A Review on Application of Biosensors for Cancer Detection

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Abstract: ***Cancer is a deadly disease that has devastated many lives over the years. Cancer, when detected in the early stage, can be cured through proper treatment, increasing the life expectancy of the patient. Thus, it is very important to detect cancer at the early stage. The current method of cancer detection is biopsy which is a total invasive medical procedure. Owing to the several limitations of the time-consuming procedure of biopsy researchers and scientist all over the globe have turned their attention towards the development of instruments for rapid and non-invasive detection of cancer through detection of clinically recognized cancer biomarkers present in blood and other body fluid of cancer patients. This paper discusses some of the novel biomarkers used for cancer diagnosis along with the potential use of biosensors in early detection of cancer.***

Keywords: Biomarkers, Biopsy, Biosensors, Cancer

1. Introduction

Cancer is a deadly disease responsible for many deaths over the years. More than 575,000 people die of cancer, and 1.5 million people are diagnosed with cancer per year only in the U.S. [1]. Cancer is caused due to uncontrolled cell growth. There are over 100 types of different cancers arising in different parts of the body [2]. Some of the common cancers are Kidney, Liver, Ovarian, Colon, Stomach etc. The exact cause of cancer is yet to be known to medical science. It is believed that cancer risk can be reduced by avoiding tobacco, limiting alcohol intake, limiting exposure to UV rays from the sun and maintaining a regular healthy diet. According to the World Health Organization, (WHO), the number of new cases is expected to rise by 70% over the next 20 years [3]. Tumor is mainly are of two types: Benign and Malignant. A benign tumor is less harmful and can be removed through surgery whereas malignant tumors are aggressive and decrease the life expectancy of the patient. A tumor when metastasized becomes cancer and spread from one organ to another throughout the body through blood. Such cancers are responsible for the majority of deaths around the world. Thus, early detection of cancer is of utmost importance. The current method of detection of cancer is biopsy which is an invasive process. A Biopsy is a medical procedure which requires the insertion of medical instruments in the patient's body for removal of certain tissues to be examined to find the presence of cancer cells. Such a process is time-consuming and further has many limitations. Patients undergoing biopsy complains of weak health, nausea, insomnia etc. with further post-biopsy effects. Thus, the need for non-invasive detection has come into importance in the modern time. In addition, the need of rapid detection is of utmost importance to give immediate results to the patients so that their treatment can be started without wasting any time. Thus, this need for rapid non-invasive detection of cancer has led the researchers to develop instruments which would detect cancer early without the need of an invasive procedure. This has led to the development of biosensors for non-invasive rapid early detection of cancer.

2. Cancer Biomarkers

Due to several disadvantages of invasive procedure of cancer detection researchers and scientist from all over the globe have turned their attention towards non-invasive diagnosis of cancer using Cancer Biomarkers. According to the National Cancer Institute, a biomarker is a biological molecule found in blood, other body fluids, or tissues that is a sign of normal or abnormal process of a condition or disease such as cancer [4]. Biomarkers may be proteins, nucleic acids or peptides. In medicine however, cancer biomarkers are limited to proteins only. The presence of biomarkers in blood or any other body fluids confirms the presence of cancer cells in the body. There are different biomarkers for different types of cancers. For example, the biomarkers CYFRA (Cytokeratin19fragments), CEA (Carcinoembryonic antigen), EGFR (epidermal growth factor response), SCC (squamous cell carcinoma antigen are used for detection of lung cancer [5]. Biomarkers MUC-1(CA27.29 and CA

15-3) and carcinoembryonic antigen are the two biomarkers that are approved by the Food and Drug Administration (FDA) for monitoring and treatment of the advanced or recurrence breast cancer [6]. Biomarkers such as CA-125, CA 72-4 have been clinically used for ovarian cancer [7]. Biomarker CA 19-9 has been clinically used to detect Pancreatic Cancer [8]. Alpha-fetoprotein biomarker is widely used for detection of hepatocellular carcinoma (HCC) [9]. Prostate Specific Antigen (PSA) is the most widely used biomarker for prostate cancer [10]. High levels of CEA, mutated KRAS, TP53, APC are recognized biomarkers for colorectal cancer [11]. Carbonic anhydrase IX (CA-IX) biomarker is used to Renal Cell Carcinoma [12]. The recognized biomarkers for oral cancer are IL-8, IL-1-β and S100P [13]. High levels of epidermal growth factor receptor (EGFR) alongwith expression of 0-6 methylguanine-DNA methyltransferase (MGMT) have been clinically used as a biomarker for malignant brain cancer (gliblastomas) [14]. Mutation of oncogenes such as FLT3, KIT are considered as biomarkers for acute leukemia [15]. Human papillomavirus (HPV) is the single most important etiological agent in cervical cancer, contributing to neoplastic progression through the action of viral oncoproteins, mainly E6 and E7 [16]. Classic biomarkers for gastric cancer diagnosis include carcinoembryonic antigen and cancer antigen 19-9, while microRNA and DNA hypomethylation are proposed as novel biomarkers [17]. RASSF1A methylation has been considered as a biomarker in melanoma (skin cancer) patients [18]. In the modern era the two disciplines of proteomics and genomics have helped the researchers to identify novel biomarkers for cancer detection [19]. Today different biomarkers have been used clinically for screening, diagnosis and monitoring for different cancers. Biomarkers are found in different quantities in blood, saliva and other body fluids [20]. Biomarkers have been recognized as a novel approach for early cancer detection.

3. Biosensors

Owing to the non-invasive early detection of cancer researchers over the globe have started to design and develop biosensors that could detect cancer efficiently. Biosensors are devices that are designed to detect a specific biological analyte by essentially converting a biological entity (protein, DNA, RNA) into an electrical signal that can be detected and analyzed [21]. Since the sensor senses biological materials the word “Bio” comes into play. The biological material can be enzymes, antibodies, micro-organisms, nucleic acids etc. Prof. Leland C. Clark Jr. is known as the “father of biosensors” and the modern day glucose sensor is based on his research [22]. The three most important elements of a biosensor are a biological recognition element, a transducer and a signal processing system [23]. The biological element must be highly specific, stable and immobilized. Based on the biological recognition element biosensors are classified into the following categories: enzymatic, protein, receptor based, DNA and whole cell biosensors [24]. The transducer converts recognition signal events into electrical signals. Based on the signal transduction mechanism biosensors are further classified into the following categories: Electrochemical, Thermal, Optical and Mass Sensitive Sensors [25]. Electrochemical transducers are the most widely used in sensor technology but however, optical transducers are gaining importance in the modern era due to their several advantages. Signals from the transducer are passed to an electronic system for amplification and display.

4. Biosensors for Cancer Marker Detection

Researchers and scientist are trying to design and develop biosensors for detecting cancer markers to detect early cancer. The use of biosensors for protein biomarker analysis has been developed as an attractive and cost effective technique for the development of point of care devices [26]. Electrochemical biosensors have played a significant role in cancer marker detection [27]. Sensors based on spectroscopy of surface plasmons, sometimes referred to as surface plasmons resonance sensors (SPR) are being used for label free detection of cancer markers [28]. Piezoelectric biosensors have also been exploited for cancer marker detection due to their light weight, high sensitivity and low power requirement [29]. W. Tan *et al.* [30] have developed a surfaced immobilized optical protein sensor to detect an IL-8 marker for oral cancer detection. J. Yuan *et al.* [31] have developed an SPR based biosensor for the detection of cancer markers in ovarian cancer. T. Kumeria *et al.* [32] have developed a microchip biosensor based on nanoporous aluminia for detection of circulating tumor cells. A. Malima *et al.* [33] have developed a highly sensitive microscale in-vivo sensor enabled by the electrophoretic assembly of nano particles for multiple biomarker detections. Optical Biosensors are gaining importance in the modern era for detection of biomarkers due to its high sensitivity, specificity, small size, rapid and cost effectiveness [34]. High multi disciplinary approaches like nanotechnology, MEMS (micro electro mechnaical systems), NEMS, biotechnology etc have been used in the implementation of new optical biosensors.

5. Conclusion

Due to the several limitations in conventional detection techniques of cancer researchers and scientist are turning their attention towards the development of biosensors for efficient rapid non-invasive detection of cancer markers. Cancer markers confirm the presence of cancer cells in the body. These markers are present in blood, saliva or any other body fluids. Novel biomarkers for different cancers are still in the process of research, although a few of them have been clinically used for screening and monitoring of cancer patients. The development of biosensors paves a new novel approach for rapid early detection of cancer. Different biosensors have been designed by researchers for efficient of the cancer markers. Optical biosensors are gaining importance over other biosensors due to its several advantages. However, the development of biosensors for multiple cancer marker detection is still a big challenge to the scientist and researchers. Integration of high multi disciplinary approaches along with the use of nanomaterials in development of biosensors will enhance the sensitivity of these devices and make it more efficient for early detection of cancer which is the need of the hour.

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