machine learning (ML) are increasingly integrated into biomarker research, enabling the analysis of complex, multidimensional datasets—such as genomic, proteomic, and radiologic data—to uncover novel biomarker patterns and predictive models [12]. Liquid biopsy, a non-invasive technique for detecting tumor-derived materials such as ctDNA, exosomes, or circulating tumor cells in bodily fluids, holds particular promise for early cancer detection in tumors that are difficult to biopsy, such as those in the pancreas or brain [13].

In conclusion, the integration of protein, nucleic acid, and metabolite biomarkers into clinical practice represents a promising avenue for advancing early cancer detection, guiding therapeutic strategies, and improving patient outcomes. However, further standardisation, validation in large-scale studies, and technological accessibility are essential to translate these advances into widespread clinical benefit.

Future Directions

The field of cancer biomarker research is undergoing rapid advancement, driven by technological innovations and an increasing demand for early, accurate, and personalised diagnostic tools. One of the most promising directions is the development of multi-omic profiling platforms, which integrate data from genomics, proteomics, metabolomics, and transcriptomics. By capturing information at multiple molecular levels, these platforms offer a more comprehensive understanding of tumor biology and significantly enhance the precision of early cancer detection.

Another emerging trend is the creation of personalized biomarker signatures, which take into account an individual's genetic predisposition, environmental exposures, and lifestyle factors. Such individualised profiles enable the stratification of patients based on their unique risk levels, thus allowing for targeted screening strategies and tailored therapeutic interventions that improve clinical outcomes.

Moreover, there is increasing interest in point-of-care diagnostic technologies, particularly those based on microfluidics and biosensors. These innovations aim to bring diagnostic capabilities directly to the patient’s bedside or outpatient setting. By enabling rapid, low-cost, and minimally invasive detection of cancer biomarkers from small volumes of blood or other body fluids, these tools have the potential to transform early diagnosis, especially in resource-limited settings where access to centralized laboratories is restricted.

Vol.9, No. 04; 2025

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Collectively, these future directions reflect a broader shift toward precision oncology, where biomarker-driven approaches will play a pivotal role in the early identification, risk assessment, and personalized management of cancer.

Conclusion

Biochemical markers hold immense promise for revolutionizing cancer detection and management. While several biomarkers are already in clinical use, ongoing research aims to refine their specificity, sensitivity, and cost-effectiveness. Future developments in omics technologies and computational biology are expected to usher in a new era of precision oncology.

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