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REVIEW ARTICLE

Biomaterial-Assisted Detection of Cancer Stem Cell Markers for Early Cancer Diagnosis

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Abstract

Cancer stem cells are a small population of cells present within tumors. These cells play an important role in tumor initiation, progression, and metastasis. It also shows strong resistance to chemotherapy and radiotherapy. Due to these properties, cancer stem cells are considered important targets for early cancer diagnosis and prognosis. However, their detection is difficult because they are present in very low numbers and show high heterogeneity. Traditional diagnostic methods are often not sufficient to detect these cells accurately. This review focuses on the role of biomaterial assisted platforms for the detection of cancer stem cell markers. Biomaterials such as nanoparticles, nanocomposites, and hydrogels have gained attention due to their unique properties. These materials provide a high surface area and improved signal response. This helps in the efficient capture and detection of cancer stem cells. Different nanomaterial based platforms are discussed in this review. These include optical systems, electrochemical systems, and hybrid platforms. These approaches allow sensitive and specific detection of important cancer stem cell markers such as CD44, CD133, ALDH1, and EpCAM. The review also describes various biosensing strategies used for detection. These include surface plasmon resonance, fluorescence based methods, and aptamer or antibody mediated techniques. These methods support real time analysis and non-invasive diagnosis. In addition, the importance of surface engineering and functionalization techniques is discussed. These approaches improve target specificity and enhance detection efficiency. Despite recent progress, several challenges still remain. The heterogeneity of cancer stem cells makes detection complex. Surface fouling can affect accuracy and some biomaterials show toxicity. Clinical translation of these platforms is also limited. Addressing these challenges is important for developing reliable and reproducible diagnostic tools. Biomaterial assisted detection platforms show strong potential for early cancer diagnosis and personalized treatment strategies.

1. Introduction

Cancer stem cells are a small group of cells present within heterogeneous tumors. These cells have the ability to self renew and differentiate into multiple cell types. It plays a major role in tumor growth and progression (Singh et al., 2015). Even a small number of these cells can regenerate a complete tumor mass. It shows similarities to normal stem cells but they grow in an uncontrolled manner. Cancer stem cells also contribute to metastasis through epithelial mesenchymal transition. This process increases their ability to migrate and invade other tissues. Their stem like nature and adaptability make them an important factor in tumor heterogeneity and aggressive disease behavior (Liang and Kaufmann, 2023; Tang et al., 2015). Cancer stem cells also show strong resistance to conventional treatments of chemotherapy and radiotherapy. This resistance is due to improved DNA repair, drug efflux activity, and their inactive cell cycle state. It can also escape programmed cell death and lead to tumor recurrence of patient outcomes (Patil et al., 2023). Early detection of these cells is important for better clinical management. However, their low number and variable nature make detection difficult. Traditional

methods such as imaging and biopsy are not always effective. Recent advances in nanobiotechnology have improved the detection of cancer stem cells. Nanomaterials such as nanoparticles, nanocomposites, and hydrogels are widely studied. These materials have high surface area and flexible surface properties (Sun et al., 2024a). This helps in better interaction with target cells. Nanoparticles such as gold nanoparticles, magnetic nanoparticles, and quantum dots can be modified with specific ligands. These ligands help in targeting cancer stem cell markers and allows selective capture and sensitive detection (Ellis et al., 2020). Hybrid nanocomposite systems can detect multiple markers at the same time. Hydrogel and microfluidic platforms provide suitable environments for cell capture and analysis (Zhu and Yang, 2017). These systems also support real time monitoring of biomarkers. Overall, nanomaterial based platforms show strong potential for early cancer detection and improved treatment strategies.

2. Cancer Stem Cells: Biology and Diagnostic Relevance

Cancer stem cells are a distinct group of cells present within tumors. These cells show stem like properties such as self renewal and differentiation. It also shows resistance to common cancer treatments. Cancer stem cells play a key role in tumor initiation, progression, metastasis, and recurrence. Unlike other tumor cells, they can survive chemotherapy and radiotherapy (Huang et al., 2020; Liu et al., 2020). This is due to better DNA repair ability and high drug efflux activity. It also remains in a low metabolic state which helps them escape treatment. Because of this, it can regenerate tumors after therapy and contribute to aggressive disease (Moitra et al., 2011). Cancer stem cells are identified by specific surface and functional markers. CD44 is one of the most widely studied markers which involved in cell adhesion and migration. High expression of CD44 is linked with advanced tumor stage and poor survival in many cancers (Senbanjo and Chellaiah, 2017). CD133 is another important marker found in colorectal, brain, pancreatic, and lung cancers. Increased CD133 expression is associated with tumor aggressiveness and recurrence (Chen et al., 2013). ALDH1 is a functional marker that is linked with self renewal and drug resistance. Its expression is often related to poor prognosis (Chen et al., 2013). EpCAM is also used as a marker for isolating circulating tumor cells. High EpCAM expression is associated with metastasis and poor clinical outcome (Schulze et al., 2013).

In addition to surface markers, transcription factors also regulate cancer stem cell behavior which includes Oct4, Nanog, and Sox2. These factors help to maintain differentiation and support tumor progression (Kashyap et al., 2009). Their increased expression is linked with therapy resistance and aggressive cancer types. Other markers such as LGR5 and CD24 are used along with CD44 or ALDH1 to improve detection. Since no single marker is sufficient, a combination of markers is used for accurate identification of cancer stem cells. Cancer stem cell markers have strong clinical importance. In colorectal cancer, combined expression of CD44 and ALDH1 is linked with higher metastatic potential. In gastric cancer, CD44 and CD133 are associated with advanced disease stage and poor survival (Wakamatsu et al., 2012). In ovarian cancer, ALDH1 expression indicates poor prognosis. These markers help in early detection and provide important prognostic information (Zhao et al., 2018). It also supports personalized treatment strategies and improves clinical decision making.

3. Biomaterials in Cancer Diagnostics

Biomaterials have improved cancer diagnostics by providing sensitive and specific detection platforms. These systems can identify tumor cells and tumor related biomarkers including cancer stem cells (Yun et al., 2024). Traditional methods such as histopathology and imaging have limitations. It shows low sensitivity in early stages and cannot easily detect rare cancer stem cells. In contrast, engineered biomaterials offer better performance. These include nanoparticles, nanocomposites, polymers, and hybrid systems. It provides high surface area and adjustable physical properties to provide good biocompatibility. These features help in improving detection efficiency. Biomaterials can be functionalized with antibodies, aptamers, peptides, or small molecules. These targeting agents help in the specific detection of cancer stem cell markers such as CD44, CD133, and ALDH1 (Grover et al., 2023; Tiwari et al., 2023). This improves both capture efficiency and signal strength.

Nanoparticles are widely used in cancer diagnostics. Metallic nanoparticles such as gold and silver show strong optical properties. These properties help in sensitive detection of biomarkers. Gold nanoparticles functionalized with anti CD44 antibodies have shown high sensitivity in detecting cancer stem cells (Liang et al., 2015). Magnetic nanoparticles can capture rare cancer stem cells using an external magnetic and it allows separation of target cells from complex samples. Magnetic nanoparticles targeting CD133 have improved detection of aggressive tumor cells (Liang et al., 2015). Polymeric nanoparticles and lipid based carriers are used for multiplex detection. These

systems can detect more than one marker in a single test. For example, nanoprobes targeting EpCAM and CD44 improve detection of circulating tumor cells with stem cell features (Han et al., 2023). Quantum dots are another important class of biomaterials. It shows high brightness and stable fluorescence. These properties make them suitable for detecting multiple cancer stem cell markers. Quantum dots targeting CD133 and ALDH1 are used to visualize cancer stem cells in tissue samples (Ju et al., 2016). Upconversion nanoparticles are also used to improve detection accuracy. It can reduce background signal and allow better analysis in complex samples. Hybrid biomaterial systems combine different functions in a single platform. These systems can include magnetic and optical properties together. This allows both capture and detection of cancer stem cells. Electrochemical biosensors are also widely studied. These sensors use materials such as graphene and carbon nanotubes. It can detect very low levels of tumor markers and are useful for point of care testing. Biomaterials are also used in microfluidic systems and these systems act as lab on chip devices. It allows sample processing and detection in a single platform (Guttenplan et al., 2021). Nanostructured surfaces improve the capture of rare cancer stem cells. Microfluidic chips functionalized with specific markers can isolate circulating cancer stem cells from blood samples (Guttenplan et al., 2021). This supports non-invasive liquid biopsy and disease monitoring. Despite these advantages, some challenges remain. Certain nanomaterials may show toxicity and need proper safety evaluation. There is also a need for standard methods to ensure consistent results. Large scale production and regulatory approval are still difficult. Clinical validation in large patient groups is required. Even with these limitations, biomaterial based platforms show strong potential and can improve early cancer detection and support personalized treatment strategies.

4. Nanomaterial-Based Platforms for CSC Marker Detection

Nanomaterial based platforms play an important role in the detection of cancer stem cell markers. These platforms provide high sensitivity and specificity. It also supports detection of multiple markers at the same time (Kim et al., 2024). Unlike conventional approaches, these systems integrate nanomaterials into functional devices. This helps in identifying rare cancer stem cells in tumor samples and blood. Nanomaterials offer large surface area and adjustable physical properties. It also allows easy surface modification to improve target capture and signal generation. Optical nanoplatforms are widely used for cancer stem cell detection. Quantum dots are semiconductor nanoparticles with strong fluorescence properties and it has high stability and narrow emission signals. These features make them suitable for detecting multiple markers such as CD44, CD133, and ALDH1 (Figure 1 & Table 1). Quantum dots can be functionalized with antibodies or aptamers. This allows selective detection of cancer stem cells in tissue and blood samples (Mir et al., 2024; Xu et al., 2012). Upconversion nanoparticles are also used in optical detection and it convert infrared light into visible signals. This reduces background noise and improves detection accuracy in complex samples.

Electrochemical nanoplatforms are another important approach and these systems use materials such as graphene and carbon nanotubes. These materials are attached to electrode surfaces and functionalized with molecules that recognize cancer stem cell markers (Khan et al., 2024). When the target binds to the surface, changes in electrical signals are observed and these changes can be measured easily. These platforms provide very high sensitivity and can detect markers at very low concentrations. It is cost effective and suitable for clinical purpose. Hybrid and multifunctional platforms combine different detection methods and these systems improve both sensitivity and specificity. Magnetic plasmonic composites are one example. It allows capture of cancer stem cells and their optical detection in the same system. This reduces false results and improves accuracy. Nano metal organic frameworks are also used to target multiple markers at the same time and helps in addressing tumor heterogeneity (Cai et al., 2025; Deng et al., 2025).

Microfluidic platforms are also important in cancer stem cell detection. These systems use small channels for fluid handling. Nanostructured surfaces are used to improve cell capture and surfaces are functionalized with specific antibodies or aptamers. This allows efficient isolation of circulating cancer stem cells from blood. These platforms combine several steps in a single device to support rapid and non-invasive testing for early diagnosis and disease monitoring (Varillas et al., 2019; Wu et al., 2024). Recent developments also focus on signal amplification methods. Techniques such as enzyme based amplification and DNA based reactions are used to increase detection sensitivity. For example, magnetic nanoparticles with amplified DNA probes show much higher sensitivity compared to traditional methods. This helps in detecting very rare cancer stem cells (Wang et al., 2024). Overall, nanomaterial based platforms provide high throughput and sensitive detection of cancer stem cell markers. It helps in overcoming challenges related to low cell number and heterogeneity. However, issues related to biocompatibility and standardization still remain. Clinical application also requires further validation and these platforms have strong potential in personalized cancer diagnosis.

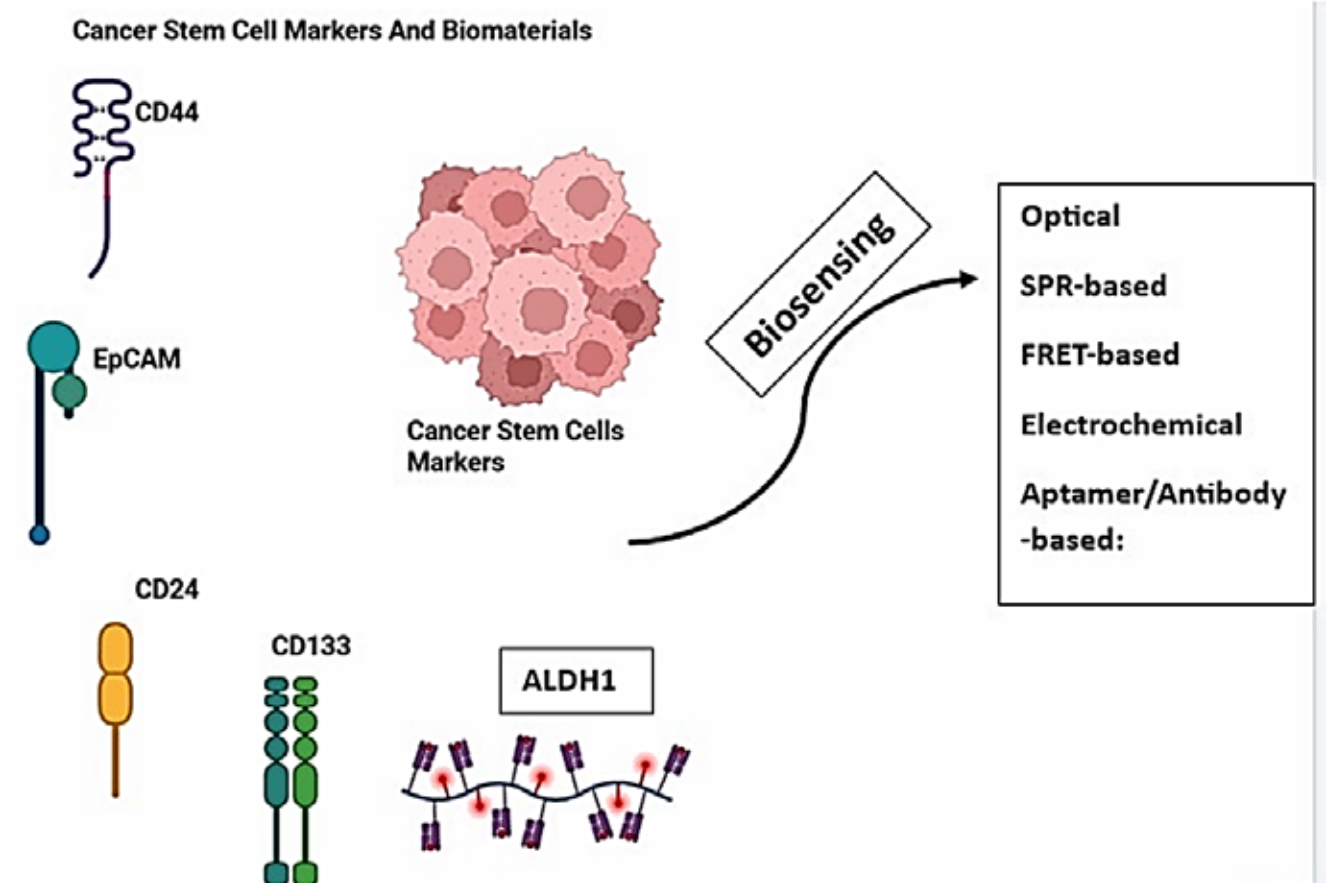

Figure 1: Key CSC markers such as CD44, EpCAM, CD24, CD133, and ALDH1 are targeted using biomaterial-based platforms for detection of cancer stem cells. The figure also highlights major biosensing approaches including optical methods, surface plasmon resonance (SPR), fluorescence resonance energy transfer (FRET), electrochemical detection, and aptamer or antibody-based techniques used for sensitive and specific identification of CSCs.

Table 1: Nanomaterial-Based Biosensing Strategies for Cancer Stem Cell Detection

Biosensing Strategy	Principle	Nanomaterials	Target Markers	Key Advantages	Clinical Use
Optical Biosensors	Detect changes in light absorption, emission, or scattering	Quantum dots, upconversion nanoparticles (UCNPs), gold nanoparticles	CD44, CD133, ALDH1	High sensitivity; multiplex detection; real-time imaging	Early diagnosis; point-of-care testing
Colorimetric Sensors	Visual color change from nanoparticle aggregation or dispersal	Gold nanoparticles	CSC surface markers	Rapid; simple; low cost	Point-of-care diagnostics
SPR-Based Sensors	Measure refractive index changes on a metal surface	Gold-coated chips; nanostructured surfaces	CD44, CD133	Label-free; real-time detection; kinetic analysis	Liquid biopsy; CSC quantification
FRET-Based Sensors	Energy transfer between donor and acceptor fluorophores	Quantum dots; graphene oxide	Various CSC markers	Single-cell sensitivity; high specificity	Cellular-level CSC detection
	Detect changes in current, voltage, or impedance	Graphene; carbon nanotubes; metal nanostructures	Multiple CSC markers	Femtomolar sensitivity; quantitative; scalable	Point-of-care and clinical diagnostics

Aptamer-Based Sensors	DNA/RNA aptamers bind to specific CSC markers	Aptamer-functionalized nanoparticles	CD133 and others	High specificity; stable; easy to modify	Targeted CSC capture and detection
Antibody-Based Sensors	Antibody-antigen interaction	Antibody-coated electrodes and nanoparticles	CD44, CD133, EpCAM	High binding affinity; clinically validated	Standard diagnostic use
Magnetic Nanoparticle Systems	Magnetic separation followed by detection	Magnetic nanoparticles (MNPs)	CD133	Efficient enrichment of rare CSCs	Liquid biopsy; sample preparation
Signal Amplification	Enhance signal from low-abundance targets	Rolling circle amplification; enzymatic methods	CSC markers (various)	Ultra-high sensitivity; detects rare cells	Early-stage cancer detection; MRD monitoring

5. Biosensing Strategies for CSC Marker Detection

Biosensing methods for cancer stem cell markers use nanomaterials for biomolecular recognition elements. These methods allow for highly sensitivity and multiplexed detection. The key strategies include optical and electrochemical methods. These techniques detect rare CSCs in circulating tumor cells or biofluids. This supports early cancer diagnosis and real-time disease monitoring (Tang et al., 2020; Wang et al., 2024). Optical biosensors detect CSC markers with light. Fluorescence-based systems use quantum dots and also use upconversion nanoparticles. It detects multiple markers like CD44 and CD133 to provide qualitative and quantitative data (Juzenas et al., 2011). Quantum dots have narrow emission spectra and high photostability. This enables simultaneous tracking of markers. Upconversion nanoparticles reduce background autofluorescence for high-contrast detection in complex samples. Colorimetric platforms use gold nanoparticles and produce visible signals through aggregation. It produces signals through dispersion to yields rapid and interpretable outputs (Yang et al., 2022). These are ideal for point-of-care settings.

Surface plasmon resonance biosensors monitor refractive index changes. These changes happen on a metallic surface and result from CSC marker binding (Nguyen et al., 2015). SPR platforms enable real-time label-free detection to support kinetic investigations. Gold-coated SPR chips use anti-CD44 antibodies and anti-CD133 antibodies. It captures CSCs from liquid biopsies (Sun et al., 2024b). Binding causes a shift in the resonance angle and is proportional to CSC concentration. Advanced SPR uses nanostructured surfaces to boost sensitivity and enhances detection of rare CSCs. FRET-based sensors use energy transfer between fluorophores. A donor and an acceptor are involved. Nanomaterials like quantum dots act as donors. Dyes or small molecules function as acceptors (Xu et al., 2010). CSC-specific ligand binding causes conformational changes to affect FRET efficiency. This generates a detectable signal and has high sensitivity. It discerns single-cell differences in marker expression to enables accurate characterization of heterogeneous CSCs.

Electrochemical biosensing detects markers through electrical changes at functionalized electrodes. Common materials like graphene, carbon nanotubes, and metallic nanostructures enhance electron transfer and increase surface area for marker binding (Kuswandi et al., 2025; Zhu, 2017). CSC-specific antibodies are immobilized on electrodes and aptamers are also immobilized. Target binding yields measurable electrochemical responses. Methods like differential pulse voltammetry provide quantitative measurements and achieves femtomolar sensitivity. Multiplexed platforms detect various CSC markers simultaneously and improve accuracy in evaluating tumor heterogeneity. Aptamer and antibody biosensors use high-specificity molecular recognition. Aptamers are single-stranded DNA or RNA sequences for target binding. It offers benefits like small size and chemical stability to easily modify. Antibody-functionalized platforms have high binding affinity to established clinical relevance. Both strategies integrate with optical systems, electrochemical systems, and microfluidic systems to enables ultrasensitive detection. For example aptamer-functionalized magnetic nanoparticles capture CD133-positive CSCs from blood samples (Fu and Xiang, 2020; Poonaki et al., 2022). Electrochemical readouts facilitate rapid quantification. Signal amplification techniques are vital to enhance sensitivity in CSC detection. Approaches such as rolling circle amplification, hybridization chain reaction, and enzyme-assisted amplification can be incorporated into biosensors. It boosts the detectable signal from rare CSCs.

For example, rolling circle amplification integrates with magnetic nanoparticle sensors. This allows CSC detection at low concentrations on few cells per milliliter (Ding et al., 2013; He et al., 2019). This makes it possible to monitor minimal residual disease to monitor at early-stage tumors.

6. Surface Engineering and Functionalization Techniques

The performance of cancer stem cell detection platforms depends on surface engineering and functionalization of nanomaterials. These processes control target binding, specificity, and signal generation. Surface engineering involves modifying physical and chemical properties of nanoparticles, electrodes, and microfluidic devices. This improves the capture and detection of cancer stem cells (Bargahi et al., 2022; Huang et al., 2023). Advanced approaches include nanostructuring and use of multifunctional coatings. These methods improve selectivity and performance under biological conditions. Covalent functionalization is a widely used method. It provides stable attachment of targeting molecules to surfaces. Techniques such as EDC NHS coupling and click chemistry are commonly used. These methods attach antibodies, aptamers, or peptides to nanomaterials. This ensures strong binding and reduces loss of ligands during experiments. For example, anti CD44 antibodies on gold nanoparticles help in selective capture of cancer stem cells. Dual targeting using aptamers can detect markers such as CD133 and ALDH1 at the same time (Huang et al., 2019; Subramanian et al., 2016). Non covalent functionalization is also used in some platforms. This method allows flexible and reversible attachment of molecules. It helps in maintaining the biological activity of ligands. Common methods include physical adsorption and electrostatic interaction. These are often used with materials such as graphene and carbon nanotubes. Aptamers can bind to these surfaces and still maintain their structure for target recognition. This method is useful in systems where ligands need to be replaced or reused. Polymeric and biomimetic coatings improve stability and compatibility. Materials such as polyethylene glycol and polydopamine reduce non-specific binding. These coatings also improve performance in biological samples. Biomimetic coatings derived from cell membranes help in better interaction with target cells. They also reduce immune response. These features improve the capture of cancer stem cells in complex samples (Omidian and Wilson, 2024; Ren et al., 2025; Savari et al., 2025).

Nanostructuring of surfaces further improves detection efficiency. Structures such as nanofibers and nanopillars increase surface area. This allows more ligands to attach to the surface. It also improves interaction with cell membranes. These structures help in capturing rare cancer stem cells more effectively. Hierarchical designs combine micro and nanoscale features. This improves stability and reduces cell loss during flow based analysis. Multifunctional surface engineering combines different properties in one system. For example, magnetic plasmonic nanoparticles can capture and detect cells in a single step. These systems improve sensitivity and reduce assay time. Surfaces with multiple ligands can target different cancer stem cell markers. This helps in better identification of diverse cell populations (Rodriguez-Nieves et al., 2025; Usman et al., 2023). Advanced methods such as bioorthogonal reactions allow fast and specific attachment of ligands. They work under mild conditions and preserve ligand activity. Stimuli responsive coatings are another approach. These coatings respond to changes in pH or enzymes. This helps in controlled detection and signal improvement. Overall, surface engineering plays a key role in cancer stem cell detection. Proper design improves binding efficiency and detection accuracy. These strategies help in overcoming challenges such as low cell number and heterogeneity. They also support the development of reliable diagnostic tools for clinical use.

7. Challenges and Limitations

Biomaterial based platforms offer many advantages for early detection of cancer stem cells. However, several challenges limit their use in clinical practice. One major issue is the very low number of cancer stem cells in patient samples. These cells are often less than 0.1 percent of the total cell population. This makes their detection very difficult (Hakala et al., 2025). Even with specific ligands such as antibodies or aptamers, non-specific binding can occur. This can lead to false positive results and reduce accuracy. Another challenge is the heterogeneity of cancer stem cells. These cells express different markers such as CD44, CD133, ALDH1, and EpCAM. The expression varies with tumor type and stage. Platforms designed for a limited number of markers may miss other important cell populations. Multiplex detection can improve this issue. However, adding multiple ligands increases design complexity. It can also reduce binding efficiency due to competition between ligands. Surface fouling is another important problem. Proteins and other components in biological samples can stick to nanomaterial surfaces. This blocks the active sites and reduces detection sensitivity. Anti fouling coatings can help reduce this problem. However, these coatings may affect ligand

activity and binding strength. Careful optimization is required for each system. Biocompatibility and stability of nanomaterials are also major concerns. Some materials may release toxic substances or degrade in biological conditions. This can affect both safety and performance. In addition, it is difficult to maintain consistency during large scale production. Small changes in particle size or ligand density can affect detection results. This creates problems in reproducibility between batches. Another limitation is the need for advanced instruments. Many detection platforms require specialized equipment such as fluorescence systems or electrochemical devices. These tools are not always available in clinical settings. Microfluidic systems show promise but they require precise handling. This limits their widespread use. Regulatory approval is also a major challenge. Nanomaterial based platforms require detailed safety and performance evaluation. There is also a lack of standard protocols for sample preparation and detection methods. This makes comparison between studies difficult. It also delays approval for clinical use.

8. Conclusion

Biomaterial assisted platforms are useful for early detection of cancer stem cells. These cells are rare and show high variation. They play an important role in tumor growth and therapy resistance. Advanced surface engineering methods improve detection performance. These include ligand immobilization and antifouling coatings. Nanostructuring and multifunctional designs also enhance detection. These approaches help in identifying markers such as CD44, CD133, ALDH1, and EpCAM with high sensitivity. Several challenges still need to be addressed. These include low number of cancer stem cells and their heterogeneity. Surface fouling and material stability also affect performance. Integration of these platforms into clinical use is another limitation. Proper optimization is required to improve reproducibility and reliability. These platforms have strong potential for early cancer diagnosis. They can also support personalized treatment strategies.

Declarations

Ethics approval statement

Not applicable

Consent to participate

Not applicable

Consent to publish

Not applicable

Data Availability Statement

The data are available from the corresponding author upon reasonable request

Competing Interests

The authors declare that they have no conflict of interest

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References

1. Bargahi, N., Ghasemali, S., Jahandar-Lashaki, S., Nazari, A., 2022. Recent advances for cancer detection and treatment by microfluidic technology, review and update. Biol. Proced. Online 24, 5. https://doi.org/10.1186/s12575-022-00166-y
2. Cai, M., Yang, Y., Kong, J., Zhang, Y., Li, S., Zhang, H., Xv, X., Ni, J., Yin, X., 2025. Nanoscale metal-organic frameworks as a versatile platform for synergistic combination tumor therapy. J. Nanobiotechnology 23, 601. https://doi.org/10.1186/s12951-025-03625-2
3. Chen, S., Song, X., Chen, Z., Li, X., Li, M., Liu, H., Li, J., 2013. CD133 Expression and the Prognosis of Colorectal Cancer: A Systematic Review and Meta-Analysis. PLoS One 8, e56380. https://doi.org/10.1371/journal.pone.0056380
4. Deng, X., Liu, X., Zhao, L., 2025. Multifunctional nanoplatforms for tumor microenvironment remodeling: Toward precision and intelligent cancer therapy. Mater. Today Bio 35, 102385. https://doi.org/10.1016/j.mtbio.2025.102385
5. Ding, C., Wang, N., Zhang, J., Wang, Z., 2013. Rolling circle amplification combined with nanoparticle aggregates for highly sensitive identification of DNA and cancercells. Biosens. Bioelectron. 42, 486–491. https://doi.org/10.1016/j.bios.2012.10.015
6. Ellis, G.A., Dean, S.N., Walper, S.A., Medintz, I.L., 2020. Quantum Dots and Gold Nanoparticles as Scaffolds for Enzymatic Enhancement: Recent Advances and the Influence of Nanoparticle Size. Catalysts 10, 83. https://doi.org/10.3390/catal10010083
7. Fu, Z., Xiang, J., 2020. Aptamer-Functionalized Nanoparticles in Targeted Delivery and Cancer Therapy. Int. J. Mol. Sci. 21, 9123. https://doi.org/10.3390/ijms21239123
8. Grover, R., Drall, S., Poonia, N., Kumar Jain, G., Aggarwal,

G., Lather, V., Kesharwani, P., Pandita, D., Goyal, R.K., 2023. CD44 and CD133 aptamer directed nanocarriers for cancer stem cells targeting. Eur. Polym. J. 183, 111770. https://doi.org/10.1016/j.eurpolymj.2022.111770

9. Guttenplan, A.P.M., Tahmasebi Birgani, Z., Giselbrecht, S., Truckenmüller, R.K., Habibović, P., 2021. Chips for Biomaterials and Biomaterials for Chips: Recent Advances at the Interface between Microfabrication and Biomaterials Research. Adv. Healthc. Mater. 10. https://doi.org/10.1002/adhm.202100371
10. Hakala, S., Hämäläinen, A., Sandelin, S., Giannareas, N., Närvä, E., 2025. Detection of Cancer Stem Cells from Patient Samples. Cells 14, 148. https://doi.org/10.3390/cells14020148
11. Han, D., Ren, X.-H., Liao, X.-R., He, X.-Y., Guo, T., Chen, X.-S., Pang, X., Cheng, S.-X., 2023. A Multiple Targeting Nanoprobe for Identifying Cancer Metastatic Sites Based on Detection of Various mRNAs in Circulating Tumor Cells. Nano Lett. 23, 3678–3686. https://doi.org/10.1021/acs.nanolett.2c04643
12. He, Y., Chen, S., Huang, L., Wang, Z., Wu, Y., Fu, F., 2019. Combination of Magnetic-Beads-Based Multiple Metal Nanoparticles Labeling with Hybridization Chain Reaction Amplification for Simultaneous Detection of Multiple Cancer Cells with Inductively Coupled Plasma Mass Spectrometry. Anal. Chem. 91, 1171–1177. https://doi.org/10.1021/acs.analchem.8b05085
13. Huang, P., Wang, C., Deng, H., Zhou, Y., Chen, X., 2023. Surface Engineering of Nanoparticles toward Cancer Theranostics. Acc. Chem. Res. 56, 1766–1779. https://doi.org/10.1021/acs.accounts.3c00122
14. Huang, T., Song, X., Xu, D., Tiek, D., Goenka, A., Wu, B., Sastry, N., Hu, B., Cheng, S.-Y., 2020. Stem cell programs in cancer initiation, progression, and therapy resistance. Theranostics 10, 8721–8743. https://doi.org/10.7150/thno.41648
15. Huang, X., Wan, J., Leng, D., Zhang, Y., Yang, S., 2019. Dualtargeting nanomicelles with CD133 and CD44 aptamers for enhanced delivery of gefitinib to two populations of lung cancerinitiating cells. Exp. Ther. Med. https://doi.org/10.3892/etm.2019.8220
16. Ju, H., Shim, Y., Arumugam, P., Song, J.M., 2016. Crosstalk-eliminated quantitative determination of aflatoxin B1-induced hepatocellular cancer stem cells based on concurrent monitoring of CD133, CD44, and aldehyde dehydrogenase1. Toxicol. Lett. 243, 31–39. https://doi.org/10.1016/j.toxlet.2015.12.006
17. Juzenas, P., Steponkiene, Kavaliauskiene, S., Purviniene, Rotomskis, 2011. Quantum dots affect expression of CD133 surface antigen in melanoma cells. Int. J. Nanomedicine 2437. https://doi.org/10.2147/IJN.S24477
18. Kashyap, V., Rezende, N.C., Scotland, K.B., Shaffer, S.M., Persson, J.L., Gudas, L.J., Mongan, N.P., 2009. Regulation of Stem Cell Pluripotency and Differentiation Involves a Mutual Regulatory Circuit of the Nanog, OCT4, and SOX2 Pluripotency Transcription Factors With Polycomb Repressive Complexes and Stem Cell microRNAs. Stem Cells Dev. 18, 1093–1108. https://doi.org/10.1089/scd.2009.0113
19. Khan, M.Z., Tahir, D., Asim, M., Israr, M., Haider, A., Xu, D.D., 2024. Revolutionizing Cancer Care: Advances in Carbon-Based Materials for Diagnosis and Treatment. Cureus. https://doi.org/10.7759/cureus.52511
20. Kim, C.-D., Koo, K.-M., Kim, H.-J., Kim, T.-H., 2024. Recent Advances in Nanomaterials for Modulation of Stem Cell Differentiation and Its Therapeutic Applications. Biosensors (Basel). 14, 407. https://doi.org/10.3390/bios14080407
21. Kuswandi, B., Amalia, R., Pitaloka, D.A.E., Murti, B.T., Hidayat, M.A., 2025. Electrochemical nanobiosensors for low-cost clinical diagnosis. Int. J. Electrochem. Sci. 20, 101205. https://doi.org/10.1016/j.ijoes.2025.101205
22. Liang, L., Kaufmann, A.M., 2023. The Significance of Cancer Stem Cells and Epithelial–Mesenchymal Transition in Metastasis and Anti-Cancer Therapy. Int. J. Mol. Sci. 24, 2555. https://doi.org/10.3390/ijms24032555
23. Liang, S., Li, C., Zhang, C., Chen, Y., Xu, L., Bao, C., Wang, X., liu, G., zhang, F., Cui, D., 2015. CD44v6 Monoclonal Antibody-Conjugated Gold Nanostars for Targeted Photoacoustic Imaging and Plasmonic Photothermal Therapy of Gastric Cancer Stem-like Cells. Theranostics 5, 970–984. https://doi.org/10.7150/thno.11632
24. Liu, Y., Yang, M., Luo, J., Zhou, H., 2020. Radiotherapy targeting cancer stem cells "awakens" them to induce tumour relapse and metastasis in oral cancer. Int. J. Oral Sci. 12, 19. https://doi.org/10.1038/s41368-020-00087-0
25. Mir, Gh.J., Manzoor, I., Islam, A. ul, Ganie, S.A., Hamid, R., 2024. Cancer Stem Cells as Promising Nanotherapeutic Targets, in: Personalized and Precision Nanomedicine for Cancer Treatment. Springer Nature Singapore, Singapore, pp. 27–68. https://doi.org/10.1007/978-981-97-3545-7_4
26. Moitra, K., Lou, H., Dean, M., 2011. Multidrug Efflux Pumps and Cancer Stem Cells: Insights Into Multidrug Resistance and Therapeutic Development. Clin. Pharmacol. Ther. 89, 491–502. https://doi.org/10.1038/clpt.2011.14
27. Nguyen, H., Park, J., Kang, S., Kim, M., 2015. Surface Plasmon Resonance: A Versatile Technique for Biosensor Applications. Sensors 15, 10481–10510. https://doi.org/10.3390/s150510481
28. Omidian, H., Wilson, R.L., 2024. Polydopamine Applications in Biomedicine and Environmental Science. Materials 17, 3916. https://doi.org/10.3390/ma17163916

29. Patil, T., Rohiwal, S.S., Tiwari, A.P., 2023. Stem Cells: Therapeutic Implications in Chemotherapy and Radiotherapy Resistance in Cancer Therapy. Curr. Stem Cell Res. Ther. 18, 750–765. https://doi.org/10.2174/1574888X17666221003125208
30. Poonaki, E., Nickel, A.-C., Shafiee Ardestani, M., Rademacher, L., Kaul, M., Apartsin, E., Meuth, S.G., Gorji, A., Janiak, C., Kahlert, U.D., 2022. CD133-Functionalized Gold Nanoparticles as a Carrier Platform for Telaglenastat (CB-839) against Tumor Stem Cells. Int. J. Mol. Sci. 23, 5479. https://doi.org/10.3390/ijms23105479
31. Ren, X., Zhang, B., Guo, G., Yu, T., Yang, L., Li, G., Luo, R., Wang, Y., 2025. Research and prospects of strategies for surface-modified coatings on blood-contacting materials. Med-X 3, 14. https://doi.org/10.1007/s44258-025-00056-4
32. Rodriguez-Nieves, A.L., Shah, S., Taylor, M.L., Alle, M., Huang, X., 2025. Magnetic–Plasmonic Core–Shell Nanoparticles: Properties, Synthesis and Applications for Cancer Detection and Treatment. Nanomaterials 15, 264. https://doi.org/10.3390/nano15040264
33. Savari, A., Tahir, B.S., Ahmed, A.M., Foroutan, R., Ramavandi, B., 2025. Application of polydopamine-based materials for advanced techniques in water and wastewater treatment. Results Chem. 15, 102256. https://doi.org/10.1016/j.rechem.2025.102256
34. Schulze, K., Gasch, C., Staufer, K., Nashan, B., Lohse, A.W., Pantel, K., Riethdorf, S., Wege, H., 2013. Presence of EpCAM-positive circulating tumor cells as biomarker for systemic disease strongly correlates to survival in patients with hepatocellular carcinoma. Int. J. Cancer 133, 2165–2171. https://doi.org/10.1002/ijc.28230
35. Senbanjo, L.T., Chellaiah, M.A., 2017. CD44: A Multifunctional Cell Surface Adhesion Receptor Is a Regulator of Progression and Metastasis of Cancer Cells. Front. Cell Dev. Biol. 5. https://doi.org/10.3389/fcell.2017.00018
36. Singh, A.K., Arya, R.K., Maheshwari, S., Singh, A., Meena, S., Pandey, P., Dormond, O., Datta, D., 2015. Tumor heterogeneity and cancer stem cell paradigm: Updates in concept, controversies and clinical relevance. Int. J. Cancer 136, 1991–2000. https://doi.org/10.1002/ijc.28804
37. Subramanian, N., Akilandeswari, B., Bhutra, A., Alameen, M., Vetrivel, U., Khetan, V., Kanwar, R.K., Kanwar, J.R., Krishnakumar, S., 2016. Targeting CD44, ABCG2 and CD133 markers using aptamers: in silico analysis of CD133 extracellular domain 2 and its aptamer. RSC Adv. 6, 32115–32123. https://doi.org/10.1039/C5RA27072C
38. Sun, S., Yang, Q., Jiang, D., Zhang, Y., 2024a. Nanobiotechnology augmented cancer stem cell guided management of cancer: liquid-biopsy, imaging, and treatment. J. Nanobiotechnology 22, 176. https://doi.org/10.1186/s12951-024-02432-5
39. Sun, S., Yang, Q., Jiang, D., Zhang, Y., 2024b. Nanobiotechnology augmented cancer stem cell guided management of cancer: liquid-biopsy, imaging, and treatment. J. Nanobiotechnology 22, 176. https://doi.org/10.1186/s12951-024-02432-5
40. Tang, Y., Wang, S., Jiang, J., Liang, X., 2015. Links between cancer stem cells and epithelial– mesenchymal transition. Onco. Targets. Ther. 2973. https://doi.org/10.2147/OTT.S91863
41. Tang, Z., Huang, J., He, H., Ma, C., Wang, K., 2020. Contributing to liquid biopsy: Optical and electrochemical methods in cancer biomarker analysis. Coord. Chem. Rev. 415, 213317. https://doi.org/10.1016/j.ccr.2020.213317
42. Tiwari, H., Rai, N., Singh, S., Gupta, P., Verma, A., Singh, A.K., Kajal, Salvi, P., Singh, S.K., Gautam, V., 2023. Recent Advances in Nanomaterials-Based Targeted Drug Delivery for Preclinical Cancer Diagnosis and Therapeutics. Bioengineering 10, 760. https://doi.org/10.3390/bioengineering10070760
43. Usman, F., Ghazali, K.H., Muda, R., Johari, N.H., Dennis, J.O., Tamam, N., Sulieman, A., Ji, Y., 2023. Magnetoresistance and magneto-plasmonic sensors for the detection of cancer biomarkers: A bibliometric analysis and recent advances. Sensors and Actuators Reports 6, 100172. https://doi.org/10.1016/j.snr.2023.100172
44. Varillas, J.I., Zhang, J., Chen, K., Barnes, I.I., Liu, C., George, T.J., Fan, Z.H., 2019. Microfluidic Isolation of Circulating Tumor Cells and Cancer Stem-Like Cells from Patients with Pancreatic Ductal Adenocarcinoma. Theranostics 9, 1417–1425. https://doi.org/10.7150/thno.28745
45. Wakamatsu, Y., Sakamoto, N., Oo, H.Z., Naito, Y., Uraoka, N., Anami, K., Sentani, K., Oue, N., Yasui, W., 2012. Expression of cancer stem cell markers ALDH1, CD44 and CD133 in primary tumor and lymph node metastasis of gastric cancer. Pathol. Int. 62, 112–119. https://doi.org/10.1111/j.1440-1827.2011.02760.x
46. Wang, M., Jin, L., Hang-Mei Leung, P., Wang-Ngai Chow, F., Zhao, X., Chen, H., Pan, W., Liu, H., Li, S., 2024. Advancements in magnetic nanoparticle-based biosensors for point-of-care testing. Front. Bioeng. Biotechnol. 12. https://doi.org/10.3389/fbioe.2024.1393789
47. Wu, F., Kong, X., Liu, Y., Wang, S., Chen, Z., Hou, X., 2024. Microfluidic-based isolation of circulating tumor cells with high-efficiency and high-purity. Chinese Chemical Letters 35, 109754. https://doi.org/10.1016/j.cclet.2024.109754
48. Xu, H., Huang, X., Zhang, W., Chen, G., Zhu, W., Zhong, X., 2010. Quantum Dots Acting as Energy Acceptors with Organic Dyes as Donors in Solution. ChemPhysChem 11, 3167–3171. https://doi.org/10.1002/cphc.201000287
49. Xu, J., Müller, S., Nannapaneni, S., Pan, L., Wang, Y., Peng, X., Wang, D., Tighiouart, M., Chen, Z., Saba, N.F., Beitler, J.J., Shin,

D.M., Chen, Z. (Georgia), 2012. Comparison of quantum dot technology with conventional immunohistochemistry in examining aldehyde dehydrogenase 1A1 as a potential biomarker for lymph node metastasis of head and neck cancer. Eur. J. Cancer 48, 1682–1691. https://doi.org/10.1016/j.ejca.2011.12.029

50. Yang, J., Wang, X., Sun, Y., Chen, B., Hu, F., Guo, C., Yang, T., 2022. Recent Advances in Colorimetric Sensors Based on Gold Nanoparticles for Pathogen Detection. Biosensors (Basel). 13, 29. https://doi.org/10.3390/bios13010029
51. Yun, Y., Kim, S., Lee, S.-N., Cho, H.-Y., Choi, J.-W., 2024. Nanomaterial-based detection of circulating tumor cells and circulating cancer stem cells for cancer immunotherapy. Nano Converg. 11, 56. https://doi.org/10.1186/s40580-024-00466-x
52. Zhao, W., Zang, C., Zhang, T., Li, J., Liu, R., Feng, F., Lv, Q., Zheng, L., Tian, J., Sun, C., 2018. Clinicopathological characteristics and prognostic value of the cancer stem cell marker ALDH1 in ovarian cancer: a meta-analysis. Onco. Targets. Ther. Volume 11, 1821–1831. https://doi.org/10.2147/OTT.S160207
53. Zhu, Z., 2017. An Overview of Carbon Nanotubes and Graphene for Biosensing Applications. Nanomicro Lett. 9, 25. https://doi.org/10.1007/s40820-017-0128-6
54. Zhu, Z., Yang, C.J., 2017. Hydrogel Droplet Microfluidics for High-Throughput Single Molecule/Cell Analysis. Acc. Chem. Res. 50, 22–31. https://doi.org/10.1021/acs.accounts.6b00370