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Gold Nanoparticles (Aunps)-Based Biosensors for Cancer Detection

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Abstract. Gold nanomaterials have shown unique advantages in constructing biosensors due to their special optical and electrochemical properties, and have been widely used. This paper investigates improved gold nanoparticles (AuNPs) applications in biosensors for early cancer detection, focusing on the use of AuNPs to improve diagnostic sensitivity and specificity. The introduction emphasizes the critical need for precise early detection technology that can improve cancer treatment outcomes. It describes several biosensing technologies, including aptasensors and microcantilever sensors, where they use AuNPs to improve cancer biomarker detection at low concentrations. Techniques like the green-synthesized AuNPs-based optical fiber ball resonator biosensor are praised for their biocompatibility and environmental benefits, as well as their superior diagnostic performance. Surface-enhanced Raman scattering (SERS) biosensors are also reviewed, demonstrating their capability for high-resolution, multiplexed imaging of cancer cells. This work emphasizes gold nanoparticles' great potential for transforming cancer diagnostics by improving the early detection capabilities of biosensors, which is critical for effective cancer management and therapy.

Keywords: AuNPs; Biosensors; Cancer; Detection.

1. Introduction

Cancer is one of the deadliest diseases in the world. Clinic data shows that it has high mortality rate and incidence, so early detection of cancer is significant for effective treatment. To realize early detection, the key is to detect biomarkers of cancer. Biomarkers of cancer are measurable substances, which includes proteins, genes, enzymes, hormones, DNA or other substances found in blood or other body fluids. They also indicate the development or spread of cancer. For example, PSA is the biomarker of prostate cancer, and CA-125 is biomarker of ovarian cancer. There are couples' common ways to detect these biomarkers, including blood test and imaging test. These methods can often be used individually or in combination to improve early diagnosis and treatment outcomes for cancer. However, some of these detection methods have limitations in sensitivity, specificity, accuracy and reaction time. As a result, new diagnostic techniques are desperately needed to overcome these obstacles.

Cancer detection has always been an issue bothering doctors from all parts of the world. Nevertheless, introducing nanoparticle into the realm has brought hope to totally change conventional ways of detection. Nanoparticles could play a significant role in drug transportation, generating images of lesion locations, and synthesizing vaccines. Some nanoparticles themselves own unique functions in treating diseases, such as reducing toxicity of pathogens and promoting the metabolism of human body. Some treatments aiming at suppressing and eliminating cancer have already shown promising results in clinical treatments. Several therapeutic nanoplatforms have been licensed for cancer treatment, such as liposomes, albumin nanoparticles, and polymer vesicles, and more therapeutic modalities are undergoing clinical trials, such as chemotherapy, hyperthermia, radiation therapy, gene or RNA interference (RNAi) therapy, and immunotherapy [1, 2]. In recent years, biosensor had been regarded as a viable technique to identify cancer biomarkers. Biosensors can transform a biological response into a calculated signal. The sensitivity of biosensors based on nanomaterial is outstanding, and they are able to detect cancer biomarkers at very low concentrations. The advantages of nanomaterials are significant, such as variable surface chemistry, exceptional chemical physicochemical properties, high sensitivity, high selectivity, rapid response, portability and cost-effectiveness. Therefore, nanomaterials can provide strong support for a wide range of detection.

For the past few years, biosensors that are developed based on gold nanoparticles (AuNPs) have influenced the field of biosensing greatly. AuNPs have certain advantages that makes it possible to shed light on new ways of detecting and analyzing certain biomolecules. Their high sensitivity is the reason why they are being frequently utilized in many early disease diagnoses, such as cancer detection. This feature originates from the collective oscillation of free electrons exposed to light and the great electric field enhancement, resulting in various light-matter interactions, such as local surface plasmon resonance (LSPR) and surface-enhanced Raman scattering [1]. These interactions can generate high absorption of lights of different frequencies, which can then be clearly distinguished by optical instruments and analyzed to lead to certain conclusions. Based on the formal discussion, it is not hard to draw to the conclusion that noble metal and cancer treatment stand a chance of combination, which would greatly enhance the chance of detecting and treating cancer successfully. This research will discuss the application of AuNPs-based biosensors for the detection of cancer. In the application process, the advantages and disadvantages of these sensors will also be discussed and analyzed.

2. AuNPs-based biosensing methods for detection of cancer

Two major biosensing techniques introduced include optical biosensing and enzyme-dependent biosensing. The optical method could detect amounts of miR-17 inside cancer cells or serve as an amplification method for miR-21-AuNPs with the combination of NaYF4. Based on different photon frequencies and amounts of electrons released by cancer cells, AuNPs would show various states of resonance due to the absorption of the photons and electrons. The two forms of AuNPs include concentrated form and dispersed form. This process of accepting electrons and photons is often followed with colour changes which could be detected. Then the optical signal induced by AuNPs could be translated into electric signals or be directly analyzed inside a computer. On the other hand, this biosensing technique not only detects the amounts of miDNA but also plays a role of delivering certain drugs, with the presence of resonance, the AuNPs could release doxorubicin, a kind of tumor chemotherapy agent that is toxic to cells, to a desired location, which could then treat a patient [3].

AuNPs could be a promising way of detecting various diseases that are lethal to humans, including HIV, AIDS, and cancer. The biological amplification methods based on AuNPs has undergone progresses in recent years, and they can now detect pathogens at very low concentrations (about 10-15 pg/mL as a limit of detection). These ways of robust and effective detection include many specific sections, one of them is through imaging and microscopy techniques. The general way of performing such technique is through utilizing AuNPs wrapped by dendrimers. These specifically designed nanoparticles that are modified by FA and FI could easily form covalent bonds with KB cells, a kind of cancer cell in human's skins. The particles could easily reach the lysosomes of the KB cells within about two hours, providing a quick and easy way of detection. These discoveries indicate that dendrimer entrapped AuNPs can serve as fundamental methods for treating and imaging cancer. Using different sizes of AuNPs, this model provides an efficient way of detecting cancer cells through optical imaging.

Another way of detecting cancer using AuNPs is the immunoassay and electrochemical-based method. Combining ELISA and AuNPs, the new method of using AuNPs as enhancer is far more sensitive and efficient compared with conventional methods of detection. A noncrosslinking aggregation mechanism with a specific peptide substrate was developed, which is used as a coagulant of AuNPs with anionic surface. A stable AuNPs-modified high-binding ELISA plate method for the representative biomarker carcinoembryonic antigen (CEA) detection was also developed. They have proved that the AuNPs could enhance the message transmitted by the ELISA to a great magnitude, thus breaking the limit of detection [4].

The reported research discussed the detection of breast cancer using AuNPs. The major method presented is the detection of microRNAs in cancer cells. The miRNA is of great importance in regulating a cell's life cycle. Thus, it is an effective sensing method of monitoring whether a person has cancer related diseases through detecting their specific miRNAs. Nanomaterials can greatly increase various sensors' sensitivity through increasing their surface area contacting with the tested sample. Therefore, AuNPs have been utilized to form electrode coating outside of the miRNA needles to enhance electric signals. Based on this, a detector that directly tells whether a person has cancer could be developed through examining the miRNA of cancer cells. The needle of the detector transmits signals from samples into electric signals that could be analyzed on a computer [5].

AuNPs can be used to detect prostate cancer, where the detection process is basically a procedure of sample taking and sample analyzing. Through analyzing urine samples, doctors can get to know whether somebody has prostate cancer. The gold surface would be passivated with 0.1 mM of MCH to reduce the move of electrons so as to get a better and more accurate result. At last the process is repeated with FcSH replacing the MCH as the blocking reagent. The final product would go through a series of electrochemical processes until statistics have been clearly shown [6].

Early diagnosis for curing pancreatic cancer is pivotal, therefore an electrospun nanofiber biosensor combined with AuNPs has been developed. This biosensor could detect a biomarker named Lewis antigen, also known as CA19-9, the only approved antigen for detecting pancreatic cancer. Blood samples are detected by nanofibers coating with AuNPs. The sample, together with $HAuCl_4$ solution and sodium citrate solution are heated at a temperature of 90 ℃ until the solution turns into red, indicating that AuNPs have formed. Then the nanofibers attract the particles through hydrogen bonding and interactions with electrons. This would allow the fibers to bind with antigens which could be detected. This way, a simple and efficient method for detecting pancreatic cancer and other diseases characterized with antigen CA19-9 is developed, using nanofiber coated with AuNPs [7].

The use of sensitive sensors based on AuNPs in the early identification of cancer biomarkers is explored [1]. The research talks about how sensitive sensor technology has advanced recently and the way early cancer detection can benefit from it. It describes how aptasensors use single-stranded RNA or DNA molecules called aptamers to connect to target biomarkers in a targeted manner. AuNPs are used to strengthen these aptamers in order to increase their endurance and sensitivity. Because AuNPs have superior electrical and optical qualities, they can detect biomarkers in very low concentrations. Their capacity to detect biomarkers at extremely low concentrations is essential for early identification. These sensors offer outstanding selectivity because they are also very resistant against interference from other substances in the detecting environment. The excellent biocompatibility, simplicity of synthesis, and optical characteristic adaptation of AuNPs-based sensitive sensors are the main benefits of using them. These sensors might also be able to perform rapid, high-throughput on-site diagnostic examinations. Despite these benefits, there are drawbacks as well, such as the challenge of developing aptamers that perform effectively in a variety of biological environments. The long-term stability and reproducibility of these sensors can also be impacted by outside variables as well as the chemical and physical stability of the nanoparticles [1].

AuNPs are used by the microcantilever biosensor to enhance the signal for protein biomarker detection. At the end of the cantilever, the device incorporates a microcavity to maximize the local biological response space. This arrangement improves binding efficiency by strengthening the relationship between the biomarker and the detecting system. The biosensor's sensitivity has been greatly increased, with a detection limit of 21 pg/mL. This method shows low detection and high sensitivity limit, enabling the detection of extremely low biomarker concentrations, which are essential for an early diagnosis. It also shows quick reaction time and large throughput, which can be used for real-time monitoring and clinical situations. It also shows complex manufacture and design, which may make biosensor maintenance and production more difficult. Although beneficial, reliance on AuNPs may raise costs for operations and compromise the biosensor's scalability [2].

By incorporating AuNPs into the fiber optic ball resonator's surface, the biosensor takes advantage of their special optical qualities. The biosensor surface's refractive index changes as a result of the interaction between these nanoparticles and the cancer biomarker, causing a discernible shift in light intensity. This shift can be carefully assessed and is directly correlated with the biomarker's concentration. By incorporating AuNPs into the fiber optic ball resonator's surface, the biosensor takes advantage of their special optical qualities. The biosensor surface's refractive index changes as a result of the interaction between these nanoparticles and the cancer biomarker, causing a discernible shift in light intensity. This shift can be carefully determined and is directly correlated with the biomarker's concentration. The biosensor can identify CD44 cancer indicators over a broad range of concentrations, from sub-picomolar to nanomolar levels, and has an extremely low detection limit of 0.111 pM. This method shows excellent sensitivity and low detection limit, and it facilitates precise and timely biomarker identification, which is essential for efficient cancer diagnosis and therapy. The use of green synthetic AuNPs can be used to guarantee environmental friendliness and safety. This method simplifies and lowers production costs by using a readily available direct synthesis method based on green tea extract. Depending on the traits of the biomarker and its particular interactions with the AuNPs, performance of this method may differ. Although the platform is very successful at detecting CD44, more research is needed to see whether it can also be used to detect additional biomarkers or complicated biological samples [8].

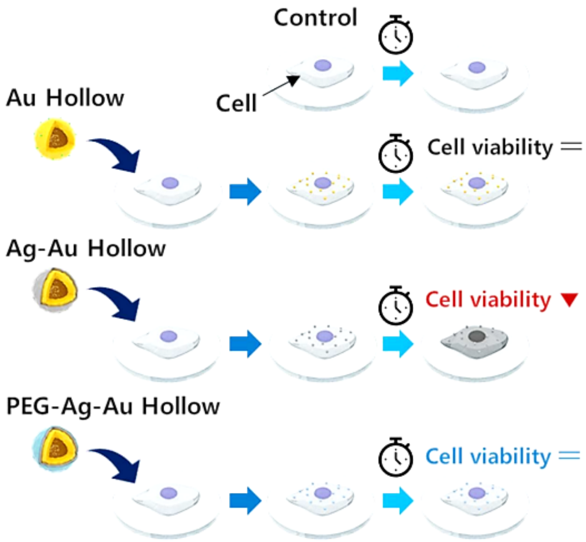

Fig. 1 Cell viability analysis in the presence of various types of SERS nanotags [9].

PEGylated silver-gold hollow nanospheres are used in this biosensor to increase the SERS effect, allowing more accurate and reproducible imaging of cancer cells. Raman reporter molecules are positioned in the nanogap between the silver shell and the gold hollow spheres to increase SERS. With this arrangement, the Raman signal is greatly amplified and protein biomarkers at extremely low concentrations can be found effectively [9]. The biosensor shows extremely high specificity and sensitivity while imaging and analyzing many biomarkers all at once. To ensure dependable functioning in various situations, the optical sensitivity and stability of the synthesized SERS nanotags have been extensively evaluated under a range of circumstances, including variations in temperature, pH, and salt concentration. This method shows excellent sensitivity and specificity that identifies biomarkers at sub-picomolar concentrations, which is essential for the early identification of cancer. By using materials that are less hazardous, biosensors used in clinical settings can be used with greater safety. As shown in Fig. 1, for a thorough grasp of the phenotypic of cancer cells, several biomarkers can be found at the same time. The exact control required in the manufacturing process of nanotags makes them difficult to design, which could impede their rapid production and dispersion.

Although not stated specifically, using sophisticated materials and techniques may be more expensive than using conventional biomarker detection techniques [9].

3. Concluosion

This research has investigated various ways of detecting cancer biomarkers using AuNPs-based biosensors. The biggest advantage for these biosensors lies in its high sensitivity and selectivity. AuNPs could easily detect proteins and other cancer biomarkers at very low concentrations, which is important for early cancer diagnosis. As for how it works, these particles could serve directly as a key element of a detector through its surface resonance effect or as coating to enhance the effect of numerous equipment such as needles and nanofibers. But there still are many properties of AuNPs left to be explored. Its current application is not fully developed either. Hence, for such a promising technology, there is still a long way to go. AuNPs should play a bigger role in future cancer treatments and benefit more and more people suffering due to cancer related diseases.

Authors Contribution

All the authors contributed equally, and their names were listed in alphabetical order.

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