

Nanomaterial-Based Biosensors for Early Breast Cancer Detection: A Comprehensive Review of Technologies and Biomarkers

Ibtihal Riyadh Najeeb¹, Assist Prof. Saba Abd AL Mutleb Hamood², Baneen chasib gabal³, Narimann Neamah Hussein⁴

¹Department of pathological analyses, Collage of science, University of Kufa, Iraq.

²Department of Medical Physics, Faculty of Medical Sciences, Jabir Ibn Hayyan University for Medical and Pharmaceutical Sciences, Najaf, Iraq

³Department of pathological analyses, Faculty of Medical Sciences, Jabir Ibn Hayyan University for Medical and Pharmaceutical Sciences, Najaf, Iraq.

⁴Department of Medical Physics, Faculty of Medical Sciences, Jabir Ibn Hayyan University for Medical and Pharmaceutical Sciences, Najaf, Iraq.

ABSTRACT

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Nanomaterial based biosensor have emerged a promising approach that demonstrates great progress in the diagnosis of breast cancer with increased sensitivity and selectivity compared to conventional detection methods. These nanomaterials may allow for combinatorial detection capabilities that could provide simultaneous identification of multiple biomarkers in order to reach an accurate tumor classification, by using quantum dot imaging and carbon nanotube electrical sensing. However, this field faces challenges that must be addressed before widespread application of clinical. Key among these is the need to standardize methods and protocols to ensure reproducibility and minimize non-specific correlations. Furthermore, ensuring the nanomaterial's safety and biocompatibility, as well as the toxicity of a diagnostic methods, are essential elements for their success in future patient care.

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Corresponding Author:
Ibtihal Riyadh Najeeb

1. INTRODUCTION

In 2020, female breast cancer ranks fifth globally in terms of cancer death and is the primary cause of cancer incidence worldwide. Based on the expression of biomarkers including progesterone receptors (PR), human epidermal growth factor receptor 2 and estrogen receptors (ER), breast cancer can be divided into several subtypes. Decisions about systemic treatment for breast cancer also depend heavily on the examination of these biomarkers [1]. Nanotechnology has become one of the most significant fields in the development of novel treatment approaches for breast cancer in the past 20 years [4-6]. The use of nuclear medicine has proven its therapeutic effectiveness in treating various types of breast cancer tumors, and targeted drug delivery has been achieved through the study of different types of nanoparticles such as polymer nanoparticles, micelles, and carbon nanotubes. A tumor marker as the target molecule, a bioreceptor as the recognition element, and an appropriate biotransducer that is highly selective and affinity-oriented are the usual components of a cancer detection biosensor [7]. Numerous biosensing platforms, including physical, optical, and electrochemical biosensors, have been developed and used to detect the targeted biomarkers in order to get around the earlier challenges [8]. Nanomaterials can be used to create biosensing platforms with remarkable mechanical, optical, magnetic, and electrical characteristics. By expanding the transducing area of the sensors, nanomaterials can improve catalytic activity. Nanoparticles' electroactive qualities toward specific reactions have been extensively used in biosensing applications. When sample size is critical, nanoscale structures offer distinct advantages due to their enormous surface area-to-volume ratio, regular shape, and

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compact structure, making them suitable for use in biosensors [9]. However, to attain more specificity in biosensing, developments in nanomaterial biofunctionalization are essential. In order to provide particular recognition for biosensing, nanomaterials can be "decorated" with various (bio)receptors [10-15]. This comprehensive review paper describes Nanomaterial-based biosensors for early breast cancer detection.

2. TYPES OF NANOMATERIALS USED IN BIOSENSOR

Numerous nanomaterial kinds have been thoroughly investigated for the creation of biosensors to identify breast cancer biomarkers. The target biomarker, the intended sensing mechanism, and the particular needs of the biosensing platform are some of the variables that influence the choice of nanomaterials[16].

2.1. Carbon-based nanomaterials

Carbon-based nanomaterials, like carbon nanotubes, graphene and its derivatives, nanodiamonds, fullerenes, and other nanosized carbon allotropes, have been growing rapidly in recent years, leading to an exponential growth. Their large specific surface area, high electrical and thermal conductivity, special optical qualities, and superior mechanical properties are all attributed to their small size and comparable size to many basic biomolecules. A wide range of applications can be opened up due to the endless possibilities for modification and customization offered by carbon nanomaterials. Fullerene derivatives are used for solar energy scavenging, and graphene is widely used in flexible electronics. Molecular recognition capabilities have been incorporated into carbon nanotubes and graphene quantum dots have gained widespread usage for bio-imaging and sensing due to their photoluminescence properties. It has been proven that nanodiamonds are advantageous for nanoscale temperature sensing and super-resolution imaging[17-20] and figure1[21].

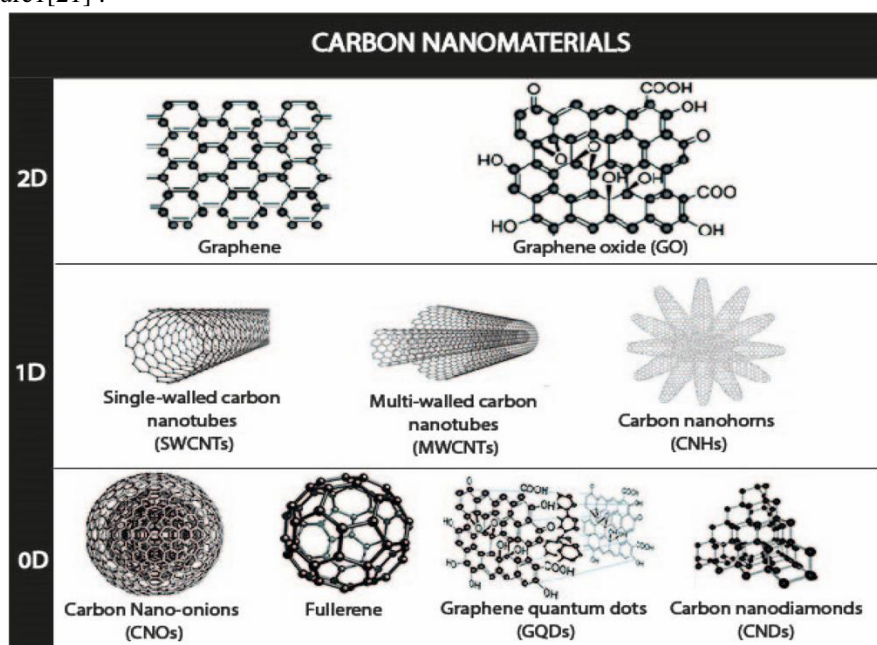


Figure 1: Carbon-based nanomaterials[21]

2.2. Nanoparticles

The physical properties of nanoparticles are unique. Gold nanoparticles (AuNPs), silver nanoparticles (AgNPs), palladium nanoparticles (PdNPs), and platinum nanoparticles (PtNPs) are widely used due to their excellent optical properties, This includes surface plasmonic resonance, which can be used for colorimetric detection or detection via surface-enhanced Raman scattering. [22–25].

2.3. Nanowires and nanotubes

Due to their one-dimensionality, nanowires and nanotubes have a unique function. Van Hove singularities are singularities in the electronic density of states that appear at specific energies when the diameter of a nanowire or nanotube decreases. These singularities are more similar to the case of molecules and atoms, but they appear to be very different from the case of crystalline solids or even two-dimensional systems. Thus, new quantum phenomena related to this distinctive 1-D density of states feature are seen in the limit of small diameters, The topics covered in this article include bismuth nanowires and single-wall carbon nanotubes. Generally, it is anticipated that a long thin nanowire [26] or a single wall nanotube constructed from a single atomic layer shell [27] will display significant quantum effects at small diameters. Because of their distinct electrical characteristics and high surface-to-volume ratios, semiconductor nanowires and nanotubes are ideal for detection, sensitive electrochemical detection methods are

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used; for example, nuclear silicon wires can be modified using components known to develop highly sensitive biosensors for detecting cancer biomarkers. [28,29].

2.4. Magnetic nanoparticles

Particles that can be controlled by magnetic fields are known as magnetic nanoparticles. These particles have a functional chemical coating on top of a core composed of magnetic materials including iron, nickel, and cobalt. Due to their superparamagnetic nature, magnetic nanoparticles lose their magnetization when exposed to a magnetic field. The presence of this feature makes particle aggregation less likely. The use of magnetic nanoparticles as MRI contrast agents is feasible due to their super paramagnetism and super ferromagnetism properties with respect to magnet moment in an applied magnetic field. Magnetic nanoparticles can be used for a variety of medical purposes, including treating hyperthermia, delivering medication for cancer treatment, bioseparation, gene transport, biosensors, protein purification, immunoassays, and cell labeling. Illustrates the good physical and chemical properties of magnetic nanoparticles, such as iron oxide nanoparticles, which are frequently employed for magnetic biosensing applications. To extract cancer biomarkers from complicated biological materials, they can be functionalized using certain ligands. Techniques such as magnetic relaxation can be used to quantify recorded biomarkers magnetic particle detection (MPD) or magnetic resonance imaging (MRI) [31–33].

3. PREPARATION NANOMATERIALS USED IN BIOSENSOR

The "top-down" approach, which restructures bulk materials to form nanomaterials, and the "bottom-up" approach, which assembles nanomaterials at the molecular level, are just two of the many methods and techniques [34] that have been developed and chosen for the preparation of nanomaterials [35]. Sol-gel, spinning, pyrolysis, biosynthesis, hydrothermal synthesis, chemical vapor deposition (CVD), and other processes are among them. Similar to this, a range of techniques like mechanical milling, lithography, laser ablation, sputtering, pyrolysis, and others are included in the top-down approach. This wide spectrum of approaches underlines the diversity, as well as complexity, of top-down and bottom-up strategies in nanomaterials synthesis. Advanced systematic and an investigation engineering of a metal oxide based nanoparticles (NRs, CNTs, QDs [quantum dots], composite nanodendrimers) might revolutionize biosensor technology. By exploring the synthesis and design, show figure 2[36].

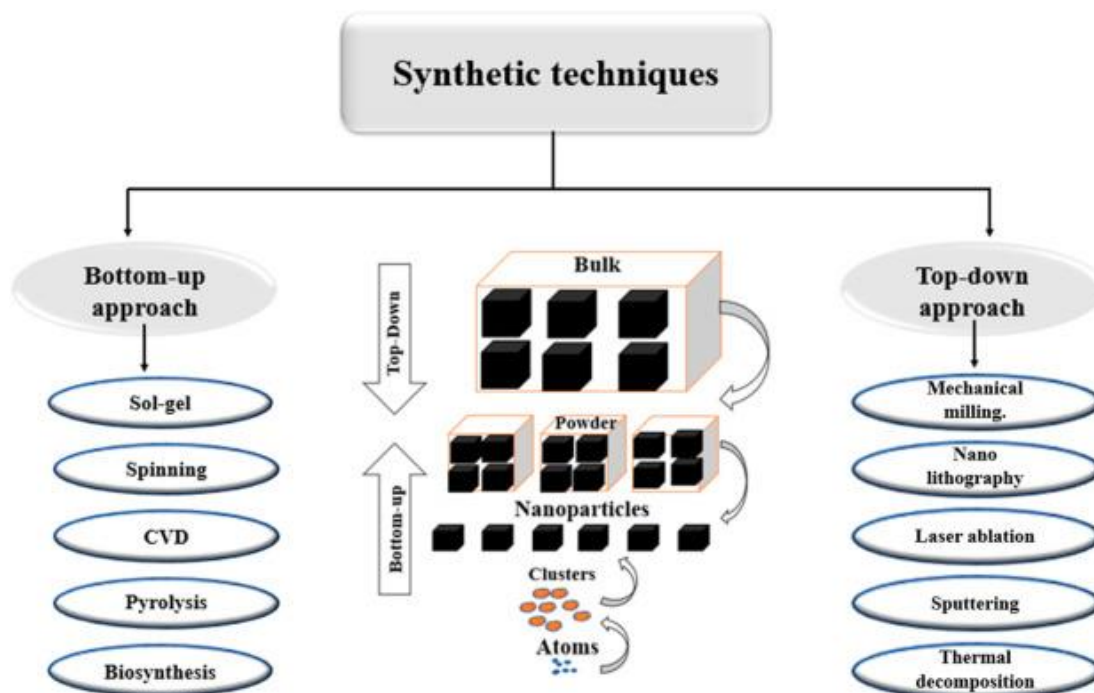


Figure 2: Preparation nanomaterials used in biosensor[36].

4. NANOSENSORS

Nanosensor: This refers to an electrical device which is fabricated at the nanoscale and proves data that can detect small changes in chemical or physical quantities, process data received from experiments. They are used to detect small changes in physical or chemical quantities, process the measurements taken and convert those into a signal. Nanosensors require the synthesis of materials, characterization of their properties and device fabrication. Nanosensors and their applications Nanosensors are used in diverse applications these days, from environmental monitoring to medical diagnostics[37]. Sensors classified based on Application: chemical sensors, deployable nanosensors, electrometers and biosensors. [38].

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4.1. Biosensor

To measure or investigate biochemical substances, a nanobiosensor is a tool used at the nanoscale level for analysis. A sensing element called a 'bio-receptor' is commonly used to detect and quantify analytes, and it is usually comprised of a sensing element called a 'bio-receptor' that interacts with the targeted analyte to create a detectable physical signal that can be converted and quantified using optical means. Methods that use electronic, thermal, or magnetic technology. The advancement of nanotechnology-based biosensors is rapid and they are being utilized extensively in a variety of sectors, such as analytical chemistry, biomedicine, environmental monitoring, and national security. Innovative nanomaterials are being designed and produced in large quantities for possible biosensing and theranostic uses, but their possible health concerns have not been thoroughly evaluated [39].

5. TYPES OF BIOSENSORS

- 5.1. Miniaturized biosensors that use magnetic resistance to detect micro magnetic and nanoparticles in microfluidic channels are a promising option for both size and sensitivity [43].
- 5.2. Thermal or calorimetric biosensors can be created by incorporating the biosensor materials previously mentioned into a physical transducer[43].
- 5.3. The acoustic surface wave device and quartz crystal scales are considered two types of electro-optical sensors are available, and the measurement of the resonant frequency of the electro-optical crystal changes as a result of mass changes in the crystal structure. These devices operate on this basis[43].
- 5.4. In optical biosensors, light sources and a set of optical components are used to help generate a light beam with specific characteristics and direct it towards a modulating agent, a modulating sensor head, and a photodetector. [43].
- 5.5. Electrochemical Biosensors: The benefits of using electrochemical biosensors are that they are easy to instrument, fast and highly sensitive in detecting bacteria. Electrodes made of carbon nanotube and graphene offer a great electrical conductivity and surface area where the biomolecules can be immobilized. Metallic nanoparticles incorporated in electrochemical sensors improve the electron transfer kinetics as well as increase the detection signals[43]

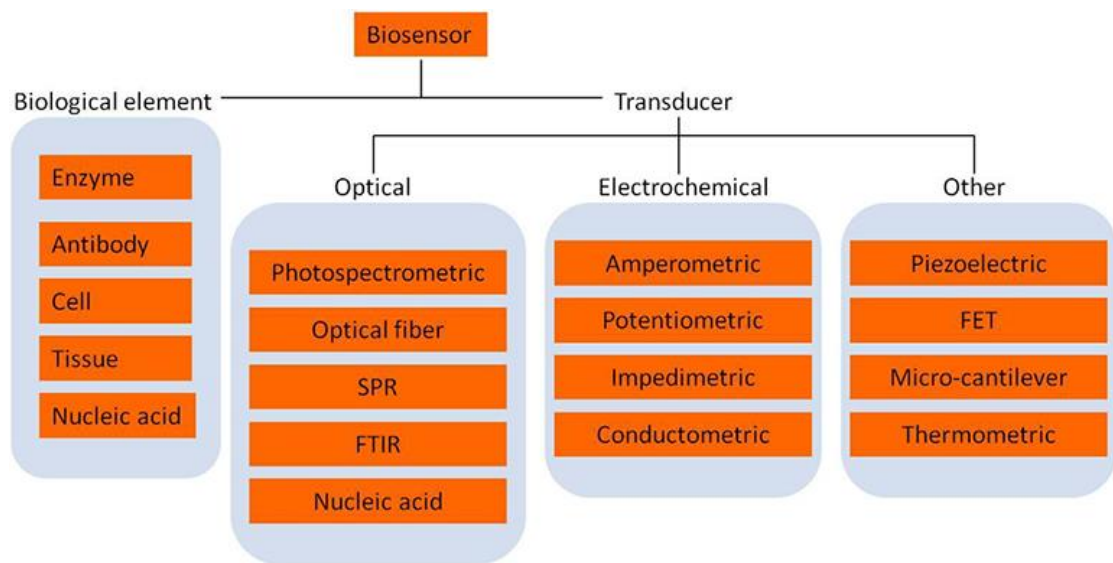


Figure 3 : Types of Biosensors[43]

6. FEATURES AND CATEGORIZATION OF BIOSENSORS

In order to accomplish the intended outcomes for the improvement of society's health, the biosensor prototype that has been built and prepared must have the following qualities.

6.1. Selectivity: Before building any biosensor, the major consideration in the mind of the designer is to think about the selectivity of the biosensor so that it can detect the required analytical materials are from samples containing either nearly identical or different analytical materials. /contaminants [44].

6.2. Reproducibility: It is extremely concerning if the biosensor can consistently yield the same results for repeated trials [45]. Currently, there is a great demand for biosensors with good repeatability quality. The results should be highly accurate and precise in addition to being repeatable; all of these characteristics make the biosensor more reliable[45].

6.3. Stability: The biosensor's commercial success is largely dependent on its stability. Age does cause the biosensor's signals to weaken, therefore this element requires additional thought and care [44]. Additionally, when the temperature rises, aging or instability accelerates; in other words, aging is directly correlated with temperature [44].

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6.4. Only biosensors with high sensitivity are given a high rating. During modern times, a ppm level is essential for detecting pollutants in the air, water, and soil, but in the medical field, it fluctuates between nanograms per milliliter and femtograms per milliliter [45].

7. WORKING PRINCIPLE OF BIOSENSORS

Depending on the particular design and detection method, biosensors for the identification of cancer biomarkers in human fluids function according to a variety of functioning principles. Nonetheless, the main idea is identifying the target of biomarker by the biological receptor, and this a recognition event's translation into a quantifiable indication[16].

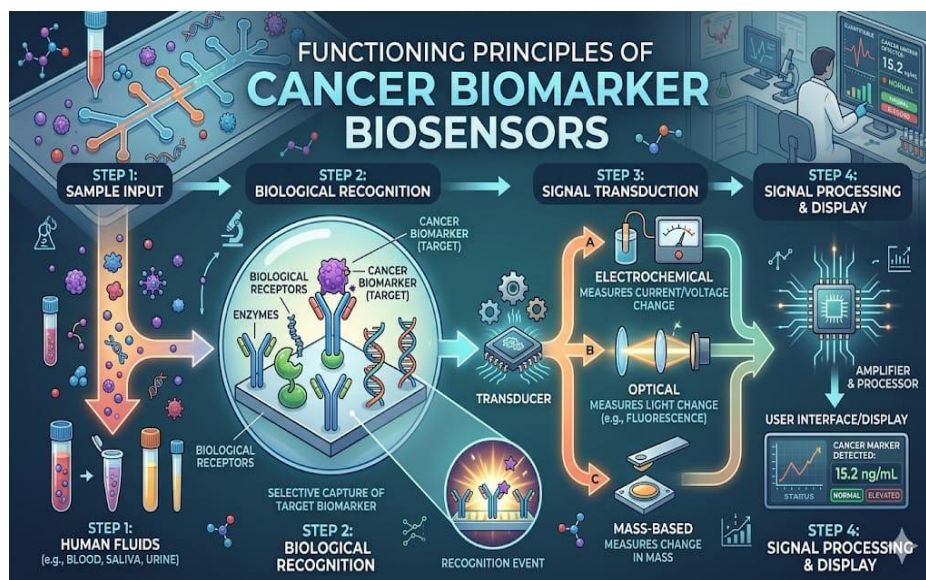


Figure 4 : Working principle of biosensors

8. BIOSENSOR IN THE DIAGNOSIS OF BREAST CANCER

The use of nanomaterial-based biosensors for early cancer detection, precise characterization, and tailored cancer treatment is a promising method. These biosensors use the special qualities of nanomaterials to identify particular cancer biomarkers with great selectivity and sensitivity. Certain cancer biomarkers Proteins, nucleic acids, or metabolites that suggest cancer may be present or progressing can be sensed with nanomaterial-based biosensors[46-49]. These biosensors employ nanomaterials like nanowires, nanoparticles or nanotubes that are afunctionalized with a recognition elements like aptamers, peptides or antibodies that bind to a target the biomarkers mentioned, above. A presence and concentration of the biomarkers are revealed through the detection and quantification of the signal produced by the binding event. For liquid biopsies, which include analyzing, urine, blood or other body fluids to find cancer the biomarkers, nanomaterial-based biosensors are very useful. Compared to typical tissue biopsies, liquid biopsies are non-invasive or minimally invasive and can provide real-time information regarding the genetic properties of the tumor, the response to treatment, and the development of drug resistance. allowing for the sensitive and precise identification of exosomes, cell-free DNA, circulating tumor cells (CTCs), and other components associated with cancer in liquid biopsies [50–54].

Multiple cancer biomarkers can be concurrently detected by nanomaterial-based biosensors, enabling a thorough evaluation of the illness. Biosensors can identify panels of biomarkers linked to various cancer kinds or particular molecular signatures by functionalizing various nanomaterials with particular recognition elements [55–58]. Multiplexed detection enables more accurate tumor characterization and classification, thus enhancing cancer diagnosis specificity and reliability. These refractive-oriented nanoparticles, such as a quantum dots [59], magnetic- nanoparticles [60] and carbon-nanotubes [61], can act as a contrast agent for cancer imaging and positioning. These nanoparticles functionalized with a specific label can attach to the target or receptor which can also be a cancer cell or tissue, and this representation enhances localization and causes accurate extra cellular or intracellular tumor imaging. Nanomaterial-based imaging techniques, such as surface-enhanced Raman scattering (SERS), magnetic resonance imaging (MRI), and fluorescence imaging, also enhance a sensitivity and specificity of cancer adagnosis by providing accurate a chemical information and spatial [62–64].

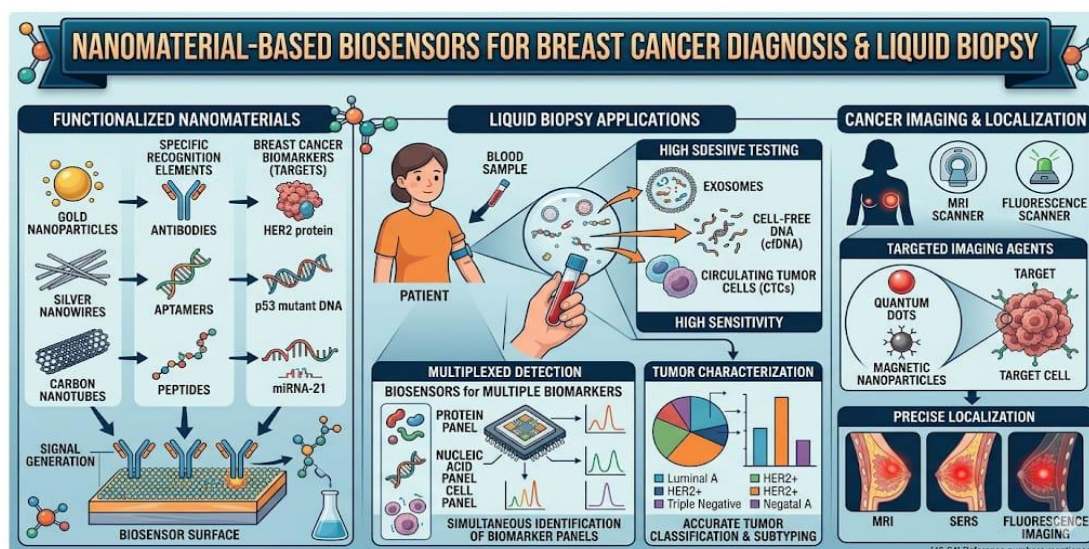


Figure 5: Biosensor in the diagnosis of breast cancer

9. CHALLENGES THE USE OF NANOMATERIAL-BASED BIOSENSORS

Nanomaterial-mediated biosensors ultimately hold considerable promise for the cancer biomarkers of detection, but more challenges must be addressed prior to their effective use. There is a crucial need for establishing-standardized methods and methodologies for nanomaterial-based biosensors to ensure inter- and intra-laboratory reproducibility of results in different research groups, as well as equivalency of clinical contexts. Biomarker detection is highly sensitive to sample preparation, assay settings and data analysis. Sensitive and specific detection of cancer biomarkers is important. Nanomaterial-based biosensors must be modified to achieve the proper sensitivity and specificity, preventing false-positive, as well as false-negative rates. Improving the sensing performance of biosensors is required to solve issues such as nonspecific a binding, interferent effects from changeable levels of target biomarker and complex biological matrices. Most importantly, the biomarker discovered by using these nanomaterial-based biosensors must be validated for reliable accuracy and clinical significance. All of the identified biomarkers need to be verified in large studies conducted on heterogeneous cohorts of patients to assess their clinical utility and prognostic impact. Also, to validate the reliability of biosensor-based detection and an accuracy and, it needs to be correlated with gold standard diagnostic methods. In addition, a close evaluation of the biocompatibility and possible toxicity of nanoscale materials used in biosensors is needed [16].

10. CONCLUSION

Substantive early breast cancer detection strategies based on integration of nanomaterials into biosensor technologies results demonstrated in this area a true breakthrough the fact that certain materials like carbon nanotubes or nuclear wires feature an enormous relative surface area to their volume offers the potential for superior sensitivity to biomarker concentrations as low as just a few copies can be detected using these methods and ultimately improves diagnostic accuracy but also enables a new generation of minimally invasive liquid biopsies enabling real time monitoring during treatment without painful surgical biopsy their ultimate success depends. This extensive characterization is necessary since non-specific binding and complex interactions with body fluids render much desired activity of nanomaterials a potential toxicity concern preventing patient safety.

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