Application of Nanomedicine in Diagnostic Technology

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Abstract. In both diagnoses and treatments of diseases, nanomaterials play a critical role. They can be used to detect and target specific cells and proteins in the body, and to deliver drugs and other therapeutic agents directly to these cells and proteins. Nanomaterials can also be used to create new diagnostic tools, such as sensors that can detect the presence of disease-causing agents in the body, and to develop new and more effective treatments for diseases. Nanomaterials have a number of advantages over traditional disease diagnostic methods. They are more sensitive, more specific, and more accurate. Nanomaterials can also be used to detect a wider range of diseases and conditions. Nanomaterials also have the potential to be used in drug delivery. Finally, nanomaterials are less expensive and easier to use than traditional methods. Nanomaterials have made some progress in medical diagnosis, especially in regard to the prevention and treatment of cancer. By using nanomaterials, doctors can detect cancer earlier and more accurately than ever before. Nanomaterials can also help doctors treat cancer more effectively, by killing the cancer cells and preventing them from spreading. In this paper, the characteristics of nanomaterials, the role of nanomaterials in the preparation of biosensors and nanoprobes, and some common nanoimaging techniques are reviewed.

Keywords: Nano-biosensor, Nanomaterials, Oxide nanomaterials, Nanoprobes, Nano-imaging technology.

1. Introduction

Malignant tumors are currently mostly diagnosed via biological detection and imaging techniques. However, the majority of these conventional diagnoses which have a low sensitivity and specificity, are unable to pinpoint cells, need invasive biopsy procedures, and have a finite number of specimens. Imaging techniques are ineffective against tumors with a diameter of less than 0.5 cm and are constrained by expense and risk [1]. Therefore, for early diagnosis and monitoring, the development of new technology is quite important. The physiology, pathological conditions, and metabolic levels of the body can now be revealed at the cellular and molecular levels using targeted nanomaterials as nanocontrast agents or nanoprobes for various types of imaging equipment. This has shown and is showing good application prospects in diagnosis and prognosis evaluation. Therefore, accurate diagnosis and timely treatment are particularly important to control the development of tumors to malignancy. In order to improve the diagnosis and treatment effect, nanodrug delivery systems have been extensively studied because of their advantages of targeted delivery capabilities, improved pharmacokinetic properties, and responsive fixed-point drug release. Because of their outstanding biocompatibility and relative chemical inertness. nanomaterials have shown great potential in biomedicine, materials, industrial catalysis, bioanalytical chemistry and other fields, especially in tumor treatment and tumor imaging. Large specific surface areas, enhanced catalytic capabilities, and ease of surface modification with a range of functional groups are characteristics of nanomaterials. Their huge specific surface area enables the biomolecule to be effectively immobilized on the transducer surface, increasing the sensitivity of the sensors. It can be utilized to build imaging techniques as well as biosensors and nano probes. Nanomaterials are also known to increase the transducer surface's rate of electron transfer. Numerous nanomaterials have been thoroughly investigated in order to create sensors that are interesting for a wide range of applications. These nanomaterials include nanoparticles made of carbon, metal/metal oxide, composite materials, etc. Nanomaterials with diverse morphologies, sizes, forms, and compositions are anticipated to play a significant role in carrying out a variety of tasks in sensing systems. To achieve the intended functionality, however, regulated synthesis of nanomaterials is essential. By designing nanodrug delivery systems and controlling their size, topography and surface modifications, probes can be efficiently loaded and delivered to targets while prolonging blood circulation time, enhancing biocompatibility, lowering immunogenicity and toxicity while overcoming medication resistance. The development of diversified nanoplatforms has enabled the creation of composite probes with medicinal and imaging capabilities. The difficulty of attaining targeted absorption by particular cells has been highlighted by recent breakthroughs in the field. For instance, it has been demonstrated that when nanoparticles are introduced into biological environments, biomolecules on them become adsorbed, and the ensuing corona can be used to screen the targeting molecules [2]. While this is happening, it has been discovered that cell membrane receptors can recognize the corona itself, and this primary recognition may affect the method cells use to absorb the nanoparticles [3]. There are still several unanswered questions regarding the molecular mechanisms underlying the first identification of nanoscale objects by cell receptors as well as their absorption and intracellular processing. Designing more intelligent nanomedicines and achieving better targeting may benefit from a greater knowledge of these processes.

In this study, the most recent knowledge concerning the initial interactions between nanoscale materials and cells will be summarised. The preparatory identification to the cell membrane and subsequent internalization mechanisms by the cells will receive special attention. Regarding the accomplishment of nanoscale materials for nanomedicine, these factors are examined. An insight into known endocytic processes in cells will be given, along with challenges in describing these initial activities. By introducing the application of nanomedicine in diagnostic technology, this paper reflects the discovery space and potential of nanomaterials.

2. Nano-biosensor

Nanobiosensor includes nanotechenology and biosensor, and biosensor is sensing device used to detect bio-components based on biospecific identification. Nanobiosensor can help clinical doctors detect cancer cell and tumor markers rapidly and achieve an early diagnosis of cancer.

Research of nanobiosensor involves biotechnology, nanotechnology, information technology, surface technology, etc. It sums up many kinds of advanced detection technology, such as optical, ultrasonic, and radionuclide, so it becomes increasingly appealing. Its design and development provide many ideas of innovation, and it will make the detection of tumors more efficient and easier, and bring a revolutionary effect.

The detection performance of biosensors is improved once nanoparticles are added. and some new biosensors have been produced. Magnetic nanoparticles are a new kind of material that develops in recent years. Because magnetic nanoparticles have special superparamagnetism, and they can also combine the molecules with many functions. it has comprehensive research and application in nucleic acid analysis, clinical diagnosis, enzyme immobilization, cell isolation, and targeted therapy.

The significant characteristics of nanobiosensor are high-speed, efficiency, accuracy, smartness, portability, and multi-functionality. they cannot only detect bacteria, viruses, ferment, protein, blood sugar, toxic and harmful small molecules, and heavy metal ions, but also explore the inside of atom and molecule. As the biosensor, it needs to equip with these characteristics: 1) small size, quick response and ability of accurate continuous detection. 2) the uniform separation and detection of the tested components without pretreatment. 3) ability of analyzing the living body.

Salahandish et al. used electrochemical methods to fix silver nanoparticles (AgNPs) and polyaniline (PANI) on graphene biosensors, and then combined with DNA probes complementary to miRNA on the nanocomposite, and used electrochemical voltammetry to detect miRNA precisely, with a linear range of 10 fmol/L ~ 10 μmol/L and a detection limit of 0.2 fmol/L with high sensitivity [4]. The high selectivity of graphene nanobiosensors is not affected by the matrix effects of the detection buffer. The experimental results above show that the graphene nanobiosensor can be directly used to detect miR-21 in clinical samples without the need for further analysis.

Nanomaterial is a sensitive chemical and biological sensor, it can combine with the biochip, and chooses the target molecule selectively, which makes molecular detection more efficient and convenient. Nanomaterials show their peculiar chemical and physical characteristics, such as the effect of small size, surface, quantum dimension, and macroscopic quantum orbital. Because the methods of preparation are easy, the surface is easy to embellish and the size of it can be controlled. In addition, as the material of biosensors, it requests fast response speed, wide detection range and function, and nanomaterials are in accordance with these characteristics. Therefore, it has been widely used in analytical chemistry and clinical diagnosis.

The typical usage of nanotechnology in biological testing is made of nanochips. Nanochip is setting multiple bioactive molecules in surface area, just using less bioactive molecules, and it can detect and study different biological cells, biological cells and DNA properties and find out the interaction of them, knowing about the law of microscopic activity of life. Traditional biochips have many limitations, they cannot set DNA very well, need many samples and have low sensitivity, but when applying the nanotechnology to biochips, the limitations will be overcome significantly.

3. Nanomaterials

3.1. Gold nanomaterials

Because metal nanomaterials have a variety of species and are easy to prepare, they are extensively studied in life sciences. Gold nanomaterial is in common use. The particle diameter of nano gold is between 1 nm and 250 nm. Nano gold is a very versatile metal that can be used in many different applications. For example, it is easily synthesized and has good biocompatibility. Additionally, it is easy to be modified with functional molecules which are used to target specific cells. This makes nano gold a very versatile metal that can be used in a variety of applications. Because of its small size, it can be modified by various groups and its optical properties, nano-gold has become a popular research object in the early diagnosis of diseases.

Laser speckle pattern recognition and signal enhancement techniques have been extensively used in medical imaging for decades. Recently, the use of laser speckle pattern recognition and signal enhancement techniques for imaging diagnosis of cells and living bodies has become more prevalent. Laser speckle pattern recognition and signal enhancement techniques offer several advantages over other medical imaging techniques, such as the ability to image small objects and the lack of radiation exposure. Gold nanomaterials not only have great special surface area and strong catalytic activity, but also it has strong adsorption capacity, so it can set the biological macromolecules, many enzymes can be adsorbed to the gold nanomaterials' surface and retain catalytic activity. In addition, He et al. found that gold nanosheets exhibit excellent catalytic activity in the decomposition of hydrogen peroxide to generate non-toxic oxygen, and using this, on the surface of gold nanosheets through HS-PEG-NH2 coupled with folic acid (FA), in a closed container, the specific interaction between FA and folate receptor (FR) overexpressed by tumor cells enables tumor cells to take up folate-conjugated gold nanosheets [5]. The catalytic action of intracellular gold nanosheets causes H_2O_2 to break down into more O2, the pressure in the container changes, and the sensor detects the pressure signal to interpret the presence of tumor cells.

Through the transfer of energy or electron, gold nanomaterials can transfer the photon energy to other small molecules like oxygen and hydrogen peroxide surrounding it. Photodynamic therapy of tumor can be achieved by photochemical reaction producing reactive oxygen and achieving. Compared with normal tissue, the blood vessel wall at the site of the tumor has a big gap, and its permeability is better. After intravenous injection, gold nanomaterials passively target to the tumor tissue. Within the body, nanomaterials can easily be swallowed by macrophages and influence their targeted delivery. Therefore, they need to be modified on the surface to improve biocompatibility and reduce the possibility of being swallowed by macrophages.

Using body fluids such as blood and urine to diagnose diseases is more convenient that using Photoacoustic Imaging (PAI), CT, Fluorescence Imaging and Raman Imaging. Du et al. found that mercury ion can induce creatinine gold nanoparticles which are modified by and uric acid produces sensitive color changes and lay the foundation for using gold nanomaterials for detection outside the body [6].

3.2. Oxide nanomaterials

3.2.1. Graphene oxide (GO)

GO is a new reagent used to diagnose and cure cancer and shows huge potential in the biomedical domain [7,8]. Compared with other nanomaterials, GO has its special advantages. 1)It has low production costs, and can be prepared by using cheap carbon materials and a simple chemical reaction. 2)2D plane shape makes GO a huge specific surface area, which can be used to deliver all kinds of treatment medicine [9]. 3)Because the surface of GO is rich in negative charge, it has good water solubility. 4)Special 2D structure applies to the establishment of nanocomposite which is based on GO as well [10]. 5) In contrast to Au nanomaterials, carbon nanotubes, quantum dots, etc, GO shows better biocompatibility [11].

GO and its derivatives show good potential in the diagnosis, imaging, and treatment of tumors. GO cannot only be a fluorescence quenching platform, but also mix with precious metal materials to diagnose the tumor. The good photoluminescence characteristics and Raman features make GO show its value in fluorescence imaging and Raman imaging of tumors [12]. However, because of the toxicity of GO materials, especially some composite materials, the direction in which GO has gone is also a matter and relative if it can be used in human beings' bodies.

3.2.2. Mesoporous silica nanoparticles (MSNs)

By virtue of their special physicochemical property and low toxicity, MSN s are getting more attention. Compared with traditional nanomedicine carrier, such as polymer nanoparticles and liposomes, MSNs have significant advantages. According to the report, the amount of MSNs loading DOX can reach 100 times the loading capacity of liposomes of the same size [13]. It has a highly ordered pore structure that can take different materials efficiently. High specific surface area achieves large loading. Mesoporous shapes are diverse. More importantly, the ability of high loading capacity of MSNs makes overcoming multidrug resistance possible. Another advantage that cannot be ignored is that the synthetic process of MSNs is economical and practical, which also makes the possibility of putting it into industrial production much higher than the traditional nano-carrier.

3.3. Carbon nanotubes (CNTs)

CNTs are found accidentally by an electron microscope specialist called Lijima from NEC company's basic research laboratory in Japan when he used the high-resolution transmission electron microscope to try out globular carbon molecules produced in graphite arc equipment [14].

CNTs are commonly used in biomedicine. Especially in antitumor drug carrier, CNTs show their special advantages. 1) Tubular structure makes CNTs have a dominant ability to cross the membrane, without damaging cells. 2) They have a huge specific surface area, and can load many medicines onto the external wall and inside the cavity. 3) Their chemical property is stable and easy to modify to bond with many kinds of biological molecules, improve the targeting, and achieve the goal of treatment successfully. 4) The complex of CNTs can improve the treatment time of medicine in vitro [15].

CNTs as biosensor, because it has excellent tensile strength, chemical stability, electrical conductivity and surface catalytic activity, the research of carbon nanotube modification materials has become one of the hot topics about biosensors. Cai et al. introduced CNTs to biosensors, improved the response current value of GC electrode, enhanced the current response sensitivity of sensors, and obtained the direct electrochemistry of Horseradish Peroxidase, HRP in the electrode [16]. Their experimental results show that HRP can perform effective and stable direct electron table on the superficial appearance of CNT/GC electrode, and its cyclic voltammetry curve shows a couple of nearly symmetrical good redox peaks. The formula potential hardly changed with the sweep speed, the apparent rate constant for direct electron transfer was (2.07 ± 0.56) s^{-1}. Further experimental results show that HRP stationary on the CNT/GC electrode table may maintain its bioelectrocatalytic activity against H_2O_2 reduction and can quickly respond to H2O2 concentration changes.

There are also some limitations. For example, carbon nanotubes tend to agglomerate, so that they are difficult to disperse. Single wall carbon nanotubes (SWCNTs) are insoluble, which may affect their applications in biosensors [17,18].

4. Nanoprobes

In clinical testing, traditional imaging methods can reflect the location of the tumor and its structure of anatomy, but traditional imaging methods are hard to determine the molecular pathology. Although the pathological biopsy can obtain the molecular characteristics of the tumor, it gains the samples through the traumatic means of treatment. By contrast, tumor molecular imaging which borrowed specific probe imaging, analyzes directly molecular markers of tumor pathology at the molecular level, and has a unique advantage in the precise treatment of tumors.

Molecular probe system is the premise of achieving molecular imaging. It should meet the requirements that magnify valid information, have good biocompatibility, excellently targeted enrichment capability and have biodegradability.

Nanoprobes are different from small molecule materials. Nanoprobes have a larger hydrate particle size, cannot pass through freely vascular endothelial space and are excreted in the urine by the glomeruli, so they circulate with blood for a longer time. Benefiting from huge specific surface area and liberal surface sites, nanomaterials can be used to fabricate nanoprobes that have the ability of tumor targeting. Compared with small molecules, they have enough time to target tumors.

Through Enhanced Permeability and Retention (EPR), nanoprobes enrich passively in the tumor, and also identify specific molecular targets associated with tumors. These two characteristics improve the imaging contrast of the tumor diagnosis together. It is expected to achieve a high sensitivity diagnosis of tinier tumor nidus.

5. Nano-imaging technology

Nanomaterials can be used to produce nano contrast agents and nanoprobes, from the cell and molecular level to reveal the physiology of the engine body, metabolism and pathology. Magnetic Resonance Imaging (MRI) has some characteristics, such as high resolution, security and noninvasivity, and it is also good for soft tissue imaging. Gadolinium is usually used as T1 weighted imaging contrast medium, but gadolinium is toxic. Fe_3O_4 nanoparticles are known as non-toxic T2 weighted imaging contrast medium [19]. Compared with gadolinium, Fe_3O_4 is more sensitive, has better bio-compatibility and superparamagnetism.

Optical imaging usually uses fluorescein and produces a fluorescent signal for imaging. It is very safe, nonradiative, noninvasive, of high resolution and good controllability. In addition, photoacoustic imaging (PAI) is a new kind of imaging. As one of the fastest discoveries, it uses the differences in light absorption by biological tissues [20]. PAI can overcome the lack of pure optical image resolution and pure contrast agents for ultrasound imaging, greatly improving the penetrability of tissue and spatial resolution. PAI is obtained by measuring the real-time of PA signal. The amplitude of PA reflects the absorption of optical energy and the structure of absorbent. The change of tissue associated with pathology and viscoelastic property is important to medical diagnosis, and biological tissue is viscoelastic rather than inelastic, so there is a phase delay between PA wave and exciting light [21]. Therefore, PA technology which can represent the viscoelastic properties of tissues has great potential in clinical diagnosis. Using ultrasound signals to capture this difference, and the imaging shows the anatomical information of tissue, and provides information on the body's metabolism.

At present, different types of imaging methods are used to diagnose jointly, and integration of different measures, can have a synergetic effect, presenting more accurate and comprehensive imaging. This multimodal imaging of tumors will become a new direction of tumor diagnosis in the future.

Compared with traditional biological diagnosis, nanomaterials are more efficient, sensitive, accurate, comprehensive, and less invasive. They can help clinical doctors find out and detect the cancer cell and tumor markers, achieve early treatment, and reduce the mortality rate. However, some of them are toxic, and might affect cell activity, and is slightly invasive and the degree of damage to the organism is unmanageable. Because of the dissociation of the tumor and cancer cells, nanomaterials distributed inside the body still bring some inevitable harm to the tissue, and for some nanocomposite materials, biocompatibility is also a problem that needs to be solved. Nanomaterials' distribution and direction in the body are related to whether some nanomaterials can be used in the human body, and the experiment research about integration of diagnosis and treatment is still not sufficient. The diagnosis of a tumor is also the challenge of nanomaterial using in clinical medical diagnosis. Hopefully, there are some harmless and non-toxic nanomaterials which have been developed.

6. Conclusion

This paper introduces some of the ways nanomaterials are used fordiagnosis in medicine. Nanomaterials are increasingly being used in medicine for diagnosis. They offer a lot of benefits over traditional diagnostic methods, including the ability to provide real-time information about the body and to target specific cells or tissues. Nanomaterials are also less invasive than many traditional diagnostic methods and can be used to detect many conditions, including cancer and heart disease. Nanomaterials can also be applied in nanobiosensors that detect biological molecules One of the most common uses for biosensors is in the clinical detection of diseases. The application of nanomaterials in biosensors makes them more efficient, faster and more sensitive at detecting diseases. This article also introduces the application and research progress of some nanomaterials in disease diagnosis. The common point of these nanomaterials is targeting, and their targeting properties allow them to be well used for cell recognition. Nanomaterials can be used to diagnose a lot of diseases, including cancer, and neurological disorders, and cardiovascular disease. In addition, Nanomaterials are also being studied for possible use in drug administration and tissue engineering. Nanoprobes make good use of targeting as well. Nanoimaging technology is the use of nanomaterials and their properties comprehensive imaging to help clinically better diagnose and analyze the location and pathology of tumors. All above this, the article follows these points to introduce the principles, methods, and applications of nanomaterials.

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