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Research Article

Biomarkers

Clinical Significance of Biomarkers in Oncology and its Application in Advanced Biosensing Technology- A Comprehensive Review

Das S.[1], Roy S.[2], Bose A.[3], Choudhury S.[4], Kumar Pal T.[5], Mondal S.[6*]

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[1] Sourav Das, School of Pharmacy, The Neotia University, West Bengal, India.

[2] Sukanta Roy, School of Pharmacy, The Neotia University, West Bengal, India.

[3] Anirbandeep Bose, Taab Biostudy Services, India.

[4] Sangeeta Choudhury, Taab Biostudy Services, India.

[5] Tapan Kumar Pal, Bioequivalence Study Centre, Jadavpur University, Kolkata, West Bengal, India.

[6*] Subhasish Mondal, School of Pharmacy, The Neotia University, West Bengal, India.

Cancer detection in early stages may decrease the death rate as initial treatments may be employed which will minimise the chance of becoming metastasis. After mutation few specific proteins, enzymes are overexpressed for different cancers, which are identical for different cancers. The presence of those specific bio-molecules and concentrations of those bio-molecules in biological sample, known as biomarkers can be an important tool in detecting cancer. Apart from the earlier detection techniques, new detection trends has been employed in cancer research. Sensors for biological molecules i.e., optical, electrochemical, magnetic sensors are employed which provides digital signals against biological samples via different mechanisms. These bio sensing technologies enables cost effective, simple, sensitive outcomes, which minimises cancer detection complications. Herein, we have discussed various biomarkers employed in detection cancers with new detection trends using biosensors of different mechanisms like microfluidic chips in smartphone, nano molecule based biosensors etc. On the verge of twenty first century, introduction of artificial intelligence (AI) based approach for detection of biomarker for cancer detection has brought new beam hope for early detection of camcer. Those emerging strategies also have been discussed in this context.

Keywords: Biomarkers, Biosensor, Electrochemical Biosensor, Optical Biosensors, Nano Technology

Corresponding Author

Subhasish Mondal, , School of Pharmacy, The Neotia University, , West Bengal, India.
Email: subhasish.mondal@tnu.in

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Introduction

Cancer is the second lethal cause of human death globally and based on published literatures, approximately 9.6 million deaths accounted in 2018.[1] There are several major causes of cancers: which includes, tobacco and alcohol consumption, poor hygiene less fibrous diet, lack of physical activity or some chronic infections caused by Helicobacter pylori, Human papilloma virus (HPV), Hepatitis B and C virus and Epstein-Barr virus etc.[2-5]According to World Health Organization report, (WHO, 12 September 2018) the most common cancers are lung, breast, colorectal, prostate, skin (non-melanoma) and stomach cancer. Aging and poor hygienic condition causes formation of free radical leading to oxidative damage to mature cells. Formation of free radicals are responsible for genomic alteration and attenuates age related oxidative damage repair mechanism in our body by suppressing different cytokines and other immunomodulaents; which is closely related to progression of different kind of cancers.[6] Apart from that, different other causative mechanisms; i.e., microbial attack in host cells, viral infection, cell necrosis caused by radiations also contributes mutation in specific cells employed in the pathogenesis of different types of cancers. Among the Different therapeutic modalities of cancer, surgery has been proved to be most effective globally, before metastatic stage.[7] However, detection of the disease in pre-invasive is very crucial for optimal treatment for the patient. Similarly chemotherapy (i.e., Hormonal modulators, cytotoxic agents, different antibiotics etc) and radiotherapy have been successfully implemented worldwide for a variety of cancer types; specifically Cisplatin and its analogues have found global application.[8-11]Furthermore photodynamic therapy (PDT), a relatively modern and minimally invasive treatment modality has been developed and found appreciable success against oral and skin cancers. Photofrin® is a FDA approved drug which is based on PDT.[12]Additionally, these treatment minimises suffer from several adverse side-effects; namely, prolonged skin sensitivity, hepatotoxicity, nephrotoxicity, neurotoxicity and ototoxicity.[13-14]

However, in most of the cases of advanced or metastatic cancer, the effectiveness is very disappointing for these therapeutic methods.

In last two decades, immunotherapy has been emerged as a potential alternative and/or, complementary therapeutic method which involves either enhancement of patient's immune system by activating specific cytotoxic lymphocytes or de-activating immune regulator cells.[15]On the whole, mass awareness and early detection of cancer involving a rapid and proper diagnosis, can lead to change the scenario for betterment. The novel approach towards the early detection and treatment of cancer, monitoring the progress of the disease was implicated with use of biomarkers, which is a genetic reference of specific amino acids sequence. The altered gene expression is measured with this specific standard. The definition of biomarker as given by National Cancer Institute (NCI): "A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. This also called molecular marker and signature molecule." Biomarkers also contribute to appropriate treatment modalities for individuals and finding the chance of reoccurrence of the diseases.[16-18]

Characteristics and Classifications of Biomarkers:

According to some opinions, biomarkers are restricted to distinguishable and quantifiable proteins obtained from the blood, body fluids, tissue or urine. The term is commonly used to cover a wide range of bio-chemical identities, i.e., biochemical, physiological, anatomical qualitative, or quantitive elements that can be measured. Omics, a modern immerging tool based on high throughput techniques are known to have epitomized the major path for biomarker discovery.[19] Most Biomarkers have been identified following allocation of genetic signatures in biopsy tissue. Other Omics and deep-sequencing strategies are involved to reveal noteworthy information, related not only to protein-coding genes but also to non-coding elements such as microRNAs, as well as proteins and metabolites.[20,21] Biomarkers are measurable either in tumor tissue while executing biopsy, or circulating in the blood, urine, and other body fluids. They can be formed either by the tumor itself or physiological response to it. There are some essential characteristics of any potential biomarker [22]:

- It should be involved in cancer-causing process;
- Alterations in it should be related unequivocally with changes in the disease;
- Its quantity should be high enough to measure easily and consistently;
- The extent or occurrence of biomarkers should be readily able to distinguish between normal, cancerous, and precancerous tissue;
- Effective treatment of cancer should cause an alteration of the level of the biomarker;
- The level of the biomarker should not change spontaneously or in response to other factors which are not related to the successful treatment of cancer; the level of biomarkers should vary with different stages of carcinogenesis
- Quantification of biomarkers should be reproducible, highly specific, and sensitive.

Based on the functionality, biomarkers can be broadly classified into three types [23,24]:

A. Diagnostic: This kind is to detect the early stage of carcinogenesis;

B. Prognostic: This type provides a conjecture of a patient's disease progression, irrespective of treatment modality;

C. Predictive: This kind is to predict how well a patient will respond to a treatment modality i.e. provides insight into the response or resistance of a therapeutic drug for an individual. It also predicts the chance of reoccurrence of the disease after successful treatment.

Another classification of Biomarkers was done, and based on Bio-chemical characteristics summarized in Fig 1.

Some biomarkers can be diagnostic, prognostic, and/or, predictive simultaneously. For example, E-cadherin and estrogen receptor (ER) could be recognized for the diagnosis of a patient having breast cancer. The prognostic biomarkers, ER and progesterone receptor (PR) could be recommended that the patient had a superior chance of survival than a comparable patient whose tumor did not exhibit those biomarkers. The occurrence of the predictive biomarker, HER-2 could suggest that trastuzumab might be an effective treatment for this tumor. [25]

Table 1 and Fig 2 representing different cancer-specific biomarkers tested from serum, tissue or, urine is given below:

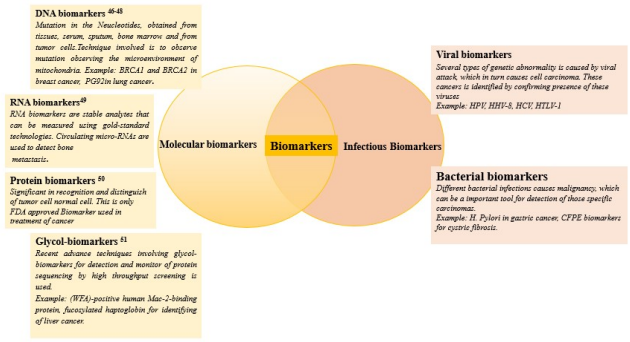

Fig 1: Classification of Biomarkers based on its biochemical nature

Table 1. List of Biomarkers isolated from serum, tissue and urine samples and their use in different carcinomas. [26-30]

Biomarker	Cancer
AFP (Alfa-fetoprotein)	Liver cancer
BCR-ABL (Philadelphia translocation)	Chronic Leukemia
BRCA1/BRCA2 (human gene and its protein product)	Breast
BRAF V600E (Proto-oncogene)	Melanoma/colorectal cancer
CA-125 (mucin 16 glycoprotein)	Ovarian cancer
CA19-9 (Antigen defined by monoclonal antibody)	Pancreatic cancer
CEA (Carcinoembryonic antigen; glycoprotein)	Colorectal cancer
EGFR (Epidermal Growth Factor Receptor)	Non-small cell lung carcinoma
HER-2/CD340 (Proto-oncogene neu)	Breast cancer
KIT/SCFR (Stem cell growth factor receptor)	Gastrointestinal cancer
PSA (Prostate Specific Antigen)	Prostate cancer
S100 (Protein)	Melanoma
Thyroglobulin	Thyroid cancer
hGC (Human Chorionic Gonadotropin)	Testicular cancer
ER (Estrogen Receptor)	Breast cancer
PR (Progesterone Receptor)	Breast cancer
BTA (Bladder Tumor Antigen)	Bladder cancer
NMP-22 (Nuclear Matrix Protein)	Bladder cancer

Techniques to Detect Cancer Biomarkers:

Chemically, biomarkers can be of different kinds; it can be genetic material (DNA or, RNA) based, protein or antibody-based and manifested as genetic/epigenetic abnormalities, altered RNA expressions, altered protein expressions, or, or antigen-antibody interactions respectively.[31-35]

DNA-related biomarkers can be optimized from chromosomal analysis by fluorescent in-situ hybridization (FISH), comparative genomic hybridization (CGH), or, methylation analysis. Again RNA based biomarkers can be detected by expressed sequence tags (EST) and sequential analysis of gene expression (SAGE) techniques.[36] The abnormal protein expressions can be identified by conventional proteomic tools i.e., 2-dimensional gel electrophoresis (2-DE), mass spectrometry(MS), matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF), Surface-enhanced laser desorption/ionization (SELDI) techniques. Antigen-antibody interactions can be monitored by immunological assays like Western blotting, frozen section immunohistochemistry, Enzyme-Linked Immunosorbent Assay (ELISA) and Radioimmunoassay (RIA).

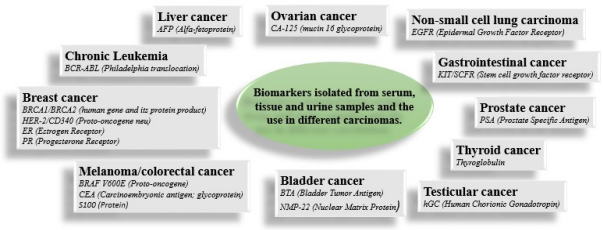

Fig 2: Schematic diagram of different biomarkers isolated from serum, tissue, and urine sample

2-Dimensional Gel Electrophoresis (2-DE) technique:

This technique involves the extraction of protein from a specific sample followed by two-dimensional gel electrophoresis (2-DE), which is known to furnish the isoelectronic point vs. molecular weight profile of the separated proteins.

This technique contributes, the quantification of a complete range of proteins (independent of pH range) through a pH gradient in both preparative and analytic amounts.[31,33,37] Downregulation of cytokeratins, psoriasin, galectin 7 and stratifin for bladder cancer, upregulation of calgranulin B for colorectal cancer, upregulation of ubiquinol cytochrome C reductase for renal carcinoma cells, upregulation of napsin for lung adenocarcinomas, upregulation of protein p19/nm23-H1 for neuroblastoma are few examples of biomarkers identified by 2-DE technique. The technique of detection is summarized in Fig 3.

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Mass Spectrometry (MS):

After resolving protein samples by the 2-DE technique, the resolved proteins get proteolyzed to peptides which can be subjected to MS for characteristic mass to charge (m/z) ratio. Selecting a particular peptide obtained from the specific protein, the tandem mass spectrometry (MS-MS) technique (summarized in Fig 4) can furnish further fragmentations of the peptide to the complementary amino acids.

This technique is capable of identification of possible post-translational modifications like phosphorylation or glycosylation of the proteins by shift in specific mass of them.[31,33] Various modified proteins had been identified in different carcinogenic conditions by this technique; specifically, upregulation of cathepsin D for lung adenocarcinoma; upregulation of retinoic acid-binding protein and carbohydrate-binding proteins for ovarian carcinoma; protein deglycase DJ-1upregulation for fibroadenoma; downregulation of 14-3-3 and upregulation of nuclear matrix, redox, and cytoskeletal proteins for primary breast carcinoma. [38]

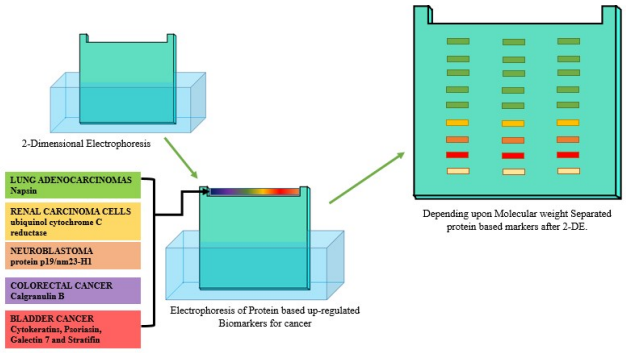

Fig 3: Diagram representing biomarker detection using two-dimensional gel electrophoresis (2-DE)

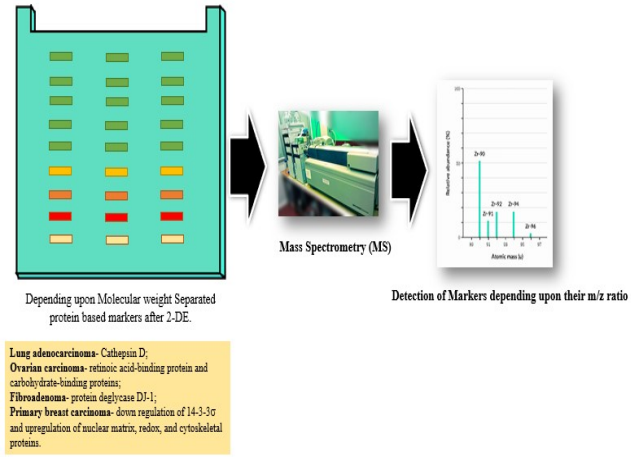

Fig 4: Diagram representing the identification of biomarker using Mass Spectrometer

Surface-Enhanced Laser Desorption/Ionization (SELDI) techniques:

This method involves a salient advantage to analyze an infinitesimally small quantity of protein (as low as 10-15 molar concentration and volume of 0.5 L) based on surface-enhanced affinity capture, through the use of explicit probe surfaces or chips. SELDI contains an immobilized metal affinity surface along with bio-chemical recognizing units like receptors or antibodies.[31,39]

SELDI coupled MS technique particularly indicates m/z peak of the resolved protein. SELDI-MS system (summarized in Fig 5) has been utilized to increase the recognition rate of bladder cancer to 75% in contrast to the 30% by traditional urine cytology technique.

SELDI technique also has been used for detecting protein-based biomarkers for breast, prostate, lung and ovarian cancer, either over expressed or present in lower amount than normal physiological condition for different age group. [40]

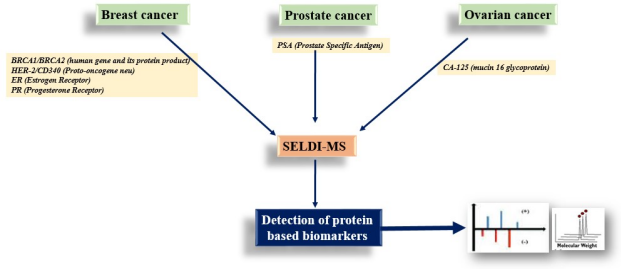

Fig 5: Schematic diagram of detection of biomarker using Surface-Enhanced Laser Desorption/Ionization (SELDI) techniques

Isotope-coded affinity tags (ICAT):

In this technique (summarized in Fig 6) cysteine residues of the protein samples are labeled with lighter ^{32}S and heavier ^{34}S tags using standard ICAT chemical tagging agents.

After that proteolytic digestion of the sample is purified through avidin affinity chromatography and subjected to mass spectrometry. Endometrial, pancreatic, prostate, and many more cancer-related biomarker proteins have been detected by this technique.[41-13]

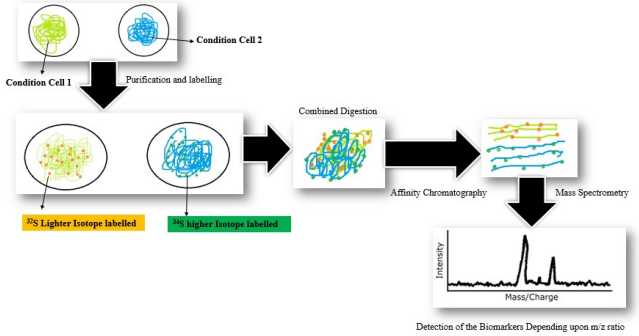

Fig 6: Diagram representing detection of biomarkers in Mass spectrometer using Isotope-coded affinity tags (ICAT)

Fluorescent In Situ Hybridization (FISH): Fluorescent in situ hybridization (FISH) is a cytogenic technique in which fluorescent-based nuclear dyes are utilized to detect a particular chromosomal location inside the nucleus and compared to normal physiological conditions and pre or, post-therapeutic scenarios (summarized in Fig 7). Fluorescence Microscopy based imaging is the key to this technique. Some gene and gene-related labeling agents are as follows: Gene: Fluorescence dye; c-myc: spectrum green; Rb1 : PF555; Chk2: PF590; p53: HyPer5; BRCA1: PF415; Different hematologic malignancies and solid tumors related genes have been identified in previous decades and thus FISH related applications also have been extended as the technique can provide a spatial-temporal pattern of gene expression in sample cell or tissue. Some specific examples are: BCR/ABL1 translocation for chronic myeloid leukemia, HER2 amplification for breast cancer, and ALK rearrangement for lung adenocarcinoma have been recognized by this technique.[43] For personalized targeted therapy, many "predictive biomarkers" have been detected and monitored by the FISH technique.

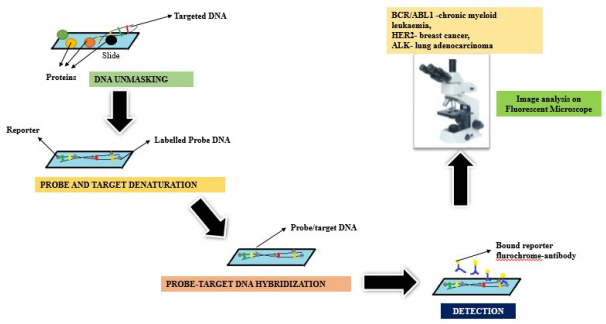

Fig 7: Simple schematic diagram of Fluorescent in situ hybridization (FISH) technique for detection of biomarkers

Comparative Genomic Hybridization (CGH):

Amplifications and deletions are some common genetic alterations that are involved in carcinogenesis and required to be monitored. The comparative Genomic Hybridization (CGH) technique (Fig 8) provides the privilege to investigate DNA-copy number variation across a whole genome. DNA extracted from the samples are subjected to co-hybridize with normal metaphase chromosomes and the fluorescence ratios along the chromosome furnish a cytogenic profile of relative DNA-copy number aberrations. For example, more than 50-fold amplification of CMYC region in copy number profile of chromosome 8 in breast cancer cell line COLO 320, is a signature of carcinogenesis identified by the CGH technique.44 Circulating tumor DNA (ct-DNA) has been extensively studied by CGH and other techniques like Single Nucleotide Polymorphism (SNP) analysis and Next-Generation Sequencing (NGS) and is recognized as a significant biomarker for breast cancer, colorectal cancer, non-small cell lung cancer and many more.

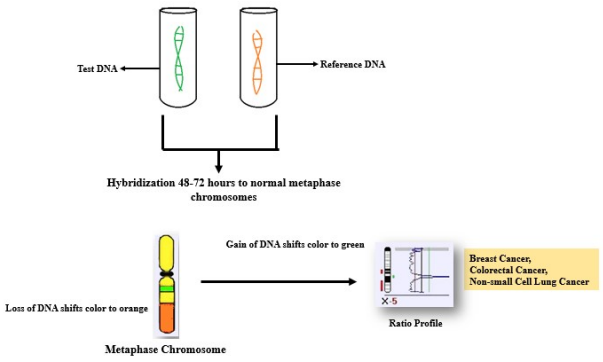

Fig 8: Schematic diagram of Comparative Genomic Hybridization (CGH) technique for detection of biomarker

Challenges associated with Biomarkers used in carcinoma:

For identification of disease, several processes has been adapted like, FNAC first (Fine needle aspiration cytology), core-needle biopsies to surgical biopsies from the centre or peripheral tissues is collected as specimen. The protein sequence was then studied in general with a standard specific sequence. Some recent techniques involved, one of them is identification of tissue block by matrix-assisted laser desorption ionization (MALDI) with imaging (MALDI imaging mass spectroscopy; MALDI-IMS). This method enables proteomics based study, which is much important for tissue study emphasized on biomarker identification and targeting peptides from specimen. 52-53 The main challenge associated with this study is low signal to noise ratio and low mass accuracy of peptides. Another vital issue accompanied with using biomarker is: for those populations who didn't undergo an early detection due to lack of awareness the tumour start to grow silently and reaches to metastasis. Detection and treatment of cancer is limited for only few type of carcinoma, i.e., breast cancer, Chronic Leukemia, Ovarian cancer, colorectal cancer, Pancreatic cancer, lung carcinoma, Gastrointestinal cancer, Prostate cancer, head and neck cancers (Mouth, tongue, hard palate, gum, mandible, parotid cancers Thyroid cancer; but for other cases the option is still very much limited. It was early demonstrated from hereditary aspect that, breast cancer and cervical carcinoma ovarian cancer are of gynecological tumours, which creates a chance to develop in their upcoming generations. But, on many occasions, it was found that the type of alteration of genomic sequence is different. This is another circumstance where detection involved with biomarkers becomes harder.

Moreover, it was observed for a few types of cancers that the progression towards the metastatic phase is very slow (for instance, breast or prostate cancer may take 15-20 years to reach in metastatic stage). Therefore, cancer detection by using may not be possible for early detection. It was also found that some biomarkers associated with some other physiological disorders, like PSA, it is associated with the detection of Prostate Cancer, but in other inflammatory condition in the prostate, the level of PSA can rise. So, this may be a difficult condition where to identify disease. 78,79 When a tumour already metastasizes, it becomes difficult to find its

Primary site of growth and a biomarker couldn't be detected for that.

Biosensors, as tool of advance Biomarker detection:

Cancer detection is a complex process, most of the patients who die in cancer is because of delay in cancer detection. As at the initial stages cancer does not give any specialised symptoms except solid tumours which are visible. Moreover, confirming the nature of solid tumour whether is benign or malignant needs complex and costly diagnosis process. To overcome such problems, attempts is being taken by researchers all over the world. Implementation of biosensors is a novel approach which may simplify the diagnosis related problems. Biosensors are nothing but biomedical devices which processes a biological response in the form of digital signal, named as transducer.[54] Biosensor tools, more specifically transducers are categorized based on detection techniques: Optical biosensors (basic principle is fluorescence, luminescent, colorimetric detection), Mass (Piezoelectric sensor used based on mass changes), Electrochemical biosensors (amperometric and potentiometric detector, electrodes detect electric charge response from biological response by means of amperometric principle), Thermal transducer (detects using exothermic heat produced). [55,56]

Advanced Cancer detection technique using smartphone:

As the modern science is improving at a very high rate the use of electronics and smartphone has been raised and it is capable of solving many sorts of problems. Nowadays, smartphones has become a mode in detection tool in diagnosis purpose of disease, especially cancer detection. High resolution cameras with extra features and improved imaging technology is capable of detecting different biological entities; like, nucleic acids, enzymes, specific proteins, DNA, RNA etc. [57,58] The camera is used here as 'Detector' whereas, complementary metal oxide semiconductor (CMOS) acts as 'Smart recorder' and the specialized App acts as the 'Final outcome'. The basic principle of detection is based on imaging, absorbance, fluorescence, surface plasmon resonance etc. Concentration of the specific biological marker as analyte is measured and the signal is converted into colorimetric outcome and recorded.

The biosensor used in the smartphone detects the obtained colour intensity and help to determine if there is any immune-complex formation or formation of any particular protein. The CMOS sensor attached to smartphone detects the biological sample by the means of optical signal and the data is processed by logical programming available in smartphone. [59] This detection technique using biosensor is capable of reducing the complication of cancer detection. This approach is cost effective, hazardless, simple and most importantly is available for all smartphone users.

Recently, use of microfluidic chips in smartphone based cancer detection is a recent trend for cancer detection. In 2020, Tiffany-Heather Ulep et al, developed Dual layer paper microfluidic chip for detection of blood cancer in human. ROR1+ (receptor tyrosine-like orphan receptor 1) was used as biomarker, which is found in buffy coat of blood sample. Among the two layers of paper microfluidic chip first layer contains a specific antigen for ROR1+ and the second layer contains cellulose chromatography paper. The flow velocity and imaging of antigens were selected as the standards of identification of cancer from complex tissue of buffy coat. [60]

Use of nano technology in Electrochemical Biosensors: Recent advancement in nanomaterial used in Electrochemical Biosensors has opened a new window in cancer detection and related research. Studies showed that, graphene or nanomaterials using carbon has prominent capability of electron transferring. Carbon nanotubes, Graphene, Carbon quantum dots, Carbon Nanohorns, Carbon Nanodiamonds, Carbon Nanofibres, Carbon black etc is nowadays used in the field of biosensors specifically Electrochemical Biosensors. These nanomaterial has few advantages, like, i) Biocompatible, ii) lower limit of detection value iii) more sensitive iv) non-toxic etc. [61,62]

Carbon nanotubes was introduced in 1991 by Japan, it is a folded carbon sheets and having a cylindrical like structure.[63] The advantages of nanotube in biosensor are, i) highly sensitive ii) enables faster electron transfer which contributes in faster detection of electronic signal iii) it has a lower (LOD) limit of detection, so, lower signal also may be identified iv) capable of capturing biological samples like protein, neuclic acid or tissue samples. [64]

The shape of Carbon nanotubes varies from zigzag to chiral due to the rolling techniques and honey comb structure of the unrolled graphene sheet. The chirality of the Carbon nanotubes offers the conductivity of carbon nanotube. [65,66,67] Carbon nanotubes has few specific physical and electrochemical properties, and the ranges varies like; Thermal conductivity- 6600 $Wm^{-1}K^{-1}$, Electrical conductivity- 2×10^{-2}–0.25 Scm^{-1} , Specific gravity- 0.8–2 $g^{-1}cm^{-2}$, surface area- 200–900 m^2J^{-1}. [68]

Mesoporous carbon compounds are being used in the field of biosensors, for identification of enzymes, proteins, DNA, RNA and other biological entities. The use of carbon in mesoporous particles is superior due to its porous nature, pore structure, surface properties, good conductivity and relatively low cost. Enzymatic sensing in biosensor containing carbon mesoporous particle is a special feature because of the presence of abundant oxygen-containing functional groups. Moreover, because of the specialized porous nature in the mesopore wall contributes higher availability of active sites, and this framework facilates greater adsorption of biological sample. Due to enhanced electron transfer it shows good conductivity, and the obtained outcome is more sensitive, reproducible and accurate. [69,70] Modified surface properties improves enzyme immobilization during enzymetic sensing. Surface properties can be modified by attaching functional groups such as amine-, thiol-, aldehyde-, carboxylic-, epoxy-, maleimide-, and nickel chelate-. The enzymes are covalently attached with the complex framework, it interacts and go through certain electron transfer mechanism, provides electrochemical response against biological samples like enzyme. [71,72]

Carbon cloth nanofibers found having successful implementation in developing biosensor, where electrodeposited gold (Au) nanostructures used in detection of biological sample. It is regarded as a good sensor tool for measuring immune responses as a form of electrical response. In a study, electrode of dimension 0.5 x 1.0 cm^2 active area immersed in $HAuCl_4$ and H_2SO_4 was used. Gold nano particle decorated over carbon cloth layer results in measuring electron transport, and Ag or AgCl is used here as reference electrode.[73] Different types of biological molecules like DNA, RNA or proteins are attached with Gold nanoparticles by means of covalent or electrostatic bond.

The following past works has been done with Gold nanoparticles to develop electrochemical biosensor:

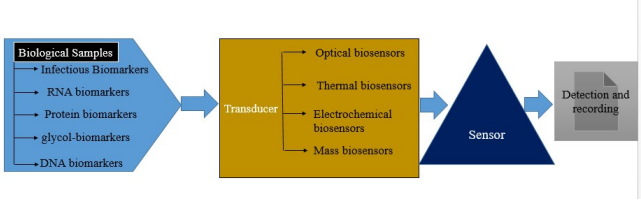

Fig 9: Schematic diagram of working principle of Biosensor

Modern application of AI based biosensors for detection of different cancers

In the modern era of advanced technology, AI (Artificial Intelligence) has a huge role in medical research. Compared to earlier cancer detection methods, sustained development of science and technology has taken it two steps ahead. Different biosensors introduced for detection of cancer biomarkers. These technologies were successfully introduced and given some positive responses. However, there were still some issues related to accuracy, reproducibility of the outcome etc. introduction of AI in the field of cancer detection has opened a window for obtaining more accurate and precise outcome.

Gliblastoma is type of aggressive brain tumour which causes death of individuals all over the world. Detection and progression of cancer in such patients using biopsy is challenging and mostly impossible. In such situation a novel technique developed based on plasma denaturation profiles obtained by a non-conventional use of differential scanning fluorimetry (DSF). Though, DSC (differential scanning colorimitry) was the earlier concept for detection of thermal degradation of biofluids including serum, plasma, CSF etc for detection of number of diseases, including several types of cancers. But technical restrictions and low throughput of DSC instruments made it difficult to be used in cancer detection. Subsequently, nanoDSF showed real promising contribution for detection purpose as, instrument requires minimal amount of plasma sample or biofluid, no need for sample preparation, and it offers faster sample handling because of disposable capillaries and high-powered fully automated (AI) data analysis using machine learning algorithms. The method involves two stages where body fluid is taken and subjected for the DSF denaturation of plasma sample, and interpreting the outcome.

. [80,81]

In first stage, DSF denaturation profile of plasma is done and the obtained data is evaluated using artificial intelligence, similarly obtained data from both patient and healthy subjects (control) used to constitute an atlas that serves as the input to train the artificial intelligence. In the later stage the plasma sample denatured by DSF technique obtained in first stage gives prompt outcome of given sample. The classical Logistic Regression (LR), the often well-performing Support Vector Machine (SVM), the Neural Networks (NN), and two different ensemble methods: Random Forest (RF) and Adaptive Boosting (AdaBoost) are the algorithm systems to conduct AI activities. Python code was used in the automation of AI. It was found that this technique provided a low-cost, rapid, more accurate and high-throughput cancer detection method

Another study which demonstrated the utility of AI in detection of prostate cancer is regarded as one another breakthrough in cancer detection techniques using AI. Earlier prostate cancer detection was carried out by measuring serum PSA (Prostate specific antigen) method and digital rectal examination (DRE), but evidentially high rate of false positive outcome is observed (about 80%). In practical, patients with high PSA is not always a marker of prostate cancer, therefore unnecessary biopsy is carried out to confirm the occurrence of cancer. [82,83] A urinary multimarker sensor system was used, to measure trace amounts of biomarkers from urine sample. The sensing signals from four different biomarkers was analyzed by two different machine learning (ML) algorithms. However, detection of prostate specific cancer biomarker was done using a drop of urine. Earlier, it was found that low concentration of biomarkers raises challenge when using urine for translational research. Therefore, highly sensitive dual-gate field-effect transistor (DGFET) was used as a urinary multimarker sensor to resolve this challenge. This DGFET is composed of a disposable four-channel extended gate, which is separated from its transducer to improve sensing performance and reliability to produce better precision. Two ML algorithms (random forest (RF) and neural network (NN)) used to extract clinically significant information from complicated biomarker sensing signals.[84,85] Specifically, RF and NN were compared to find the best algorithm and combination of biomarkers that provided the highest accuracy in prostate cancer screening. RF showed 100% accuracy, or 97.1% accuracy in terms of panels.[86]

Studies also showed ML algorithm and biosensor for the detection of breast cancer. Application of multiple algorithms based on Machine Learning approach in biosensor also contributed in the detection of breast cancer. Different types of breast cancer biomarkers like HER2, miRNA 21, miRNA 155, MCF-7 cells, DNA, BRCA1, BRCA2 was used in different biosensors i.e., FET, Electrochemical, Sandwich electrochemical and also successful implementation of algorithm as, fuzzy ELM-RBF, SVM, SVR, RVM, Naive Bayes, K-NN, DT, ANN, BPNN contributed in obtaining better accuracy and precision in detection of breast cancer.[87]

Conclusion and Future Prospect

So far many treatment options are available nowadays for cancer treatment. But detection techniques are the frequent issue involved with cancer management process. Due to lack of awareness and as we know many cancer has very mild symptoms which many people forget to pay attention, which leads to final stage of cancer; metastasis. Earlier cancer detection were expensive and complex techniques involved. People, who are already sick and unable to go anywhere are another community who rarely undergo proper diagnosis. Modern techniques or modern science should be focused on things which make life easier. However, it is believed that the recent advancements in cancer detection using specific biomarkers and employing biosensing technology would be beneficial for entire society.

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