Research Progress of Biosensors in Tumor Detection

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Abstract. Early diagnosis of malignant tumors is crucial for improving the survival rate of patients, while traditional detection methods have limitations such as being highly invasive and having insufficient sensitivity. Therefore, biosensors have shown great potential in tumor detection in recent years, thanks to their advantages such as high sensitivity, rapid, and low cost. This article reviews the latest research progress of biosensors in tumor detection, with a focus on three key technologies: conductive metal-organic framework (MOF) composite material sensors, nucleic acid aptamer sensors, and nano-field-effect transistor (such as silicon nanowires, molybdenum disulfide) sensors. By leveraging their porous structure, tunable conductivity, aptamer-specific binding ability, and charge doping or electrostatic effects, they can achieve highly sensitive detection of trace tumor markers, tumor cells, nucleic acids, proteins, and other biomolecules. The significance of this research lies not only in summarizing the current state-of-the-art in biosensor technology for tumor detection but also in highlighting the potential of these technologies to revolutionize cancer diagnosis. By providing a comprehensive overview of the latest research findings, this article aims to identify the strengths and limitations of each biosensor technology, thereby guiding future research efforts to improve their performance and practicality. Furthermore, the analysis of the challenges faced by biosensors in clinical translation, such as standardized production and stability verification, is crucial for bridging the gap between laboratory research and clinical application. Understanding these challenges can help researchers develop strategies to overcome them, thereby accelerating the commercialization and widespread use of biosensors in cancer diagnosis.

Keywords: Biosensor; Tumor detection; Conductive metal-organic framework; Nucleic acid aptamers; Field-effect transistor.

1. Introduction

Malignant tumors are one of the major diseases threatening human health, and early diagnosis is crucial for improving the survival rate of patients. However, traditional tumor detection methods (such as tissue biopsy, imaging examination, and serum marker analysis) often have problems such as high invasiveness, insufficient sensitivity, or long detection cycles, which limit the wide range of clinical applications, such as cytology and histopathology not being effectively and independently applied to the early detection of tumors [1]. In recent years, with the rapid development of nanotechnology, molecular, and micro-nano processing technology, biosensors have shown great potential in areas such as tumor marker detection, capture of circulating tumor cells, and liquid biopsy, thanks to their advantages of high sensitivity, rapid response, and low cost.

Biosensors function by combining biometric elements such as antibodies, nucleic acid aptamers, or enzymes with signal converters (including electrochemical, optical, or mechanical modules), and can achieve ultra-sensitive detection of tumor-associated molecules such as proteins, exosomes, or mutant DNA/RNA. Examples include fluorescence biosensors based on fluorescence changes [2], charge-based nanofield-effect transistor biosensors [3], etc. The ease of operation, minimal sample preparation, cost-effectiveness, and exceptional sensitivity of biosensors enhance their applicability in clinical diagnostics [4]. This article reviews the latest research progress of biosensors in tumor detection, with a focus on their design principles, performance optimization, and clinical translation challenges, aiming to provide references for the future development of high-precision, multimodal tumor diagnosis technologies.

2. Current research progress

2.1 Biosensors on Conductive MOF Composites

Conductive metal-organic frameworks (MOFs) are advanced materials that combine electrical conductivity with high porosity and exceptional catalytic capabilities, enabling diverse applications in gas adsorption and energy storage [5]. The porous structure can enhance the adsorption capacity of gases/molecules. By integrating conductive and porous MOFs through interface engineering, the response capability of the sensor to low-concentration targets can be enhanced [6]. 错误!未找到引用源。Conductive metal-organic frameworks (MOFs) have become a research hotspot in sensing due to their porous structure and tunable properties. The porosity and large surface area of conductive MOFs allow more enzymes, aptamers, electroactive, and metal nanoparticles to be anchored on their surfaces, significantly amplifying detection signals and reducing detection limits. Due to their good biocompatibility and controllable surface functionalization, conductive MOF composites show unique advantages and potential in tumor marker detection, which can serve as key components of biosensors to enable rapid diagnosis of early-stage cancers and tracking of treatment effects by detecting trace tumor markers in vivo. Biosensors based on conductive MOF composites have been proven to be good at detecting tumor markers, and with the discovery of new materials, they will move towards integration, multi-functionality, and commercialization.

Electrochemical sensors work by converting biological signals into electrical signals and detecting target substances by measuring the intensity of the electrical signals. They have the advantages of high sensitivity, good selectivity, fast response time, wide detection range, strong miniaturization ability, and are widely used in clinical cancer analysis [7]. 错误!未找到引用源。The excellent electrical conductivity of conductive MOF materials is conducive to the construction of highly sensitive electrochemical sensors. Guo et al. [8] used bimetallic conductive MOF as a sensitive scaffold for adsorption of aptamer chains to construct a bifunctional electrochemical aptamer sensor for the detection of C6 glioma cells and their marker epidermal growth factor receptor.

Photoelectrochemical sensors based on conductive MOF composites

Photoelectrochemical (PEC) sensor technology offers significant advantages, such as low background current, low cost, fast response, and high selectivity. Photoactive materials are a key factor influencing the performance of photosensors. MOFs are recognized as promising photoelectric materials. Guest molecules enhance the luminescence efficiency of MOF through energy transfer or electron transfer, with typical applications including biosensors (such as DNA and protein detection) [9]. MOFs possess not only the inherent advantages of traditional materials but also extremely high conductivity, allowing them to convert perceived stimuli into electrical signals.

2.2 Nucleic acid aptamer sensor

An aptamer is an oligonucleotide molecule that has high affinity for a variety of targets, such as proteins [10], small molecules [11], etc., because it can fold itself to form a tertiary structure. Because of its antibody-protein properties that can specifically bind to target molecules, it is widely used in disease diagnosis, nanoprobes, and drug development. Notably, nucleoproteins, which regulate cellular life processes, are selectively overexpressed on the cell membrane surface of cancer cells and are not expressed in normal cell membranes [12]. Therefore, nucleoproteins hold considerable potential as early tumor biomarkers. With the expansion of aptamer applications and the advancement of nanotechnology, nanocarriers formed by the connection of aptamers with nanomaterials have been widely used in target recognition, biosensing, and target cell imaging [13]. When the nanoprobes designed with aptamers specifically bind to the corresponding targets, the conformation of the aptamers will change, thereby generating detectable signals. Therefore, functional aptamers based on nanostructured substrates can be used as biological probes to enhance sensitive recognition of tumor cells. The sensor has good selectivity and can be used for highly sensitive detection of tumor cells, and it is expected to provide new technical means for the early diagnosis of clinical tumor patients.

2.3 Nanometer field-effect transistor sensor

In recent years, with the rapid development of nanomaterial preparation technology, more and more high-performance nanomaterials have been used in medical testing, such as silicon nanowires, graphene, and molybdenum disulfide. Nanofield-effect transistor (nano-FET) biosensors typically operate based on doping mechanisms [14, 15]. Nanofield-effect transistor biosensors have been widely used in medical tests for nucleic acids, proteins due to their high sensitivity, fast analysis speed, and ease of operation [16]. These advantages of nanofield-effect transistors are particularly suitable for the early diagnosis of tumors. The high sensitivity of the sensor enables the detection of trace markers related to early tumors, and the advantages of fast analysis speed, miniaturization, and simple operation enable rapid bedside detection of tumors, facilitating the early detection of tumors.

Recently, silicon nanowire field-effect transistors (SiNW-FETs) have demonstrated great promise in tumor biomarker detection owing to their unique electrical characteristics and surface sensitivity. Zheng et al. [17] successfully constructed a biosensor based on SiNW FET, achieving highly sensitive detection of multiple tumor markers. Including key biomarkers such as Prostate Specific Antigen (PSA), Carcinoembryonic Antigen (CEA), and Mucin, it provides new technical means for the early diagnosis of tumors.

Mansouri et al. [18] developed a high-performance field-effect transistor (FET) sensor based on a flexible polymer substrate and conductive nanomaterials for the detection of tumor marker CA125 (cancer antigen 125). This sensor uses polymethyl methacrylate (PMMA) as a flexible substrate, endowing it with excellent mechanical flexibility and biocompatibility, and is suitable for wearable or portable detection devices. Meanwhile, they selected carboxylated multi-walled carbon nanotubes (MWCNTs)/reduced graphene oxide (rGO) composites as channel materials to enhance electrical conductivity and carrier mobility, thereby increasing the sensitivity and response speed of the sensor. This study is particularly valuable due to its integration of flexible electronics and advanced nanomaterials, enhancing both sensor performance and practical applicability. In the future, this technology is expected to be further optimized for the early screening and dynamic monitoring of cancer patients, providing more accurate data support for personalized medical care.

Majd et al. [19] developed a molybdenum disulfide field effect transistor (MoS_2 FET) sensor for detecting breast cancer marker miRNA-155. Prepared molybdenum disulfide was transferred to the channel surface of the field-effect transistor by drop coating as a conductive material, and the miRNA-155 capture probe was physically adsorbed on the surface of molybdenum disulfide. The sensor also has high specificity and strong anti-interference ability, enabling the detection of miRNA in serum specimens and breast cancer cell lines, which is of great significance in clinical detection. High sensitivity and specificity are another major highlight of this sensor. In the early stage of breast cancer, the content of miRNA-155 may be very low and is often difficult to detect by traditional detection methods. The MoS_2FET sensor, with its high sensitivity, is capable of detecting extremely low concentrations of miRNA-155, thereby achieving the early diagnosis of breast cancer. Early diagnosis is crucial for the treatment and prognosis of breast cancer. It can detect the cancer in time before it spreads and take effective treatment measures, which greatly improve the survival rate and quality of life of patients.

3. Comparison and analysis of Biosensors

Conductive metal-organic framework (MOF) composite sensors, nucleic acid aptamer sensors, and nanofield-effect transistor (FET) sensors each have their characteristics in tumor detection. Conductive MOF sensors leverage their porous structure and tunable conductivity to achieve highly sensitive electrochemical detection, making them particularly effective for protein-based tumor markers; however, their resistance to interference requires improvement. Nucleic acid aptamer sensors, which use specifically bound nucleic acid aptamers, show excellent targeted recognition capabilities, especially for capturing circulating tumor cells, but have limitations such as high aptamer screening costs. Nanofet sensors (such as silicon nanowires, graphene, etc.) achieve label-free, ultrasensitive detection through charge doping effects, with sensitivity reaching the single-molecule level, but they face challenges such as complex surface modifications and ion interference. The three types of techniques each have their strengths in terms of sensitivity (nanOFET optimal), specificity (aptamer optimal), and clinical translation difficulty (MOF relatively easy), and future technology fusions (such as MOF-aptamer-FET hybrid systems) are expected to break through the limitations of a single technology and provide a more powerful tool for early tumor diagnosis.

4. Future Prospects

Biosensors show revolutionary potential in tumor detection, providing efficient, sensitive, and low-cost solutions for early diagnosis, dynamic monitoring, and precision treatment. Integration of nanomaterials, microfluidic technology, and artificial intelligence algorithms, the new generation of biosensors can achieve multi-target detection, single-cell analysis, and even real-time in vivo monitoring, significantly improving the accuracy and convenience of tumor diagnosis. However, their clinical translation still faces challenges such as standardized production, long-term stability validation and the accumulation of large-scale clinical data. In the future, with the further development of flexible electronics, bionic sensing, and intelligent diagnostic systems, biosensors are expected to be deeply integrated with personalized medicine, driving the transformation of tumor diagnosis and treatment from "passive treatment" to "active prevention." Breakthroughs in this area will not only improve patient outcomes but also potentially reshape the global paradigm for cancer screening and management.

5. Conclusion

This paper reviews recent advancements in biosensor technologies for tumor detection, with a focus on discussing three key technologies: conductive metal-organic framework (MOF) composite material sensors, nucleic acid aptamer sensors, and nano-field-effect transistor (such as silicon nanowires, graphene, and molybdenum disulfide) sensors. These biosensors utilize distinctive principles—MOFs exploit porous structures and tunable conductivity, aptamer sensors employ high-affinity binding molecules, and nano-FET sensors leverage charge doping and electrostatic phenomena—to achieve highly sensitive detection of tumor markers, circulating tumor cells, nucleic acids, and proteins. Conductive MOF composite material sensors, with their high sensitivity and signal amplification capability, are suitable for the detection of tumor markers such as proteins, but their anti-interference ability needs to be improved. Nucleic acid aptamer sensors, with their specific binding ability, demonstrate excellent targeted recognition capabilities and are particularly suitable for capturing circulating tumor cells. However, they have limitations such as high aptamer screening costs and easy degradation. Nanometer FET sensors, through label-free and ultra-sensitive detection, can achieve sensitivity at the single-molecule level and are suitable for trace nucleic acid and protein detection. However, they face challenges such as complex surface modification and ion interference. The three types of technologies each have their strengths in terms of sensitivity, specificity, and the difficulty of clinical transformation. In the future, through technology integration (such as the MOF-aptamer-FET hybrid system), it is expected to break through the limitations of a single technology and provide a more powerful tool for the early diagnosis of tumors. Ultimately, biosensors present transformative potential in cancer detection, enabling cost-effective, precise, and real-time monitoring strategies. However, widespread clinical implementation will depend on resolving issues related to standardization, sensor stability, and extensive clinical validation. In the future, with the further development of flexible electronics, bionic sensing, and intelligent diagnostic systems, Biosensors are expected to be deeply integrated with personalized medicine, promoting the transformation of tumor diagnosis and treatment from "passive treatment" to "active prevention".

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