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Biomedical Sensor Technology for Cancer Diagnosis

Madhukara S[1], Manyashree K C[2].

[1]Assistant Professor, Department of Electronics and Communication engineering, S J C Institute of Technology Chickballapur, India, madhukara2008@gmail.com

[2]UG Student, Department of Electronics and Communication engineering S J C Institute of Technology Chickballapur, India, kcmanya471@gmail.com

ABSTRACT-

By mimicking the efficient processes seen in nature, biomimetic sensors are instruments that can reproduce biological receptors and enzymes with remarkable sensitivity and accuracy. By enabling noninvasive identification of cancer-specific biomarkers in physiological fluids, they facilitate prompt diagnosis and improved therapy choices. This paper highlights the advantages of using a variety of optical and electronic biomimetic sensor types in cancer detection. Aptamers, molecularly imprinted polymers (MIPs), and immunomimetic sensors are a few of the recognition elements utilized in biomimetic sensors. Biomimetic sensors show promise for widespread usage in cancer diagnostics, despite challenges related to costeffectiveness and specificity. The implementation of wearable technologies and artificial intelligence enhances the quality of personalized cancer care even further. This review's main goal is to thoroughly investigate the field of biomimeticssensors in the context of cancer diagnostics, stressing the different kinds and components of their recognition, and underlining the important advantages of biomimetics sensors, like their sensitivity and accuracy in allowing for the non-invasive detection of cancer-specific biomarkers. All things considered, biomimetic sensors are a ground-breaking invention that expands our knowledge of early cancer diagnosis, better patient outcomes, and improved healthcare.

Keywords *– aptamers, molecularly imprinted polymers (MIPs), immunomimetic, biomimetics.*

I. INTRODUCTION

The enigma surrounding the genesis of cancer has been dispelled by several studies conducted over the past 20 years, which have advanced our understanding of the disease's molecular mechanisms. A typical, healthy body's cells interact intricately with one another to control each other's growth. The body uses this communication between cells to maintain the structure and size of the tissue. Cancerous cells cut off this connection because they are unable to abide by the standards set out by nearby cells. When they begin to propagate their unchecked growth agenda to neighboring cells, producing aggregates in both surrounding and distant tissues, they become much more deadly. Numerous factors and combinations, including genetics, environment, and lifestyle, can lead to cancer. Carcinogens, such as tobacco, radiation), hereditary reasons (e.g.., BRCA mutations for breast and ovarian cancers) and viral infections (e.g., HPV for cervical cancer). Cancer cells frequently exhibit aerobic glycolysis, a changed metabolic phenomena also referred to as the "Warburg effect." Angiogenesis is the process by which pre-existing blood vessels are recruited to produce new blood vessels in both normal and malignant cells.Neoplastic vascularization is brought on by the upregulation of VEGF, fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), and angiopoietins, and the downregulation of antiangiogenic molecules, such as endostatin, thrombospondin, and angiostatin. Tumor microenvironment factors, such as hormones (progesterone, estrogen), hypoxia, growth factors (endothelial growth factor, transforming growth factor-β, FGF, PDGF, insulin-like growth factor-1), and cytokines (interlukin-1 and interlukin-6), all affect the stimulation of VEGF expression.The complex network known as the tumor microenvironment is made up of the extracellular matriX, stromal cells like fibroblasts, adipocytes, neural and neuroendocrine cells, endothelial cells, and pericytes, as well as other cell types. This network regulates the progression of cancer cells from invasion to intravasation and metastasis. Because both stromal and epithelial processes are reversible at the interface where the stroma and inflammation meet, this is a dynamic region.

It is imperative to take use of technology improvements by merging proteomic and genomic findings with data science to improve detection and reduce the number of incorrect and delayed cancer diagnoses, given the growth in cancer incidence and mortality worldwide. It is thought that computational biology and nano-bioelectronics would be essential instruments for creating novel, targeted biomarkers with molecular association with specific human cancer types and stages.

II. TECHNOLOGIES USED IN HEALTHCARE

Microfluidic devices as point-of-care tools: These tools have drawn a lot of interest from the clinical scientific community and are seen as a promising avenue for revolutionizing medical technology. Compared to giant instruments, microfluidic point-of-care (PoC) devices are said to offer a plethora of

advantages and uses. These include the requirement for nanoliter-sized analytes, decreased sample consumption, and even smaller instrument size and maintenance costs.

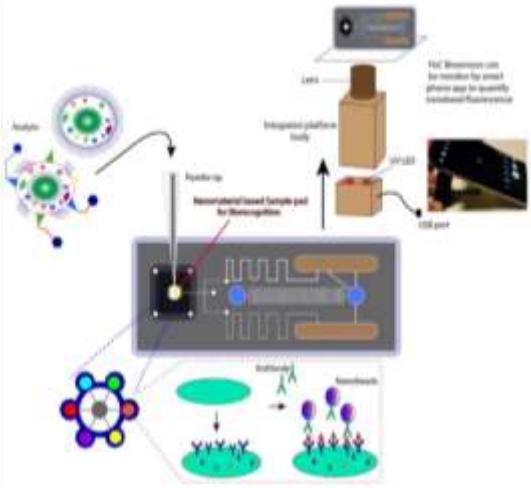

Fig. 1: Molecular point of care devices for real-time diagnosis

A crucial contender for portable point-of-care (PoC) devices is thought to be the quick in situ identification and processing of the targeted biomolecule within the micro-reactor, which has also been identified as a major contributing element during surgery. The development of liquid biopsy, which uses a simple blood sample to detect cancer, depends on the capacity to isolate cancer cells. This would do away with the expense and discomfort associated with needle-based or surgical tissue biopsies. Additionally, liquid biopsy may be helpful in monitoring the chemotherapy's efficacy over time and in identifying cancer in organs like the brain and lungs that are hard to access with conventional biopsy methods.

Drawing inspiration from biology and emulating natural sensing mechanisms: The "survival of the fittest" theory severely affects animals in the wild. In order to survive another day, animals have so evolved and developed highly sophisticated sense organs that enable them to react to a wide range of stimuli and recognize even the smallest changes in their surroundings. Researchers have studied this sensing ability in great detail in order to apply it to biomimetics sensors and benefit humanity. Biomimetic sensor technology is an innovative method inspired by the natural world. The domains of robotics, environment monitoring, and medical diagnostics have all greatly profited from this replication of the highly effective systems found in biological organisms. Biomimetics is aimed to mimic the very effective biological receptors found in organisms. The design of biomimetics to function in such a way that they perform the tasks such as ofenzymes with very high precision and efficiency just as much as real enzymes would do so.

Sensors inspired by echolocation: It is well known that animals such as dolphins and bats use sound to navigate around their environment. Numerous SONAR systems are made for underwater navigation using this complex mechanism. Advanced sonar systems with moving sonar that can interpret acoustical glints are one example of bio-inspired sonar in action. By completely reading the surroundings and employing a technology to locate and categorize random items in the surrounding area, this was done to prevent collisions. The use of biomimetic sensors has proven to be quite beneficial in the early diagnosis of numerous illnesses, particularly cancer. Unlike conventional approaches, these sensors offer a non-invasive form of detection and can identify cancer-specific biomarkers, opening up the possibility of early therapy. In one such study, Alpha-Fetoprotein (AFP) is a critical biomarker for liver cancers. The researchers at Horikawa et al. devised a technique to produce Molecularly Imprinted Polymers (MIPs), which are very sensitive and selective. They linked two readily separated functional molecules to AFP chemically to achieve this. They then incorporated two additional molecules into the AFP-imprinted polymers using a multi-step procedure called post-imprinting modification (PIM). These extra molecules performed two distinct functions: one was in charge of binding to AFP exclusively, and the other helped to convert AFP binding into a fluorescence change.

Olfactory systems inspired by insects: Many insects, including moths, butterflies, and honeybees, have highly developed and sensitive olfactory systems that enable them to identify pheromones released over great distances by possible mates and from specific flowers. Research has been conducted to replicate these old-fashioned sensors in order to create synthetic “electronic noses” that are able to precisely detect particular scents. Lu et al. developed a particular odorant-binding protein (OBP) based olfactory biosensor. They immobilized OBPs on interdigitated gold electrodes, namely Acer-ASP2 from honeybees. The purpose of this biosensor was to find ligands. connected to pheromones and floral scents via electrochemical impedance detection.

Furthermore, docking tests were carried out to verify this biosensor's efficacy. These experiments demonstrated the MIP's exceptional selectivity for AFP by showing that its reaction to these proteins was negligible. Shahinpoor's research indicates that biomimetic sensors have found use in wearables as well as robotics and artificial intelligence area. Ionic polymeric-conductor composites (IPCCs) were demonstrated by Shahinpoor as a biomimetic sensor that can be used in robotic actuators and artificial muscles. Another gadget, the Violet® Plus, is simple to clip onto any article of clothing and employs a microprocessor to measure the quantity of UV radiation that hit the skin. It then notifies the user through a mobile app of the excess UV rays to protect them from overexposure and developing skin cancer. Hence, biomimetics have a very promising future in medical and other fields.

Bionic 3D spheroid biosensors: It has been claimed that several diagnostic instruments have been created in contemporary nanomedicine to map and examine the aggressive behavior of various malignancies, including LC, which has been steadily rising globally. In the past, LC diagnosis, cancer metastatic behavior, and even the interaction between cancer cells and the tumor milieu around them have all been studied using microfluidic platforms

(2D and 3D biosensors) [122]. However, traditional drug screening methods have also been employed, involving costly and time-consuming planer grown cell models (2D) to assess the medication's efficacy and noxiousness. Due to their poor prediction capacity in drug testing clinical trials, these two-dimensional in vitro tests have been shown to be unable to replicate the in vivo complexity of three-dimensional tissues. For instance, it has been reported that novel inhibitors (MI-192) that target the migratory and invasive ability of cancer cells can be found using 3D imaging, and they are even being investigated as a viable treatment for gliomas and other cancers. In summary, because of their three-dimensional tumor architecture, 3D spheroid tests are thought to be the most effective method for both screening and identifying promising anticancer medications.

Quantum dots biosensors: Because of its numerous optical characteristics, such as great brightness, simultaneous signal detection, and long-term stability, quantum dots (QDs), which are nanoscale luminous semiconductor crystals, have been employed as promising diagnostic and therapeutic devices. Furthermore, QD has demonstrated remarkable capabilities in the areas of molecular targets, drug tracking, lymph node mapping, and fuorescence resonance energy transfer (FRET), as demonstrated in Fig. 3. In fact, QDs' optical characteristics make them perfect donors for research on FRET and other forms of photodynamic treatment. QD biosensors are seen as potentially useful instruments for different malignancies' early diagnosis. QD biosensors have proven to be quite effective for various clinical uses, including the diagnosis and detection of cancer.

Fig. 2: Application of Quantum dots[1].

For the detection and isolation of circulating tumor cells, for instance, magnetic fuorescent biosensors based on ferrosoferric oxide (Fe3O4), graphene QDs (GQDs), and molybdenum disulfide (MoS2) have been reported to be employed. It has been observed that the GQDs utilized as a probe exhibit low cytotoxicity, excellent biocompatibility, and stable photoluminescence.

Microreactors in the detection of cancer: Because of its expanding range of applications in various fields, microreactor technology is an interdisciplinary field of science and engineering that plays a critical role in biotechnology, medicine, the pharmaceutical industry, as well as clinical and environmental diagnostics. The lab on a chip platform has been made possible by the use of a single microreactor array chip for cell sorting, lysis, and analysis studies. Additionally, instruments connected to clinical diagnostics are emerging to perform a range of biochemical studies, including PCR amplification, cell lysis, separation, and detection. In a nutshell, the first and second surfaces of the sealing membrane and the array of microreactors are oriented in opposition to one another. The construction of the sealing membrane allows it to be moved, covering and sealing a variety of microreactors. A reagent gap, which allows a fluid to pass through both the second surface of the sealing membrane and the microreactor array, is also included in a microreactor array system. Additionally, there is an applicator and an injector to guide a fume against the first surface of the sealing membrane and introduce reagent into a reagent gap, respectively. Additionally, a microreactor array system has detectors.

Overview of Biometric Sensors

Biomimetic sensor technology is an innovative method inspired by the natural world. The domains of robotics, environment monitoring, and medical diagnostics have all greatly profited from this replication of the highly effective systems found in biological organisms. Biomimetics is aimed to mimic the very effective biological receptors found in organisms. The way biomimetics work is intended to replicate the high accuracy and efficiency of natural enzymes in carrying out tasks like enzymatic activity. The use of biomimetic sensors has proven to be quite beneficial in the early diagnosis of numerous illnesses, particularly cancer. Unlike conventional approaches, these sensors offer a non-invasive form of detection and can identify cancer-specific biomarkers, opening up the possibility of early therapy. In one such study, Alpha-Fetoprotein (AFP) is a critical biomarker for liver cancers. The researchers at Horikawa et al. devised a technique to produce Molecularly Imprinted Polymers (MIPs), which are very sensitive and selective. They linked two readily separated functional molecules to AFP chemically to achieve this. They then incorporated two additional molecules into the AFP-imprinted polymers using a multi-step procedure called post-imprinting modification (PIM).

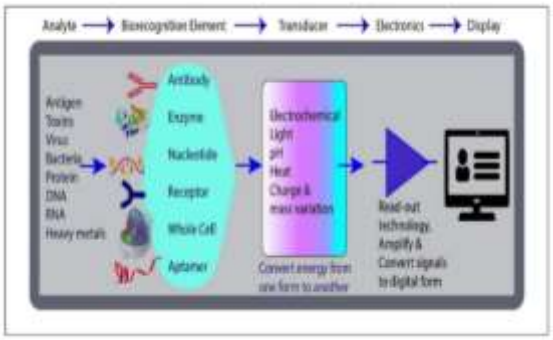

Fig. 3: Schematic representation of a biosensor

Certain imaging techniques (ultrasound, CT scan, MRI, etc.) are required to confirm the tumor recurrence if the marker levels are elevated before to the start of the treatment, normalize during or after the treatment, and then begin to grow after some time.

PET-CT scan) or alternative techniques (biopsies, fluids, tissue, etc.). Since data indicate that activation of oncogenesis pathways results in immune system impairment, limitations of tumor biomarker-based detection in clinical cases stem from the failure to identify all mutations and pathways involved in oncogenesis as well as the mechanisms that allow the tumor to evade the immune system response. In the upcoming years, a significant amount of work will be required to identify and confirm biomarkers that enable patient selection for tailored cancer care. The identification of tumor biomarkers yields valuable clinical data, but it also has drawbacks.

Biosensors and cancer diagnosis

Using a single chip, an ultrasensitive biosensing system has shown to be a great option for quick, automated, sensitive detection and analysis of biological changes in the body or surrounding environment.As digital healthcare systems gain popularity and traction, more and more groups are dedicating their efforts to creating and releasing proof-of-concept biological transmitting devices. Among these, it has been revealed that memristive biosensors may detect PSA and other cancer-related biomarkers, which will open up new possibilities for biosensing technology in the future. Nano-sensing devices are thought to represent the next technological advancement because traditional biological biomarker detection techniques, such as quantitative real-time protein chain reaction (qRT-PCR), microarray, and next-generation sequencing, are significantly more costly and time-consuming for rapid and accurateexosomal micro-RNA analysis. In short, exosomes may be isolated from bodily fluids and discharged into the extracellular surroundings during cell exocytosis. This makes them a promising diagnostic for the early identification of cancer. Among these, tumor-associated exosomes (TEXs) are novel biomarkers for the detection of non-small cell lung cancer (NSCLC) and have been shown to play a major role in carcinogenesis. To be more precise, "miR-21" and other TEXs microRNAs are exosomal biomarkers for lung cancer (LC) that may be detected quickly. TEXs have a chemical affinity for the biochip surface in microfluidic biochips because of the ion-exchange nanomembranes present. The majority of clinical microdevices on the market today require RNA, DNA, or protein extraction techniques, and a large amount of data is gathered from clinical trials that seek to directly identify.

Therapeutic perspectives on biosensors and biomarkers in cancer management

Modern sequencing tests are among the many tests that have been created to find biomarkers that may be able to predict the therapeutic response to different target therapies. Finding biomarkers is just the beginning of the fight against cancer. Before beginning treatment, tumor biomarkers can be measured to determine the best course of action. Certain biomarkers in tumor tissue are the target of specific targeted therapies. If a biomarker is prevalent enough in a particular cancerous location and is linked to a targeted therapy that has been approved by the FDA or the European Medicines Agency (EMA), selecting a treatment option that is tailored to the unique characteristics of the tumor—or, in other words, therapy that is personalized—is the inevitable outcome.

Examples of tumor tissue markers commonly used in oncological pharmacotherapeutic management:

-Progesterone and estrogen receptors (breast cancer), which are used to assess the suitability of hormone therapy.

- Examination of the genetic mutation for EGFR (non-small cell lung cancer) in order to establish a course of treatment and aprognosis. -Programmed death-ligand 1 (PD-L1) and mutational tumor load (TMI) to determine if a certain kind of targeted inhibitor therapy is the right course of action.

Personalized therapy, which is now known as precision medicine, has garnered significant attention in recent years. The action of chemicals essential to the development of cancer cells is inhibited by targeted therapy. However, this treatment targets cancer cells more than healthy ones. Traditional chemotherapy affects all fast-growing cells; tailored therapy targets specific cells. Targeted therapy comes in two primary forms. Small molecule medications are the first kind; they are tiny enough to enter cells. Monoclonal antibodies are the second type; they are too big to fit into cells. On the other hand, monoclonal antibodies target either targets on the surface of cells or targets outside of them. Target therapies include immunotherapies, hormone therapies, gene expression modulators, signal transduction inhibitors, apoptosis inducers, angiogenesis inhibitors, and monoclonal antibodies that deliver hazardous chemicals.

Tumors can exhibit a wide range of genetic abnormalities at times. Depending on the situation, different mutations or variations of a single gene may have different effects and respond differently to target therapy. One of the most notable and significant examples of personalized biomarker-based therapy is the creation of the monoclonal antibody trastuzumab and its use to breast tumors that express epidermal growth factor 2 (HER2). This treatment has significantly improved the prognosis for HER 2-positive breast malignancies. First-line trastuzumab therapy's objective response rate ranged from 34 to 37% in patients with or without HER 2 gene amplifcation, demonstrating the effectiveness of target treatments in cancers exhibiting genetic aberrations. Currently, numerous target therapies based on companion diagnostic tests have been approved in different therapy lines for cancer. The outcomes of these Tests enable each patient to select the target therapy that is most suited to them (e.g., measurement of BRAF V600 mutations for anti-RAF and anti-MEK target therapies, or BCR-ABL fusion genes for Imatinib treatment in acute or chronic myeloid leukemia). Biomarkers play a prognostic function in customized therapy, but they are also predictive in evaluating the therapeutic response, enabling the identification of individuals who are most likely to respond to a particular treatment, combining both sensitivity and resistance to different target therapies (malignant melanoma with a BRAF V600 mutation, for example, responds well to Vemurafenib therapy, but the "wild" form is resistant to it). They can also offer details on toxicity susceptibility in the context of targeted treatment. The ability to find predictive molecular biomarkers for prognosis, sensitivity or resistance to a therapeutic agent or combination therapy, and the evaluation of their related toxicity is the first step in the application of individualized cancer therapy. The goal of current efforts is to find predictive biomarkers for therapy benefit. The delivery of target regimens for each molecular change of each tumor still presents a therapeutic conundrum.

Advantages/applications of biomimetic sensors for cancer diagnosis

Biomimetic sensors have several benefits when it comes to cancer diagnosis. We'll talk about a couple of them here. When cancer arises, biological systems have a number of biomarkers. The body has defense mechanisms in place to fend off malignant cells, but occasionally they fall short. Here is where biomimetic sensors come into play since they can recognize these biomarkers, such proteins or nucleic acids, even in low concentrations, enabling accurate and timely diagnosis.

Identification of cancer

Conventional methods of detecting cancer are quite intrusive and frequently result in negative effects following therapy. In response, non-invasive methods known as biomimetic liquid-based techniques were created to detect these biomarkers in human fluids such as blood, saliva, and urine. Biomimetic sensors are more dependable than conventional techniques because of their great specificity and sensitivity. Additionally, biomimetic sensors can identify cancer biomarkers early on, enhancing the efficacy of conventional therapy. Additionally, biomimetics sensors can be used with nanotechnology to enhance their selectivity and sensitivity, which are lacking in conventional therapies. produced a novel vaccine that served as an example of biomimetic nanoparticles.They used an azide-modified tumor cell membrane to enclose a magnetic nanocluster (MNC). Before that, anti-CD205 was used to decorate the cancer cell membrane and toll-like receptor agonist CpG oligodeoxynucleotide (CpG-ODN), which is known to promote immunity, was coated on the surface of the nanocluster.

The nano-vaccine's distinct capacity to be particularly recognized by CD8+ cells was made possible by its tailored design. Its effectiveness was amply proven in five distinct cancer models in both preventive and therapeutic situations . Zhang et al. revealed another example of biomimetic nanotechnology when they were able to successfully produce adaptable artificial antigen-presenting cells (aAPCs) with a variety of uses. This was accomplished by creating a biomimetic magnetosome, which involved utilizing azide to encase magnetic nanoclusters in modified whole blood cell membrane (WBCM). They next attached T-cells to these nano aAPCs using copper-free click chemistry. These biomimetic artificial APCs demonstrated amazing capacities in cytotoxic T-cell expansion and activation with a particular antigen response. Additionally, they effectively used magnetic resonance imaging to guide cytotoxic T-lymphocytes (CTLs) to tumor areas. magnetic management. These T-cells successfully suppressed tumor growth in a mouse lymphoma experimental model, highlighting the great promise of the aAPC platform for T cell-based cancer immunotherapy. These days, point-of-care diagnostic tools are highly efficient and well-liked. In addition to avoiding the need for a trip to the doctor, portable diagnostic tools enable quick findings and real-time analysis. This is especially helpful when a patient is diagnosed with cancer, as early intervention can have a significant impact on their prognosis. In one such study, Zhang et al. modified GC surfaces with CdTe QDs, which are semiconductors that serve to expand the electrode area. This allowed for the subsequent immobilization of a DNA probe, leading to the creation of an electrochemical biosensor for the detection of certain DNA sequences associated with bladder cancer. Subsequently, target DNA sequences were hybridized, and methylene blue was used to get electrochemical data via differential pulse voltammetry. The sensor's affordability, ease of use, fast response time, high selectivity and sensitivity, and low cost make it an important tool for the medical field to succeed.

CONCLUSION

In order to improve diagnosis and treatment, technology has made it possible to gain a deeper understanding of the biological intricacies of humans, including cancer and other serious disorders. The field of study into identifying cancer cells and associated biomarkers is expanding these days, with a focus on the creation of sophisticated biosensing devices for clinical applications. In summary, biosensors engage with biological entities such as DNA, RNA, and proteins, generating a signal that is subsequently detected by a detector.Biosensors have the ability to enable more precise detection, monitoring, and trustworthy imaging of different cancer cells because they are primarily intended for use in clinical applications to identify cancer biomarkers and assess the efficacy of drugs at certain areas. The most sensitive sensing devices currently on the market are electrochemical biosensors, which are being studied in clinical settings to revolutionize clinical applications. Numerous other multifunctional sensing devices, such as optical and quantum dot biosensors, and microfluidic nanostructures as point-of-care devices, are also highly sensitive.

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