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BIOMARKERS: AN EFFICIENT APPROACH FOR CANCER DETECTION, DIAGNOSIS & PROGNOSIS

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ABSTRACT

Timely detection of cancer rescues lives and greatly lowers cancer mortality. As a result, a lot of time and energy has gone into investigating novel technologies for the early detection of the illness. A wide variety of biochemical entities, including complete tumor cells detected in bodily fluid, proteins, carbohydrates, nucleic acids, and tiny metabolites, as well as cytogenetic and cytokinetic characteristics, are included in the category of cancer biomarkers. Risk evaluation, diagnosis, prognosis, treatment toxicity and effectiveness prediction, and recurrence may all be done using them. In this review, we provide an overview of complete detail of challenges associated with detecting early-stage tumors, discovery of biomarkers, biomarkers in cancer detection, diagnosis, and prognosis, types of cancer biomarker, role of biomarkers in cancer research & medicine as well as future perspectives of biomarkers.

KEYWORDS: Biomarkers, Cancer, Tissue-imaging, Biopsy, Cytokinetic.

INTRODUCTION

A biomarker is a biological phenomena that may be hard to locate but that points to a result or interim consequence that is clinically meaningful. Applications for biomarkers include illness detection, characterization, and surveillance. Furthermore, biomarkers have the ability to predict and control adverse drug responses, serve as prognostic indicators, and guide customized therapy regimens. To properly appreciate the relevance of a biomarker, one must comprehend the underlying relationship between it and the clinical outcome.[1]

According to the National Cancer Institute, a biomarker is a biological molecule that may be detected in tissues, blood, or other bodily fluids and that can serve as an indicator of a disease or condition like cancer.[2,3] Biomarkers are often used to distinguish between individuals with an illness and those who do not. Numerous variables, including as somatic or germline mutations, transcriptional modifications, and post-translational modifications, might be the cause of the changes. Biomarkers come in a huge variety and may be classified into several categories such as proteins (such an enzyme or receptor), nucleic acids (like a microRNA or other non-coding RNA), antibodies, and peptides.[4] A group of changes, including proteomic, metabolomic, and gene expression profiles, can also be referred to as biomarkers. Biomarkers can be tissue-derived and require either a biopsy or specialized imaging for evaluation, or they can be found in the systemic circulation (whole blood, serum, or plasma) or excretions or secretions (stool, urine, sputum, or nipple discharge). All of these methods allow for easy non-invasive assessment and serial measurement. Genetic biomarkers can be somatic, recognized as mutations in DNA taken from tumor tissue, or hereditary, detectable as sequence differences in germ line DNA extracted from whole blood, sputum, or buccal cells.[5]

Cancer is a complex disease characterized by alterations in the balance between cellular growth and death caused by both genetic and epigenetic modifications. It is a serious global health problem that claims many lives annually all across the world.[6] Cancer cannot spread unless significant changes occur at the molecular and cellular levels. Analyzing biomolecules such as nucleic acids, carbohydrates, proteins, lipids, and metabolites connected to the development of cancer might yield priceless clinical data in the form of biomarkers.[7] A major factor in reducing the morbidity and death from cancer is early identification. Thus, the necessity for accurate and trustworthy cancer markers is critical. Commonly utilized cancer markers include PSA, CEA, and CA-125/MUC16; however, new sources of information are being revealed via exosomes, microRNA, and circulating tumor cells.[8]

When creating and utilizing biomarkers in healthcare settings, there are a number of things to take into account and challenges to overcome. Among the phases and components that produce a potential biomarker are analytical validity, clinical validity, and clinical usefulness.[9,10] Pre-analytical and analytical elements of the biomarker assay, such as sample preparation and assay accuracy, are included in analytical validity. Independent validation is required for clinical validity, which measures the biomarker's ability to distinguish between different groups within the target population. The clinical utility of the biomarker indicates that there is substantial evidence to support its use in patient therapy, given its efficacy and the balance between possible benefits and hazards.[10–12]

CHALLENGES ASSOCIATED WITH DETECTING EARLY-STAGE TUMORS

Early diagnosis is essential for successful cancer therapy.[13] However, the quantity of biological markers that may be released from early lesions is limited by physiological and mass transit obstacles.[14,15] Finding intrinsic biomarkers by analyzing blood and biofluids is the main goal of current studies. Bioengineered sensors and artificial markers are being developed to increase specificity. Tumor localization and detection are further aided by imaging techniques.[16–18] Because positron emission tomography (PET) scanners typically have a spatial resolution of roughly 1 cm3, they will overlook very tiny cancers (diameter < 5 mm). Three orders of magnitude (1/1000th) less than the body's entire blood volume (~5 L) is the normal blood draw volume of 5–10 mL. This implies that when the tumor is discovered, its released biomarkers will be diluted more than a thousand times. Additionally, the detection of genetic materials presents problems. Circulating tumor DNA (ctDNA), for instance, has a half-life of around 1.5 hours. Consequently, it will experience 16 half-lives in a 24-hour period. This implies that just 0.0015% of the original components will be left by the time it is discovered.[17–20] Multicompartment models and genomic chronology studies reveal a potential ten-year window for early cancer detection. On the other hand, indolent tumors that have been present for 10 years or more can be detected by current screening methods.

Triple-negative breast cancer and high-grade serous ovarian carcinoma are examples of cancers that metastasize rapidly and aggressively and have poor clinical outcomes. In synthetic biomarker research, these issues are meant to be resolved via mechanisms for early detection that are either activity-based or genetically encoded.

DISCOVERY OF BIOMARKERS

At the start of any biomarker development, biomarkers should be “discovered” and are typically validated within the same initial report. Validation based on predefined prediction rule in an independent patient series is ideal, but it is often substituted by cross-validation based methods when independent patient sets are not available.[21] The research question and plan, including the fundamental use of the biomarker, should traditionally be clearly defined prior to the analysis, although this can be challenging at the very early stages of biomarker development. In this era of ever-evolving high-throughput omics technologies where thousands of individual molecules can be easily interrogated without a priori assumptions, research hypotheses are often generated in a post hoc manner, following often serendipitous discovery from unbiased mining of the genome-wide measurements (data-driven hypothesis generation). Another relevant issue to be addressed early in biomarker development is the target population to be tested in specific clinical contexts, which will guide subsequent clinical evaluation and implementation. In general, broader target populations could lead to increased costs and risks of failure during the development stage.[22-23] Study design/setting, from which analyzed bio-specimens are derived, is the major source of bias that hampers subsequent biomarker development. Ideally, the specimens should be prospectively collected based on well-defined inclusion and exclusion criteria together with accompanying clinical annotations pre-specified in the study protocol. A cohort or case control study design is typically employed. In a cohort study, clinical characteristics of enrolled individuals as well as information of intervention and follow-up are critical in identifying molecular correlates associated with clinical outcomes of interest. In a case-control study, potential confounding factors should be properly matched between cases and controls to minimize false discovery. In practice, biomarker discovery is often based on “samples of convenience”, which were incidentally available to the investigator at the time of research and collected without prior intention of specific biomarker discovery.[24] This could introduce unrecognized confounding factors, which may contribute to the false positive associations of the biomarkers. A common cause of failure in developing robust predictive and especially prognostic biomarkers is to define them based on clinically invalid surrogate endpoints such as

objective response in oncology trials as well as short-term outcomes from retrospective studies. Biomarkers trained for poorly defined endpoints are more likely to fail in subsequent prospective evaluation.[25] A prognostic gene-expression signature trained on long-term outcome using archived specimens has been successfully validated in a series of independent clinical and experimental studies. While the most optimal setting is prospective sample collection and follow-up based on a fully predefined protocol, this requires costly and lengthy biomarker assessment, which hampers timely deployment of cancer biomarkers. As an alternative, retrospective analysis of samples archived as part of previously completed prospective trials (prospective-retrospective design) is proposed to shorten the time frame while ascertaining quality of study design. Another solution is to develop a bio-bank in which bio-specimens and complete clinical annotations are prospectively accumulated based on well-defined protocols. A recent NCI joint workshop recommended improved sharing of existing specimens and data and creation of NCI-wide inventory of prediagnostic specimens and cancer diagnosis data, ongoing engagement of the clinical, translational and basic research communities, and encouraging the development of pilot projects.[26] Robustness of sample processing and data analysis procedures is another factor that influences reproducibility of biomarker studies. For example, a high diagnostic accuracy of a peptide signature for ovarian cancer was not confirmed in subsequent independent reanalysis of the original data set possibly due to variation in sample processing. These reports highlight the importance of careful assessment of technical soundness and methodological validity and disclosure of information to the research community to enable fair evaluation of reported biomarkers and identification of candidates for further development.[27] In addition, ensuring reproducibility of bio-informatics analysis is a critical determinant of successful clinical translation of genome-based biomarkers. There have been several efforts to develop informatics infrastructure to address this issue, including public repository of datasets with relevant annotations on biological, clinical, and experimental parameters, analysis software repository, and systems to record whole process of data analysis itself to allow anyone to rerun or modify the analysis to verify robustness of reported findings.[28,29]

WHAT ARE CANCER BIOMARKERS USED FOR?

As cancer progress the cell undergoes changes. A cancer biomarker measure the chance of a cancer developing, progressive or responding to a specific therapy. Cancer biomarkers can be used to guide clinical decision making in oncology. These biomarkers are linked to specific molecular pathway deregulation and or cancer pathogenesis. The antigens used as biomarkers are expressed de novo.[30-33] They may consist of mutated protein expression, gene/protein deletion, gene/protein silencing. Cancer biomarkers can be used to screen for cancers, predict risk, developed targeted therapies and monitor patient responses to cancer treatments. Novel cancer biomarkers are continuosly being identified and validated in research. A major bottleneck in translating these biomarkers from bench to bedside is the lack of well characterized,specific antibodies. For optimal IHC analysis of cancer biomarkers antibodies should be target specific to prevent cross reactivity to ensure for studying the right protein, sensitive to allow detection of small amounts of protein in tissue sample, reproducible. Recombinant antibodies offer the greatest consistency for reliable results over the life cycle of project and beyond.[34-36]

BIOMARKERS IN CANCER DETECTION, DIAGNOSIS, AND PROGNOSIS

Imaging Biomarkers

Among the several imaging biomarkers (IBs) that are essential for clinical oncology are tumor, node, metastasis (TNM) staging, objective response, and left ventricular ejection fraction.[37] Imaging methods such as computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and ultrasonography are widely used in cancer research. To close the translational gaps, new IBs must be certified and verified.[38] To speed up the clinical translation of IBs, a total of 14 significant suggestions have been issued by the European Organization for Research and Treatment of Cancer (EORTC) and Cancer Research UK (CRUK).[39–41] Parallel validation processes, cost-effectiveness analysis, standardization, accreditation systems, precision evaluation, alternative validation frameworks, and multicenter investigations are highlighted in these recommendations for obtaining IB qualification.[42–46]

Tissue Imaging

Specific proteins or antigens in tissue samples can be examined by researchers using immunohistochemistry (IHC), a technique for tissue image processing. This process makes use of antibodies that are engineered to attach to certain protein targets in tissue slices. Once the main antibody has attached itself to its target, a secondary antibody is attached to a recognition molecule. A microscope is used to visualize the outcomes. Usually, the results show the presence and position of the target protein as a change in color or fluorescence. In pathology research and diagnosis, immunohistochemistry (IHC) is a commonly employed technique that provides valuable insights into the distribution, intensity, and location of specific proteins in tissue samples.

The demand for early cancer detection diagnostic techniques based on functional and morphological data is rising. Modern medical imaging technologies that are being investigated and verified include terahertz (THz) and infrared radiation-based techniques (FTIR and Raman). THz imaging can be used for label-free, non-invasive, and ionizing cancer detection. During operations, THz and other spectroscopic-based imaging techniques are used to determine the cancer's margins.[1]

Because THz waves are so sensitive to changes in tissue water content, hydration levels may be tracked. DNA methylation may be investigated as a possible cancer biomarker thanks to THz technology's ability to measure DNA's molecular resonance.[47] Contrast chemicals may potentially enhance THz imaging for usage in clinical and translational cancer diagnostic applications.

Needle Biopsy

Imaging studies are crucial for the detection and monitoring of cancer. These tests employ a variety of energy sources, including magnetic fields, radioactive particles, X-rays, and sound waves, to create extremely detailed pictures that provide crucial information on the location and nature of the tumor. It is important to keep in mind that imaging tests are not without limits. Their findings are not definitive, and they are unable to identify certain cancer cells. Biopsies are usually used to verify imaging tests.[48]

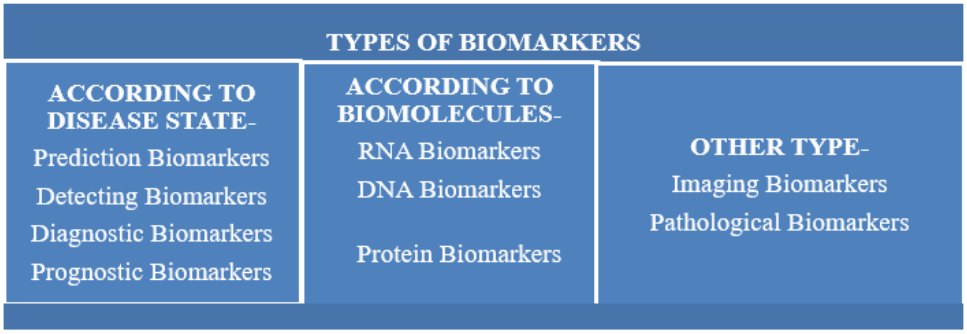
A cancer biopsy is a diagnostic procedure used to determine the kind and characteristics of the tumor cells and to either confirm or deny the presence of cancer. The results are critical in order to make further medical decisions (tumor grading; chemotherapy versus radiation treatment versus immunotherapy). Surgical, endoscopic, and needle biopsies are just a few of the methods that can be used to perform biopsies, depending on the exact location and accessibility of the questionable area.[49] A thin needle aspiration can be used to extract a little sample from cells and fluid during a needle biopsy, or a bigger needle can be used to obtain larger tissue specimens. In vacuum-assisted biopsy, a specialized needle with a suction mechanism is utilized to collect tissue samples. These techniques offer flexibility in obtaining relevant samples for analysis. A non-surgical procedure called a core needle biopsy is used to collect tissue samples for evaluation. Ultrasound- or vacuum-assisted biopsy approaches may be utilized in hard-to-reach places.[50-52]

Biofluid Biomarkers

Biofluids offer a rapid assessment and monitoring method for illnesses. Biofluids such as urine, saliva, blood, and sweat are vital sources of information about the condition that is being studied.[53] These biofluid specimens are perfect for clinical research since they are simple to obtain non-invasively. Every biofluid has particular benefits and difficulties.Urine contains salts of urea, chloride, sodium, and potassium, while saliva is easily accessible and contains electrolytes such as sodium, potassium, calcium, magnesium, bicarbonate, and phosphates. The primary components of sweat are urea, lactic acid, minerals, and salt chloride.[54, 55]

Numerous biofluids, including urine, saliva, blood, and cerebrospinal fluid (CSF), are used in the identification and tracking of cancer. KRAS, MBD3L2, ACRV1, and DPM1 have been found in studies to be biomarkers in salivary mRNA that can accurately and highly specifically identify pancreatic cancer. Calprotectin, AZGP1, and HP are salivary proteins that have a high degree of specificity and sensitivity in identifying lung cancer. Additionally, in mouth and throat malignancies, salivary DNA can identify mutations in the genes FBXW7, HRAS, KRAS, PI3K, and CDKN2A.[56–58]

TYPES OF CANCER BIOMARKER



Based on Disease State

- **Predicting Biomarkers:** This type of biomarker can ideally involve in prediction of a patient respond to a therapy or it can also use to find out an optimized drug dose. These are better suited for breast cancer because breast cancer is heterogeneous that's why other cancer may respond differently if we use same treatment.[59]
- **Detecting Biomarkers:** This type of biomarker are used for evaluation and detection of any type of cancer. Body can itself identify any tumor by triggering immunogenic factors like antibodies.[60]
- **Diagnostic Biomarkers:** It is true that diagnosis of breast tumor is confirmed only by biopsy, but biomarkers can also help in confirmation of primary cause of the cancer.[61]
- **Prognostic Biomarkers:** These are biomarker that may give knowledge about a patient's expected outcome, regardless of treatment. Biomarkers can help determine which cancers can grow faster and or metastasize because fewer breast cancers are more aggressive.[62-63]

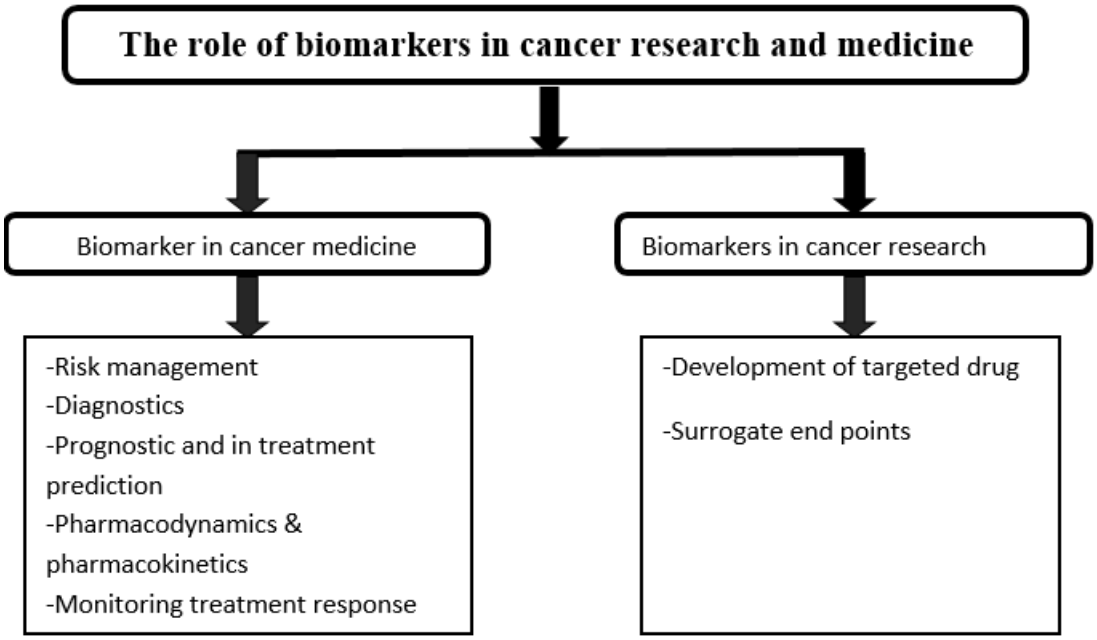
Based on Biomolecules

- **RNA Biomarkers:** Quantitative Reverse Transcription Polymerase Chain Reaction (RTPCR), differential expression, location-based methods, Serial Analysis of Gene Expression (SAGE) are mostly preferred methods for analysis of symptoms of cancer at RNA level.[64] The acquisition of pure RNA signature is experimented with LC-based microscopy in different stages and stages of treatment. Relative diagnosis of RNA expression based on temperature maps, monitored algorithms, and summaries is consistent with analysis and observation. Micro-MRNAs (miRNAs) are small, uncontrolled RNAs linked to a number of clinical features of cancer, such as blood cancer, breast carcinoma, Colorectal, prostate, and hepatic cancer. Speech profiles of miRNAs can be involved in differentiation of human carcinoma, which also promotes the link among diagnosis and treatment results. The site of symptoms of miRNAs associated with metastasis in relation to oncogenesis is growing rapidly and these symptoms have recently been termed metastamirs. MiRNAs can act as tumor inhibitor and oncogene. MRNAs can be used as biomarkers for diagnosis, prognosis, stage, risk classification and prognosis, as well as drug responses in carcinoma patients.[65]
- **DNA Biomarkers:** XRCC1, ATM, p53 for lung, head and neck carcinoma; CYP1A1, RAD1, BRCA1 and BRCA2 for breast carcinoma and PGS2 for lung cancer and Single nucleotide polymorphisms (SNPs) are major DNA markers. Other key features of DNA consists loss of hetrozygosity (LOH); variation in the rate of copying of genes; chromosomal fluctuations in cytogenetic levels, like translocation / fusion (BCR-ABL, PML-RARA translocation in leukemia's), microsatellite intensity (MSI), and epigenetic mutations. DNA nucleotide mutations in plant tumors (Ras, APC), plant suppressors (p16, p53, p19, Rb), cell cycles (cyclins) and DNA-related gene mutations (XRCC) associated with speculation and diagnosis of various cancers, although its clinical results are not yet available. DNA source may be extracted from tissue, serum, sputum, saliva, bronchial tears, CSF, and cancerous cells circulating in the blood, bone marrow, and nipple aspirate. Atoms of mitochondrial DNA (mtDNA) are also approved as biological markers for various cancers. Epigenetic modification of nucleic acids and related proteins (histones and non-histones) is important for carcinogenesis. Methylation levels in prostate cancer cells, sputum/serum from lung cancer patients, and saliva from oral cancer patients are directly affected by the size of the lesion.[66-69]
- **Protein Biomarkers:** Protein-based signals are more important biosignals in comparision to DNA or RNA-based markers due to fact that proteins are not the main killer biomolecules in tissue cells.[70] As protein molecules define cellular pathways in normal and transformed cells; therefore, proteomic symptoms are important during the onset and progression of the disease. Protein-based signatures derived from classical two-dimensional (2D) fluorescent gel electrophoresis (DIGE); polycarylamide gel electrophoresis (PAGE); and high impact forums, such as Mass Spectrometry (MS), Matrix-Related Laser Absorption Ionization Time-of-Flight (MALDITOF), Surface-enhanced Laser Absorption Ionization Time-of-Flight (MALDITOF) SELDITOF) and Microarray Phase Recovery. Quantum dots and nanoparticles are the latest additions to existing technology for testing the power of protein molecules as cancer markers.[71,72]

Based on Other Criteria

- **Imaging Biomarkers:** Current imaging techniques, such as X-ray, computed tomography (CT), ultrasound, radionuclide scan, and magnetic resonance imaging (MRI), are commonly used for screening and diagnosis. Cancer diagnosis including staging and determining the effectiveness of cancer treatment and monitoring for recurrence. Attempts have been made to link PSA citation with prostate cancer bioimaging data. Mammograms are widely used to screen for breast cancer in women over the age of 50. According to a recent report from the American Cancer Society (ACS), breast cancer rates have dropped thanks to cancer screening. Colonoscopy is routinely performed to screen populations at high risk of developing colon cancer.[73]
- **Pathological Biomarkers:** Various infectious agents, especially viral infections, account for 15-20% of all human cancers. The presence of certain tumor-bearing viruses makes them very attractive viral biomarkers. The presence of Epstein-Bair virus (EBV) has been associated with nasopharyngeal cancer and lymphoma, whereas HPV has been associated with cervical and head and neck cancers. Helicobacter pylori (H. pylori) bacterial infection causes chronic inflammation of the gastrointestinal tract. H. pylori infection is associated with the development of duodenal and gastric ulcers and is a known biomarker for gastric cancer.[74,75]

ROLE OF BIOMARKERS IN CANCER RESEARCH & MEDICINE



Examples of cancerous biomarkers for disease diagnosis and prognosi[76-80]

Biomarker	Tumour	Application	Sample type	Method of Detection
Cancer Antigen 125(CA125)	Ovarian cancers, Fallopian tube cancer	Diagnostic & Prognostic	Serum	Immunoassay
Carcinoe-mbryonic antigen	Colorectal cancer	Diagnostic & Prognostic	Serum	ELISA
Prostate specific Antigen(PSA)	Prostate cancer	Diagnostic & Prognostic	Serum	Immunoassay
Cancer Antigen 15-3(CA15-3)	Breast cancer	Diagnostic & Prognostic	Serum Lymph node Bone marrow	ELISA IHC IHC
Cancer Antigen19-9(CA19-9)	Pancreatic cancer Bladder cancer	Diagnostic & Prognostic	Serum Urine	ELISA ELISA
Alpha-Fetoprotein-(AFP)	Hepatocellular Carcinomas	Diagnostic & Prognostic	Serum	Immunoassay
Glucose metabolism	All cancers, general	Diagnostic, Prognostic & Therapeutic	Imaging	FDG-PET scan
Circulating tumour cells(CTCs)	Metastatic breast cancer etc.	Diagnostic & Prognostic	Blood	Immunocytometry
Cancer stem cell(CSCs)	AML, Melanoma, Brain tumour, Breast cancer, Prostate cancer	Diagnostic, prognostic & therapeutic	Tumour sample	Immunocytometry
Thyroglobulin (TG)	Papillary & Follicular thyroid cancer	Diagnostic & prognostic	Serum	ELISA

CONCLUSION AND FUTURE PERSPECTIVES

For a long time, cancer control researchers have been fascinated by the idea of early detection—that is, identifying tumors before they spread and become incurable. An overview of current attempts to build diverse chemical instruments for the sensitive detection of cancer biomarkers, such as proteins, enzymes, nucleic acids, small molecules, and cancer cells, is given in this article.[81] We demonstrated how transdisciplinary technology-based cancer diagnoses are becoming a more viable alternative to conventional methods by introducing many illustrative cases for each biomarker. Extensive research need to be done about the technology of the present and future for cancer diagnostics in general, and cancer biomarker detection in particular.[82] The investigation of novel technologies and biomarkers for both fundamental and sophisticated cancer diagnostics is rapidly gaining traction. The future objective is to achieve quick, portable, affordable, and user-friendly personalized point-of-care diagnostics that could be added to home disease monitoring because the analytical and molecular techniques currently employed in well-equipped clinical and professional laboratories are very sophisticated.

Even while assays for identifying cancer biomarkers have advanced significantly over the past few decades, the majority of these advancements are still proof-of-concept trials, and they can only be used in highly optimized laboratory settings.[83] Translating these sensing platforms from the clean buffered solutions of a research environment to more realistic settings and real-world clinical samples in hospitals or other medical scenarios, such cell lysate, blood serum, and urine, still faces several unresolved hurdles. First off, a biosensor's exceptional performance is contingent upon many factors such as its sensitivity, selectivity, detection range, temporal precision, repeatability, reaction time, and cost. The fundamental prerequisite for cancer diagnostics is the capacity to transduce recognition events to readout signal in a sensitive manner.[84] Both ELISA and PCR still have limitations for advanced diagnostic applications, despite being the gold standards for protein and nucleic acid tests in clinical diagnosis. Therefore, ongoing attempts have been made to either discover new and improved techniques for the assessment of cancer biomarkers or to further refine already established approaches.[85] Apart from this perspective, the application of these technologies to the clinical detection of trace cancer biomarkers requires a way to robustly and consistently increase the signal. Hybrid bio/nanostructures-based signal amplification holds great promise for achieving high sensitivity and selectivity for in situ or online biomolecule detection, given the rapid advancements in nanotechnology and nanoscience. This approach can not only accelerate signal transduction by producing a synergistic effect between catalytic activity, conductivity, and biocompatibility, but it can also enhance recognition events through high signal tag loading.[86] While promising, methods based on nanomaterials also have drawbacks, including low recognition efficiency, non-specific binding for detection in complex biological matrix, slow binding kinetics due to heterogeneous interfaces, operation complexity, and lack of generality. Without a doubt, in the future, parameters of nanomaterials will need to be significantly enhanced and refined to satisfy the demands of clinically diagnostic applications. Second, because most naturally existing biomarkers cannot reproduce themselves and exponentially increase their concentration for the purpose of detection, they are often present in low quantities and cannot be "amplified" like nucleic acids. A "game changer" in cancer monitoring would be the conversion of a particular ligandtarget recognition mechanism into DNA detection events or other encoded information recognition enabling the quick, easy, sensitive, and precise assessment of non-nucleic acid cancer indicators.

Thirdly, the development of high-throughput techniques for the parallel analysis of multiple components in samples in a single test is crucial, as simultaneous analysis is needed in practice to improve the accuracy of diagnosis and provide more efficient biological information. Fourthly, the diverse components of physiological fluidic samples have placed higher demands on sensing technologies since they have emerged as a readily accessible non-invasive liquid biopsy for cancer diagnoses. Because sample preparation, cutting-edge technologies, and biotechnologies can all be combined into a single monolithic disposable device, microfluidic chips meet the requirements of fluidic sample-based point-of-care diagnostics by allowing significant throughput portability and a high degree of integration.[87] But before commercialization is possible, these technologies still need to be optimized in the future. Consequently, the development of effective detection platforms with high sensitivity and selectivity, miniaturization, versatility, high throughput, and identification of new biomarkers specifying for early diagnosis are the future prospects in cancer biomarker detection, given the demand in the life sciences and clinical diagnostics. The collaboration and efforts of many communities of chemical engineers, scientists, researchers in biology, physicians, material scientists, engineers, and technological researchers, etc., are anticipated to bring forth new advancements and improvements.[88–91]

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