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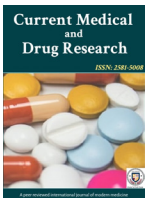

Nanoparticle-Based Liquid Biopsy Biosensors in Cancer

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ABSTRACT

Nanoparticle liquid biopsy biosensors have become a disruptive technology in cancer diagnostics, potentially substituting traditional tissue biopsies in offering a non-invasive, high sensitivity and real-time diagnostic method in a cancer patient. These biosensors hold the physicochemical characteristics of nanoparticles with that, high-surface-area, tunable optical properties, and magnetic responsiveness allow such biosensors to detect circulating tumor biomarkers, including, but not limited to, circulating tumor DNA (ctDNA), microRNAs (miRNAs), circulating tumor cells (CTCs), and extracellular vesicles Nanomaterials, especially gold nanoparticles, magnetic nanoparticles, and quantum dots, have recently been employed and improved the ability of biosensing platforms to operate by offering increased signal amplification and bio-specific recognition.

Optical, electrochemical, and subsequent lateral flow detection systems have been integrated to make its use fast and point-of-care, which has enabled early cancer detection and constant monitoring of the disease. In spite of these developments, issues like reproducibility, mass production, and medical standardization continue to be key impediments to mass adoption. Continued advances in nanoparticle-based engineering and biosensor development, however, are extending the potential of liquid biopsy technologies by making them a foundational pillar to precision oncology and personalized medicine.

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INTRODUCTION

One of the main causes of morbidity and mortality in the world is cancer, as it is often difficult to diagnose at an early stage and the heterogeneity of tumors can make the treatment more difficult. Despite being regarded as the standard of the art of cancer diagnosis, traditional tissue biopsies are invasive, time-consuming biopsies that may not be capable of reflecting the dynamic nature of the molecular environment of the tumors. These restrictions have stimulated the creation of liquid biopsy, the least invasive diagnostic modality that helps to identify tumour-related biomarkers in biological fluids like blood, urine, and saliva. Liquid biopsy enables the real-time control of the disease progression, therapeutic response, and minimal residual disease, as well as providing substantial clinical benefits over the traditional approaches (Mummareddy et al., 2021; Sardarabadi et al., 2021).

The key to the development of liquid biopsy technologies lies in the incorporation of the biosensor based on nanoparticles, which offers better analytical sensitivity, specificity, and detection rates.Nanoparticles, including gold nanoparticles (AuNPs), magnetic nanoparticles (MNPs), and quantum dots, exhibit unique physicochemical properties such as high surface-to-volume ratios, tunable optical behavior, and excellent biocompatibility. These features enable efficient

capture, enrichment, and detection of circulating tumor biomarkers, including circulating tumor DNA (ctDNA), microRNAs (miRNAs), circulating tumor cells (CTCs), and extracellular vesicles (EVs) (Martín-Gracia et al., 2020; Amri et al., 2021).

Recent advances in nanotechnology have significantly improved the performance of biosensing platforms by incorporating optical, electrochemical, and plasmonic detection mechanisms. Optical nanomaterial-based systems, for instance, leverage fluorescence and surface plasmon resonance for highly sensitive biomarker detection, while electrochemical platforms utilize nanoparticle-modified electrodes to achieve low detection limits and rapid signal transduction (Kim et al., 2024; Lee & Sim, 2024). Additionally, the emergence of point-of-care (POC) devices and lateral flow assays enhanced with nanoparticles has enabled decentralized and cost-effective cancer diagnostics (Singh et al., 2023; Jia et al., 2024).

Furthermore, nanoparticle-based biosensors have demonstrated significant potential in early cancer detection and precision oncology. By enabling multiplexed detection of biomarkers and integration with advanced analytical techniques, these systems can provide comprehensive molecular profiling of tumors. This capability is particularly important for identifying early-stage malignancies and monitoring therapeutic responses, where sensitivity and specificity are critical (Pratyusha Ghanta et al., 2023; Kalogianni, 2021). Magnetic nanoparticle-based platforms, for example, have shown promise in the selective isolation and detection of miRNAs and other nucleic acid biomarkers associated with various cancers (Balaban Hanoglu et al., 2023; Hanoglu et al., 2022).

Despite these advancements, several challenges persist, including issues related to reproducibility, scalability, and clinical standardization of nanoparticle-based biosensors. Variability in nanoparticle synthesis, functionalization, and assay conditions can affect diagnostic performance, thereby limiting widespread clinical adoption. Nonetheless, ongoing research continues to address these limitations through improved nanomaterial design, integration with microfluidics, and development of robust analytical devices (Singh et al., 2024; Marti & Huskens, 2022).

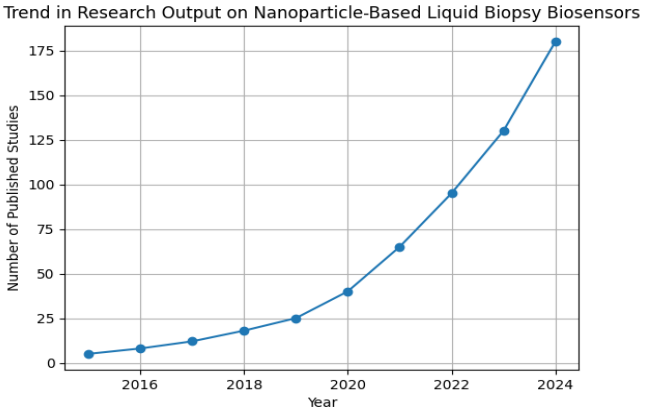

Figure 1: Data represent an illustrative trend of published studies on nanoparticle-based liquid biopsy biosensors over time. The increase reflects growing interest driven by advances in nanotechnology and precision oncology.

TYPES OF NANOPARTICLES IN LIQUID BIOPSY BIOSENSORS

Nanoparticles play a central role in enhancing the analytical performance of liquid biopsy biosensors due to their unique physicochemical properties, including high surface-to-volume ratio, tunable optical behavior, and functionalization versatility. Different classes of nanoparticles have been engineered to target and detect circulating cancer biomarkers with high specificity and sensitivity. These nanoparticle systems are typically integrated into electrochemical, optical, and hybrid biosensing platforms, enabling rapid and accurate cancer diagnostics (Kalogianni, 2021; Singh et al., 2023).

Gold Nanoparticles (AuNPs)

Gold nanoparticles are among the most widely utilized nanomaterials in liquid biopsy biosensors due to their excellent biocompatibility and strong surface plasmon resonance (SPR) properties. These features enable highly sensitive colorimetric and plasmonic detection of circulating tumor DNA (ctDNA), miRNA, and extracellular vesicles. AuNPs also facilitate signal amplification through surface functionalization with antibodies, aptamers, or nucleic acids (Kalligosfyri et al., 2020; Marti & Huskens, 2022).

Table 1: Comparison of Conventional vs. Nanoparticle-Based Liquid Biopsy Techniques

Parameter	*Conventional Liquid Biopsy Methods*	*Nanoparticle-Based Biosensors*
Sensitivity	Moderate	High due to signal amplification
Specificity	Limited by biomarker concentration	Enhanced via targeted functionalization
Detection Time	Hours to days	Minutes to hours
Sample Volume	Relatively large	Minimal sample required
Multiplexing Capability	Limited	High (simultaneous detection of multiple biomarkers)
Point-of-Care Application	Rare	Highly feasible
Cost Efficiency	Moderate to high	Potentially lower with scalable production

In addition, AuNP-based biosensors have demonstrated rapid detection capabilities in point-of-care settings, making them suitable for early cancer screening and monitoring (Martín-Gracia et al., 2020). Their integration into lateral flow assays and electrochemical platforms further enhances their diagnostic applicability (Singh et al., 2024).

Magnetic Nanoparticles (MNPs)

Magnetic nanoparticles are extensively used for biomarker isolation and enrichment due to their magnetic responsiveness. These nanoparticles enable efficient separation of low-abundance targets such as circulating tumor cells and miRNAs from complex biological matrices.

Recent developments have combined MNPs with electrochemical detection systems, improving sensitivity in early-stage cancer diagnostics. For example, ferrocene-labeled peptide nucleic acid probes coupled with MNPs have shown high specificity in detecting colorectal cancer biomarkers (Hanoglu et al., 2022). Furthermore, MNP-based biosensors have been applied in monitoring minimal residual disease and treatment response (Sardarabadi et al., 2021; Balaban Hanoglu et al., 2023).

Quantum Dots and Fluorescent Nanoparticles

Quantum dots (QDs) and other fluorescent nanomaterials offer superior optical properties, including high photostability and tunable emission spectra. These characteristics make them ideal for multiplexed detection of multiple cancer biomarkers simultaneously.

Fluorescent nanoparticle-based biosensors are particularly effective in detecting exosomes and nucleic acids with high sensitivity, enabling early cancer diagnosis. Their integration with optical biosensing platforms has significantly advanced real-time and high-throughput analysis (Amri et al., 2021; Kim et al., 2024).

Silica and Polymeric Nanoparticles

Silica and polymer-based nanoparticles provide a stable and versatile platform for biosensor fabrication. These nanoparticles are often used as carriers for signal amplification molecules or as scaffolds for immobilizing biomolecular recognition elements.

Their tunable surface chemistry allows for enhanced bioconjugation and improved detection efficiency. In liquid biopsy applications, these nanoparticles have been utilized in detecting circulating biomarkers and improving assay reproducibility (Pratyusha Ghanta et al., 2023).

Hybrid and Multifunctional Nanoparticles

Hybrid nanoparticles combine multiple functionalities, such as magnetic and optical properties, to enable multimodal detection strategies. These systems enhance diagnostic accuracy by integrating different sensing mechanisms into a single platform.

For instance, plasmonic–magnetic hybrid nanoparticles have been developed for simultaneous biomarker capture and detection, improving sensitivity and reducing assay time (Lee & Sim, 2024). Such multifunctional platforms are increasingly being explored for point-of-care applications and personalized oncology (Mummareddy et al., 2021).

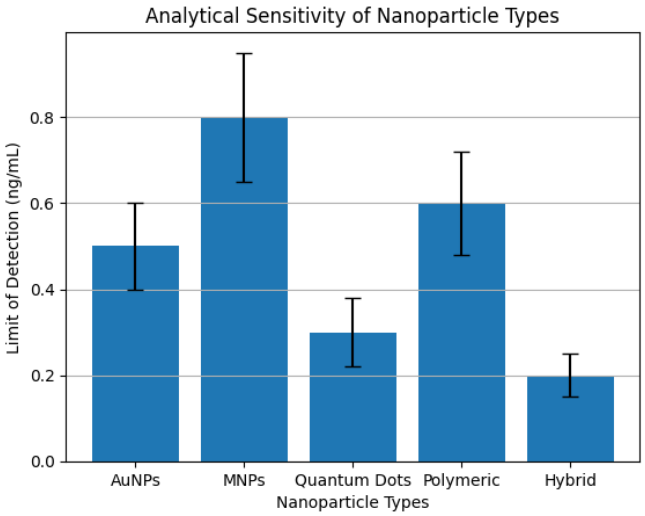

Figure 2: The above Values indicate approximate limits of detection (LoD) for different nanoparticle types, with error bars representing variability across studies. Lower LoD values correspond to higher analytical sensitivity, with hybrid and quantum dot nanoparticles demonstrating superior performance.

DETECTION STRATEGIES AND PLATFORMS

Nanoparticle-based liquid biopsy biosensors employ diverse detection strategies that integrate nanomaterial properties with advanced signal transduction mechanisms to achieve ultra-sensitive and selective identification of circulating cancer biomarkers. These platforms are broadly categorized into electrochemical, optical, and lateral flow-based systems, each offering distinct analytical advantages for clinical diagnostics and point-of-care applications.

Electrochemical Biosensors

Electrochemical detection platforms are among the most widely utilized strategies due to their high sensitivity, rapid response, and compatibility with miniaturized devices. These systems often incorporate gold nanoparticles (AuNPs) or magnetic nanoparticles (MNPs) to enhance electron transfer and signal amplification. Functionalized electrodes such as those modified with peptide nucleic acids or DNA probes enable precise detection of circulating tumor DNA (ctDNA) and microRNAs (miRNAs). For instance, MNP-based electrochemical platforms have demonstrated high specificity in colorectal cancer detection through ferrocene-labelled probes, enabling early-stage diagnosis (Hanoglu et al., 2022). Additionally, AuNP-enhanced electrode systems improve detection limits via surface plasmon-assisted electron transfer (Marti & Huskens, 2022). These approaches are particularly valuable for minimal residual disease (MRD) monitoring in cancers such as non-small cell lung cancer (Sardarabadi et al., 2021).

Table 2: Types of Nanoparticles Used in Liquid Biopsy Biosensors and Their Characteristics

Nanoparticle Type	*Key Properties*	*Detection Mechanism*	*Target Biomarkers*	*Advantages*	*Key References*
Gold Nanoparticles (AuNPs)	Surface plasmon resonance, high biocompatibility	Colorimetric, plasmonic, electrochemical	ctDNA, miRNA, exosomes	High sensitivity, rapid detection	Kalligosfyri et al., 2020; Marti & Huskens, 2022
Magnetic Nanoparticles (MNPs)	Magnetic responsiveness, easy separation	Electrochemical, magnetic enrichment	CTCs, miRNA	Efficient isolation, enhanced sensitivity	Hanoglu et al., 2022; Sardarabadi et al., 2021
Quantum Dots (QDs)	High fluorescence, photostability	Optical/fluorescence detection	Exosomes, nucleic acids	Multiplex detection, high resolution	Amri et al., 2021; Kim et al., 2024
Silica/Polymeric Nanoparticles	Chemical stability, functionalization flexibility	Signal amplification, immobilization platforms	ctDNA, proteins	Improved reproducibility, stability	Pratyusha Ghanta et al., 2023
Hybrid Nanoparticles	Combined optical and magnetic properties	Multimodal detection	Multiple biomarkers	High accuracy, multifunctionality	Lee & Sim, 2024; Mummareddy et al., 2021

Optical Biosensors

Optical biosensors exploit the unique optical properties of nanoparticles, including localized surface plasmon resonance (LSPR), fluorescence, and surface-enhanced Raman scattering (SERS). Gold nanoparticles and quantum dots are extensively used for signal generation and amplification, enabling highly sensitive detection of extracellular vesicles and nucleic acids in liquid biopsy samples (Martín-Gracia et al., 2020; Amri et al., 2021). Plasmonic sensors, in particular, offer label-free detection with real-time monitoring capabilities, making them suitable for dynamic biomarker analysis (Lee & Sim, 2024). Recent advances in optical nanomaterials have further improved multiplexing capabilities, allowing simultaneous detection of multiple cancer biomarkers with high accuracy (Kim et al., 2024).

Lateral Flow and Point-of-Care Platforms

Lateral flow assays (LFAs) enhanced with nanoparticles represent a significant advancement toward rapid and portable cancer diagnostics. These platforms utilize nanoparticle labels commonly AuNPs or magnetic nanomaterials to produce visible or instrument-readable signals. Their simplicity, low cost, and rapid turnaround time make them ideal for point-of-care testing. Recent developments integrating nucleic acid amplification techniques with nanoparticle-based LFAs have significantly improved sensitivity and specificity, enabling detection of low-abundance biomarkers (Jia et al., 2024). Furthermore, tailored point-of-care biosensors have been developed for on-demand cancer diagnostics and therapy monitoring, supporting decentralized healthcare delivery (Singh et al., 2023; Mummareddy et al., 2021).

Integrated and Hybrid Platforms

Emerging detection strategies combine multiple sensing modalities to enhance analytical performance. Hybrid systems integrating electrochemical and optical detection mechanisms leverage the strengths of both approaches, achieving improved sensitivity and robustness. Additionally, nanoparticle-assisted microfluidic platforms enable automated sample processing and multiplexed biomarker detection, advancing early cancer diagnosis (Pratyusha Ghanta et al., 2023). These integrated systems are increasingly being explored for clinical translation, offering scalable and reproducible solutions (Kalogianni, 2021; Singh et al., 2024).

Overall, detection strategies in nanoparticle-based liquid biopsy biosensors continue to evolve toward higher sensitivity, multiplexing capability, and clinical adaptability. The convergence of nanotechnology with advanced biosensing platforms is expected to further accelerate the development of robust, point-of-care diagnostic tools for cancer management.

APPLICATIONS IN CANCER DIAGNOSTICS AND MONITORING

Nanoparticle-based liquid biopsy biosensors have demonstrated substantial utility across multiple domains of cancer diagnostics and clinical monitoring, primarily due to their high sensitivity, specificity, and capability for real-time analysis of circulating biomarkers. These platforms enable the detection of tumor-derived components in biofluids such as blood, saliva, and urine, thereby facilitating non-invasive and repeatable assessments of disease status.

Early Cancer Detection

One of the most impactful applications of nanoparticle-enabled biosensors lies in early-stage cancer detection. These systems are engineered to identify low-abundance biomarkers such as circulating tumor DNA (ctDNA), microRNAs (miRNAs), and extracellular vesicles with high precision. Gold nanoparticle (AuNP)-based and optical nanomaterial-driven biosensors enhance signal amplification, enabling the detection of minute biomolecular concentrations that are often undetectable using conventional methods (Amri et al., 2021; Kim et al.,

Table 3: Comparison of Detection Strategies and Platforms in Nanoparticle-Based Liquid Biopsy Biosensors

Detection Strategy	*Nanoparticle Type*	*Target Biomarkers*	*Detection Mechanism*	*Key Advantages*	*Limitations*	*Representative Studies*
Electrochemical Biosensors	AuNPs, MNPs	ctDNA, miRNA, CTCs	Electron transfer, redox signaling	High sensitivity, rapid response, miniaturization	Electrode fouling, calibration complexity	Hanoglu et al., 2022; Marti & Huskens, 2022; Sardarabadi et al., 2021
Optical Biosensors (LSPR, SERS, Fluorescence)	AuNPs, Quantum Dots	Extracellular vesicles, nucleic acids	Optical signal modulation, plasmon resonance	Label-free detection, real-time monitoring, multiplexing	Expensive instrumentation, signal interference	Martín-Gracia et al., 2020; Amri et al., 2021; Kim et al., 2024; Lee & Sim, 2024
Lateral Flow Assays (LFAs)	AuNPs, Magnetic NPs	ctDNA, viral DNA, proteins	Colorimetric or fluorescence readout	Low cost, portability, rapid results	Lower sensitivity (without amplification), limited quantification	Jia et al., 2024; Singh et al., 2023
Magnetic Separation-Based Platforms	Magnetic NPs	CTCs, miRNA	Magnetic enrichment and detection	High specificity, efficient isolation	Requires external magnetic systems	Balaban Hanoglu et al., 2023
Hybrid/Integrated Platforms	комб. NPs (AuNPs + MNPs, QDs)	Multiple biomarkers	Multi-modal (electrochemical + optical)	Enhanced sensitivity, multiplex detection	System complexity, scalability challenges	Pratyusha Ghanta et al., 2023; Kalogianni, 2021; Singh et al., 2024

2024). Additionally, nanoparticle-functionalized platforms targeting extracellular vesicles have shown strong potential for identifying tumor-specific signatures at early disease stages (Martín-Gracia et al., 2020). This capability significantly improves early diagnosis rates and supports timely therapeutic intervention (Pratyusha Ghanta et al., 2023).

Detection of Circulating Tumor Cells and Nucleic Acids

Nanoparticle-based biosensors are also extensively applied in the detection and isolation of circulating tumor cells (CTCs) and nucleic acids. Magnetic nanoparticles, for instance, facilitate efficient enrichment and separation of CTCs from complex biological matrices, while electrochemical and plasmonic sensors enable highly sensitive detection of nucleic acid biomarkers (Lee & Sim, 2024; Hanoglu et al., 2022). These approaches are particularly valuable for characterizing tumor heterogeneity and identifying genetic mutations associated with cancer progression (Kalogianni, 2021). Furthermore, amplification strategies using nanoparticle-functionalized probes significantly enhance detection limits in DNA-based assays (Marti & Huskens, 2022).

Treatment Monitoring and Minimal Residual Disease (MRD)

Another critical application is in monitoring therapeutic response and detecting minimal residual disease (MRD). Nanoparticle-based biosensors allow continuous tracking of biomarker fluctuations during and after treatment, providing insights into treatment efficacy and early relapse detection. For example, biosensor platforms designed for non-small cell lung cancer (NSCLC) enable precise MRD monitoring through liquid biopsy analysis (Sardarabadi et al., 2021). These technologies offer clinicians the ability to make data-driven adjustments to treatment regimens, thereby improving patient outcomes.

Immunotherapy and Immune Checkpoint Monitoring

With the increasing adoption of immunotherapy, nanoparticle-based biosensors have been adapted to monitor immune checkpoint biomarkers and immune response dynamics. On-demand biosensing systems can detect changes in immune-related biomarkers, enabling evaluation of patient responsiveness to checkpoint inhibitors (Mummareddy et al., 2021). Magnetic nanoparticle-based platforms targeting miRNA and protein biomarkers further enhance the sensitivity of immune profiling in cancer patients (Balaban Hanoglu et al., 2023).

Point-of-Care and Rapid Diagnostics

Recent advancements have also enabled the development of portable, point-of-care (POC) biosensors that integrate nanoparticle technology with lateral flow assays and microfluidic devices. These systems provide rapid, cost-effective, and user-friendly diagnostic solutions suitable for clinical and decentralized healthcare settings (Singh et al., 2023; Singh et al., 2024). For instance, nanoparticle-enhanced lateral flow biosensors have demonstrated high sensitivity and rapid turnaround times for biomarker detection, supporting real-time clinical decision-making (Jia et al., 2024). Additionally, gold nanoparticle-based platforms continue to play a crucial role in rapid assay development due to their ease

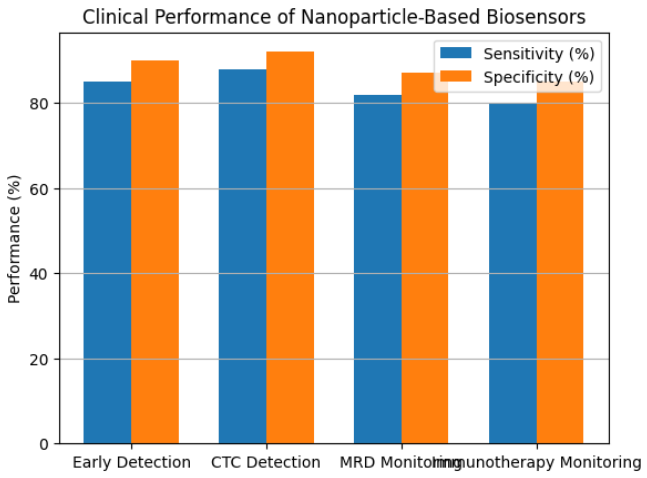

Figure 3: Sensitivity and specificity values are representative estimates based on reported ranges in the literature for nanoparticle-based liquid biopsy biosensors across different clinical applications.

of functionalization and strong optical properties (Kalligosfyri et al., 2020).

CHALLENGES AND LIMITATIONS

Despite the significant progress in nanoparticle-based liquid biopsy biosensors, several technical, translational, and clinical challenges continue to impede their widespread adoption in oncology practice.

Technical and Analytical Limitations

One of the primary challenges lies in achieving consistent analytical sensitivity and specificity across diverse biomarker types and detection platforms. Although nanoparticles enhance signal amplification, issues such as non-specific binding, background noise, and matrix interference from complex biological fluids can compromise assay accuracy (Amri et al., 2021; Kim et al., 2024). Additionally, variability in nanoparticle synthesis such as size distribution, surface functionalization, and stability can lead to batch-to-batch inconsistencies, affecting reproducibility and reliability (Kalogianni, 2021; Kalligosfyri et al., 2020).

Electrochemical and optical biosensors, while highly sensitive, may suffer from signal drift and environmental susceptibility, particularly in real-world clinical settings (Hanoglu et al., 2022; Lee & Sim, 2024). Furthermore, multiplexed detection of multiple biomarkers remains technically demanding due to cross-reactivity and signal overlap.

Standardization and Reproducibility Issues

A major barrier to clinical translation is the lack of standardized protocols for sample collection, processing, and analysis. Variations in pre-analytical factors such as blood handling, storage conditions, and isolation techniques can significantly influence biomarker integrity and detection outcomes (Martín-Gracia et al., 2020; Sardarabadi et al., 2021).

Moreover, the absence of universally accepted validation frameworks and reference standards complicates cross-study comparisons and regulatory evaluation. This challenge is particularly pronounced in emerging platforms such as lateral flow assays and point-of-care devices, where performance metrics may vary widely (Singh et al., 2023; Singh et al., 2024).

Scalability and Manufacturing Constraints

Translating nanoparticle-based biosensors from laboratory prototypes to commercially viable products requires overcoming scalability and manufacturing challenges. High-precision nanoparticle fabrication and surface modification processes can be costly and difficult to reproduce at an industrial scale (Marti & Huskens, 2022). Additionally, maintaining long-term stability and shelf-life of nanoparticle-based reagents under varying storage conditions remains a critical concern.

Integration into user-friendly, portable devices for point-of-care applications further adds complexity, particularly in ensuring robustness, miniaturization, and cost-effectiveness (Mummareddy et al., 2021; Singh et al., 2023).

Clinical Validation and Regulatory Barriers

While numerous studies demonstrate promising results, large-scale clinical validation is still limited. Many nanoparticle-based biosensors are evaluated using small patient cohorts, which may not adequately capture biological heterogeneity across cancer types and stages (Pratyusha Ghanta et al., 2023).

Regulatory approval pathways for nanotechnology-based diagnostics are also evolving, with stringent requirements for safety, efficacy, and reproducibility. Concerns regarding nanoparticle toxicity, biocompatibility, and long-term effects must be thoroughly addressed before clinical implementation (Kalogianni, 2021).

Biological Complexity and Biomarker Variability

Cancer-derived biomarkers in liquid biopsies exhibit significant heterogeneity and low abundance, particularly in early-stage disease. This poses a challenge for reliable detection, even with advanced nanoparticle amplification strategies (Martín-Gracia et al., 2020; Balaban Hanoglu et al., 2023).

Additionally, dynamic changes in biomarker expression during disease progression or treatment can complicate data interpretation and limit the predictive accuracy of biosensors (Sardarabadi et al., 2021). The coexistence of non-tumor-derived extracellular vesicles and nucleic acids further increases the risk of false-positive or false-negative results.

Integration and Data Interpretation Challenges

The integration of nanoparticle-based biosensors with digital health systems and data analytics platforms introduces challenges related to data standardization, interpretation, and clinical decision-making. High-throughput biosensing generates complex datasets that require advanced computational tools for accurate analysis and clinical translation (Jia et al., 2024).

Moreover, ensuring interoperability between biosensor

platforms and existing healthcare infrastructure remains a critical hurdle for real-world deployment.

FUTURE PERSPECTIVES AND CONCLUSION

The evolution of nanoparticle-based liquid biopsy biosensors is poised to significantly reshape the landscape of cancer diagnostics and therapeutic monitoring. Future developments are expected to focus on the design of multifunctional and hybrid nanoparticle systems capable of simultaneous detection of multiple biomarkers, including circulating tumor DNA (ctDNA), microRNAs (miRNAs), proteins, and extracellular vesicles. Such multiplexed platforms will enhance diagnostic accuracy and enable comprehensive molecular profiling, which is essential for precision oncology (Martín-Gracia et al., 2020; Kim et al., 2024).Specifically, the efficient use of plasmonic and optical nanomaterials is expected to enhance the efficiency and sensitivity of signal transduction and circulate sensitive biomarkers in the early cancer stages (Amri et al., 2021; Lee and Sim, 2024).

The other essential direction is the integration of biosensors based on nanoparticles with point-of-care and wearable diagnostics. On-site screening of cancers and continuous monitoring of the disease will be healthier and quicker with miniaturization of biosensing devices, enhanced by microfluidics, and lateral flow technologies (Singh et al., 2023; Jia et al., 2024). Moreover, real-time data analytics and inclusion of smart sensing functions may make it possible to dynamically monitor treatment reactions, especially with HI schemes like minimal residual disease (MRD) monitoring and immunotherapy monitoring (Mummareddy et al., 2021; Sardarabadi et al., 2021).

Although these encouraging improvements have been made, there are a number of issues that need to be dealt with, as a successful clinical translation. The problems associated with reproducibility, stability of nanoparticles and big scale production are major hurdles. Moreover, the non-uniformity of accepted procedures on the extraction and detection of biomarkers throws disparity in clinical performance (Kalogianni, 2021; Singh et al., 2024). Regulatory issues, such as validation, safety, and quality control, are also important issues that will impact on the implementation of these technologies in the normal clinical practice. It will also be necessary to continue to optimize nanoparticle functionalization and enhance assay robustness, and regulatory frameworks to address such restrictions (Marti & Huskens, 2022; Kalligosfyri et al., 2020).

Finally, nanoparticle-based liquid biopsy biosensors can be considered as a highly promising and the rapidly developing field in cancer diagnostics. Being able to deliver non-invasive, sensitive and real-time information about tumor biology makes them an essential facilitator of early diagnosis and individualized treatment plan. As further advances in nanotechnology and biosensor engineering, as well as integrated diagnostic platforms, unfold, these devices will soon make the transition to clinical practice, eventually leading to better patient outcomes and advancing the concept of precision medicine (Pratyusha Ghanta et al., 2023; Balaban Hanoglu et al., 2023; Hanoglu et al., 2022).

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