https://africanjournalofbiomedicalresearch.com/index.php/AJBR
Afr. J. Biomed. Res. Vol. 28(2s) (February 2025); 821-833
Research Article

Geno Sensor And Their Applications in Various Diseases Biomarkers

Rafia Batool[1*], Rahib Hassan[2], Aqsa Liaqat[2], Muhammad Ahad Tariq[2], Sidra Batool[2], Ali Hussnain[3], Hafiza Mahnoor Bughdadi[3], Muhammad Umar Aziz[3], Saim Ali[4], Faisal Mehmood[4]

[1]*Lecturer, Department of Allied Health Science, Times University Multan,
Email: rafiabatool13@gmail.com
[2]M.Phil. Scholar, Department of Pharmacy, University of Lahore
[3]Lecturer, Department of Pharmacy, Green international university, Lahore
[4]M.Phil. Scholar, Department of Pharmacy, University of Lahore

***Corresponding author:** Rafia Batool
*Email: rafiabatool13@gmail.com

Abstract
In various biological arenas such as medicine, detection of diseases, pathogenic bacteria and viruses and safety of food and quality assurance, need to provide information in certain time which encourages the search for alternative revolutionary methods. Biosensors are one of the most striking substitutes providing modest, reliable, dissolute, and comprehensive selective detection schemes compared with conservative methods like PCR, FISH, and ELISA which have some boundaries. electrochemical DNA sensors (or Geno sensors) have proved to be fascinating replacements to more intricated conventional approaches. Presently, electrochemical Geno sensors are considered very reassuring analytical tools for this motive due to their quick response, cost effectiveness, high sensitivity, affinity with microfabrication technology and easy action mode which makes them biocompatible with point-of-care (POC) testing.
This review briefly discusses the importance and current difficulties of identifying circulating biomarkers linked to related diseases like cancer, bacterial and viral infections, and neurodegenerative diseases. It also summarizes the role, analytical features, and prospects of Geno sensors as well as their efficacy as a rapid and sensitive tool for the detection of various diseases.

Keywords: Electrochemical Geno sensor, Disease markers, Nanoparticles, DNA, probe.

***Author for correspondence: Email:** *rafiabatool13@gmail.com*

Received:02/12/2024 *Accepted: 10/12/2024*

DOI: https://doi.org/10.53555/AJBR.v28i2S.6959

Introduction

We all live in a world of sensors from our own sensory body parts (nose and tongue) to various other sensing equipment use d for several applications for example to detect smoke or fire, to sense the speed of an object or vehicle, to sense alcohol consumption. Hence, in simple words, a sensor can be defined as a sophisticated device, which can identify or detect and respond towards any changes in the surrounding physical, chemical and biological environment. With the advancement in

technology, there is an increased dependence on estimating, monitoring and controlling chemical species. However, to accomplish this task, well-equipped laboratories and skilled workers are required. It becomes essentially crucial in medicines to analyze and monitor the marker analytes to diagnose and treat the disease at the early stages. So, bringing those diagnostic tests from the laboratory to the patient can make far reaching changes in the field of clinical practices [1].

Leading edge advancements in technology have authorized biosensors to developed more precise, definitive, and sensitive to biomarkers and analytes study. As these Biosensors turn out to be more innovative, there is also a drive to make them miniature and more transportable. Portable stratagem make them accessible outside of the laboratory permitting for usage in the field also transference to third world countries where the failure for early, immediate detection of disease has a major negative outcome not only on people's be present but economies on the entire. Presently, the diagnosis involves travel to a clinic as well as a protracted interval period to receive the results. Consequently, the need for biosensors has augmented, and research is engrossed on the progress of small portable devices that would let quick, precise, and site specific determination[2]

The term "**biosensor"** denotes to a significant and advanced analytical device concerning biological sensing element via extensive range of applications, such as food safety and processing drug discovery, biomedicine, diagnosis, environmental monitoring, defense, and safety. Sensors are self-contained unified devices that can measure a physical property and alter it into computable and processable signal.[3] Usually, a biosensor is consists of three main workings:
A bio receptor, a transducer in constricted assembly with bio receptor, and a signal-processing component. Binding of the analyte to a specific bio receptor as the recognition element is converted into a quantifiable output as an electrical signal by the transducer [4] sensitivity, selectivity, reproducibility, stability are fundamental characteristics of biosensors. An ideal biosensor is one which accommodate a bioreceptor that is particularly selective respective analyte and able to detect it in a sample comprising other constituents and impurities. The biosensor must hold a very precise and accurate transducers as well as other electronics to yield indistinguishable responses for a sample every time. Sensitivity is also a significant property of biosensors. it is controlled by the limit of detection which means the least amount of the sample that a biosensor can determine. Basically, an ideal biosensor should have a very rapid response period and a remarkably low detection limit (LOD)i.e. it should be capable of to detect even an extremely negligeable quantity of analyte also[[5]

Professor Leland C Clark Jnr. is considered as the father of biosensors, as he had constructed the first ever biosensor in 1956, for the detection of oxygen, which was formerly named as 'Clark electrode'. This sensor was fabricated by immobilization of glucose oxidase (GOD) enzyme onto an amperometry oxygen electrode, via dialysis membrane to detect the glucose concentration in a sample[6] after that the biosensor designed by Clark and Lyons (1962) to quantify glucose in biological samples used the approach of electrochemical determination of oxygen or hydrogen peroxide by means of immobilized glucose oxidase electrode. Meanwhile , incredible advancement has been made (together in technology and uses of biosensors with advanced applications including electrochemistry, nanotechnology to bioelectronics turmoil[7].In 1996, Tyagi and Kramer's developed a fluorescent molecular beam that emerged in the innovations of numerous routine applications/manipulations in the determination of target sequences. [8]
Classification of biosensors**:** biosensors are categories into following different way

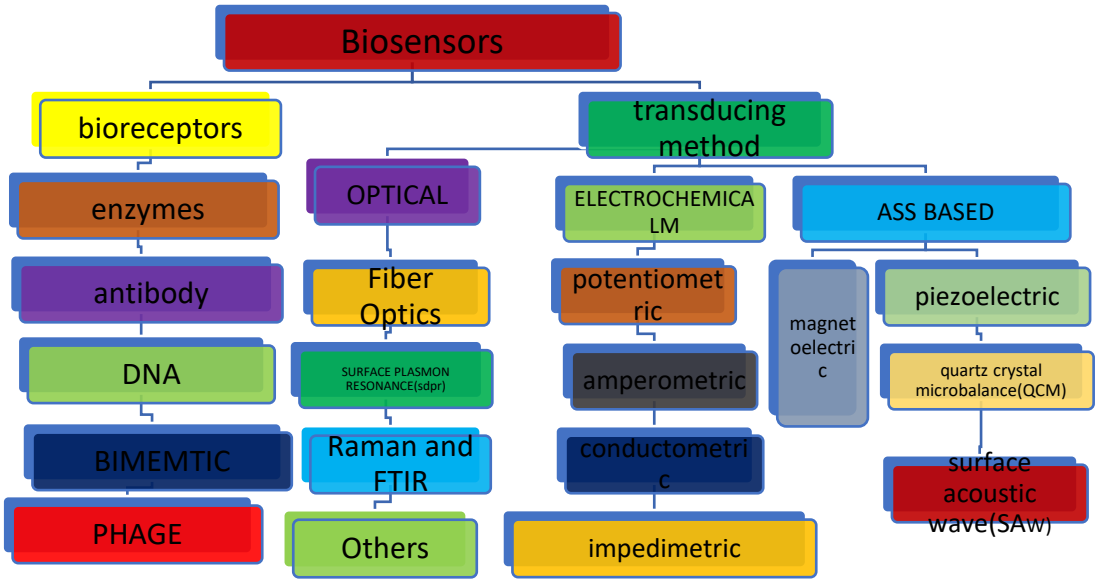


Figure 1. classification of biosensors.

Nanotechnology: has illustrated significant potentials in biomolecular-sensing applications; development of several diagnostic procedures in medicine has been possible through the beneficial application of nanomaterials, among which electrochemical nano-biosensors can be mentioned. They can be employed to quantify various clinical biomarkers in detection, evaluation, and follow up stages of the illnesses.[9]Yet, detection of valuable Nano-materials has brought about more possibilities to carry out studies in the area of bio-sensing, while it is also possible to provide considerable benefits such as being more sensitive and specific than the previous bio-diagnosis .

Since, carbon nanomaterials possess extraordinary electrical, thermal, chemical, as well as mechanical characteristics, researchers have been largely interested in them. Consequently, they have been applied in various fields including composites, energy saving and converting, sensors, administration of medicine, field emission systems, and electronic elements at nano-scale .[10] Furthermore, synthesis customization is possible through connected practical elements, while their assembly in the form of 3D arrays would help the scholars devise catalysts with more surface area along with materials possessing high levels of photo-chemical as well as electrochemical functions. They are broadly applied in designing catalysts in hydrogenation biosensors, and fuel cells due to their extraordinary features .[11]

Applying conductive polymers to modify electrodes is another novel idea, according to which the polymers and their derived forms, significantly accelerate the transmission of the electrons on the electrode. Accordingly, this results in promotion of electrochemical function of the electrode, while signaling identification is also amplified [12].

The use of nanomaterials on the surface of electrodes or electrochemical platforms in biosensor development is a very attractive strategy that mainly leads to increase the surface area, chemical stability, and numbers of binding events .In addition, electrode modification by metal nanostructures or conductive carbon-based nanomaterials such as carbon nanotubes (CNTs) and graphene offers unique advantages including enhancing the electron-transport ability, improving the surface conductivity, and increasing the biomolecule load capacity especially in electrochemical label-free biosensing .[13]

Techniques used in Geno sensor: DNA biosensor technologies are rapidly developing as an alternative to the classical gene assays, due to their potential miniaturization, portability and in situ analysis. available detection techniques, can be employed for the detection, quantification and amplification of the signal observed due to the interaction of analyte and bioreceptors, different techniques have been established for the transduction such as fluorescence, electrochemical sensing, differential pulse voltammetry radiochemical assays, cyclic voltammetry quartz crystal microbalance, electrochemical impedance spectroscopy and surface plasmon resonance spectroscopy.[14]

Fig. shows different electrochemical transduction techniques which work on different principles according to the form of input and output energy like voltage, current, charge *etc*.

Figure 2. Techniques are used in biosensors.

Biosensors in which DNA molecules are used as a subject of analysis or as sample are known as Geno sensors. Usually, single stranded DNA probe is used as bio receptor which is then hybridized with the known complementary DNA which is to be analyzed. The immobilization of single stranded DNA probe on

concern transducer surface generates a measurable electrical signal on hybridization with its complementary DNA probe. economical, rapid analysis, practicable technique, and the possibility of precision are benefit of DNA biosensors that assemble this rapidly emerging technology developing alternate way towards the genetic assays.[15] .

Immobilization of ssDNA probe onto the transducer surface DNA probe immobilized onto the transducer surface can respond the sample analyte in different ways , that includes of DNA hybridization, enzyme based interactions, antigen/antibody reactions and cellular associations amid two distinct molecules of DNA or RNA or DNA interactions with different proteins and drug molecules. [16].[17]

Geno sensors embrace incredible applications in medical science, genosensors are valuable in prognosis of several diseases and their management, valuation of cellular action of advanced complexes and compounds etc. A noteworthy collection Geno sensors have been developed over the decade for diagnostic purposes.[18]

Geno sensing of Circulating Biomarkers. Currently, Circulating biomarkers play a very major role in the diagnosis of cancer and other disease[19] Oncobiomarkers act as perfect tool for cancer detection. The current advances in the field of early phase detection of cancer reveal that specific and vigilant quantification of these biological molecules is feasible by DNA biosensors. These gene-based sensing approaches are being assembled on nucleic acid detection measures that makes them efficient, consistent and economical[15]. Electrochemical Geno sensor show mainly attractive merits such as accessible , compactness, ease, low cost, small size, quick response, ease of use, feasible of reading minute sample volumes directly over a broad choice of concentrations and affinity with POC testing [20] [21].

Cancer Biomarkers:

Cancer is a foremost public health problem globally. Global demographic features predict a growing cancer prevalence in the next decades, with **>20 million** new cancer cases yearly predicted **by 2025**.As reported by the World Health Organization, cancer is accountable for one in six deaths, that makes it the second most common reason of death universally. Cancer is still a global concern worldwide with elevated influence not only on human health, triggering morbidity and mortality, but also on commerce. Cancers of the **female breast**, **colorectal, prostate**, and **lung are** the most regularly diagnosed cancers. Lung cancer remains the leading cause of cancer incidence and mortality worldwide.[22] Advancement in diagnostic technologies and the growing familiarity of molecular tumor nature and its biology has markedly altered cancer treatment standards during the past 15 years[23]. Oncobiomarkers can display a very efficient role in the cancer prognosis that leads towards its treatments. A biomarker-based cancer diagnosis may significantly improve the initial diagnosis and successive treatment. [13]

Cancer, one of the most life-threatening diseases, has more than 200 distinct types associated with it, affecting over 60 human organs. More than 90% of all cancer-related deaths occur from metastasis of the primary cancer tumor [1]. The early stages of cancer development carry the maximum potential for therapeutic intervention. Therefore, detecting premalignant or premetastatic malignant tumors when they are still confined within organ(s) is critical to enable effective treatment and improving survival rate .[24] Recent advances in molecular biology elucidate that cancer biomarkers play an important role in diagnosis, prognosis and providing insights into the etiology of cancer. The National Cancer Institute defines a biomarker as “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.” Tumor markers are one of the most valuable tools of early cancer detection, classification, staging, progression monitoring, and assessment of resistance to chemotherapy.[24]There are more than 200 distinct diseases associated with cancer affecting different parts of the body . In the absence of a tumor, the tumor markers usually exist at low levels. Upon tumor formation, the level changes, and hence clinical assays of cancer markers must be rapid, selective, and sensitive enough to detect small changes in the level of the markers in complex biological fluids.[25] The widespread use of tumor markers in healthcare will ultimately depend upon the detection of many tumor markers with high selectivity and sensitivity. Modern electrochemical bio affinity sensors, such as Geno- or immune-sensors, offer remarkable sensitivity, essential for early cancer detection. The attractive properties of electrochemical devices are extremely promising for improving the efficiency of cancer diagnostics and therapy monitoring. With further development and resources, such portable devices are expected to speed up the diagnosis of cancer, making analytical results available at patient bedside or physician office within few minutes[26]

Breast cancer:

Breast cancer is one of the three most common cancers in females and one of the leading causes of cancer mortality among women worldwide. Since distant metastases are regarded as the major reason of death, early diagnosis becomes vital for improving this cancer type survival rate. Currently, strong efforts are being developed to monitor specific bodily fluid biomarkers for early and minimally invasive detection of this type of cancer [3]. Recent efforts by Razieh Salahandish ,worked on the very delicate and label-free nano-Geno sensor that is settled for the recognition of miRNA-21, a acknowledged breast cancer biomarker, founded on a definite construction of nitrogen-doped functionalized graphene (NFG), silver nanoparticles (AgNPs), and polyaniline (PANI) which bring about in a noteworthy outcome on signal intensification. Succeeding the efficacious functionalization of the nanostructure and immobilization of the detailed categorization of the aminated

complementary oligonucleotide of miRNA-21, the finding was completed by means of differential pulse voltammetry (DPV). The oxidation peak current of the redox probe under ideal conditions was resolute to display the incident hybridization of miRNA-21 biomarker. Put on this extremely delicate and augmented nano-biosensor allowed detection of a widespread energetic range of 10 fM–10 μM with a sensitivity of 2.5 μA cm^{-2} and a little detection edge of 0.2 fM.[27]

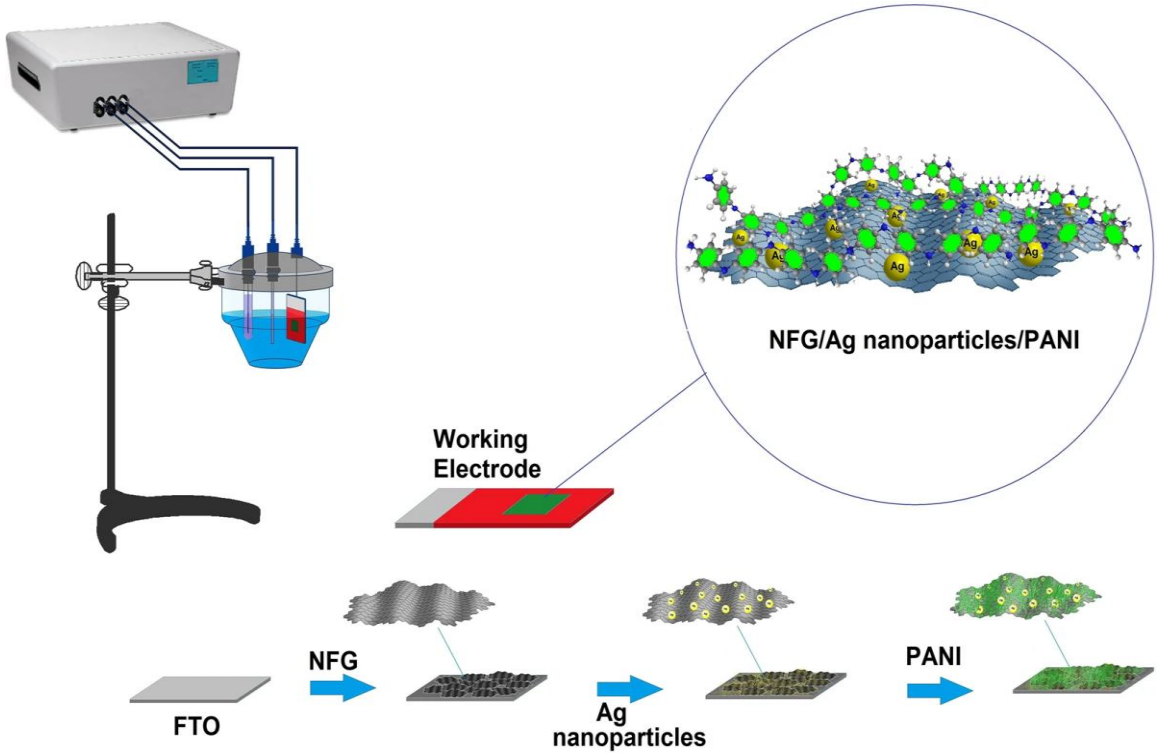


Figure 3. Schematic presentation of the synthesis procedure for metal nanoparticles (NPs)-grafted N-doped functionalized graphene (NFG)/polyaniline (PANI) nanocomposites on the fluorine doped tin oxide electrode (FTOE). The synthesis process of the nanocomposite consists of (1) coating of NFG on the FTOE substrate, (2) chronoamperometry of metal NPs on the NFG coated FTOE, and (3) cyclic voltametric electro polymerization of PANI on AgNPs modified FTOE.

The top right corner represents the final synthesized nanocomposite complex.
https://media.springernature.com/lw685/springer-static/image/art%3A10.1038%2Fs41598-018-37573-9/MediaObjects/41598_2018_37573_Fig1_HTML.png?as=webp

Liver cancer:
globally, liver cancer is the most frequent fatal malignancy; in the United States, it ranks fifth. Patients are often diagnosed with liver cancer in advanced stages, contributing to its poor prognosis.[28]
Jinng lieu et al.in their work, an innovative label-free photoelectrochemical (PEC) biosensor constructed on Au/Cs_xWO_3 heterogeneous films with less background clamor and eminent sensitive recognition of alpha-fetoprotein (AFP) was projected. and fabricated Au/Cs_xWO_3 heterogeneous films by distinct approaches involving template elimination and spin covering. The surface plasmon resonances (SPR) of Au film and Cs_xWO_3 semiconductor nanocrystals largely improved the photoelectrochemical properties of the electrodes and enhanced the photocurrent. Under the optimal conditions, the prepared PEC biosensor exhibited a linear response between photocurrent differences and the logarithm of AFP concentration in the range from 0.01 ng/mL to 500 ng/mL with a LOD of 7 pg./mL. moreover, the proposed PEC biosensor had great specificity, repeatability, durable stability and displayed reasonable results in the analysis of human serum samples, which would have inordinate idea in clinical enactment and biological analysis in upcoming studies.[29]

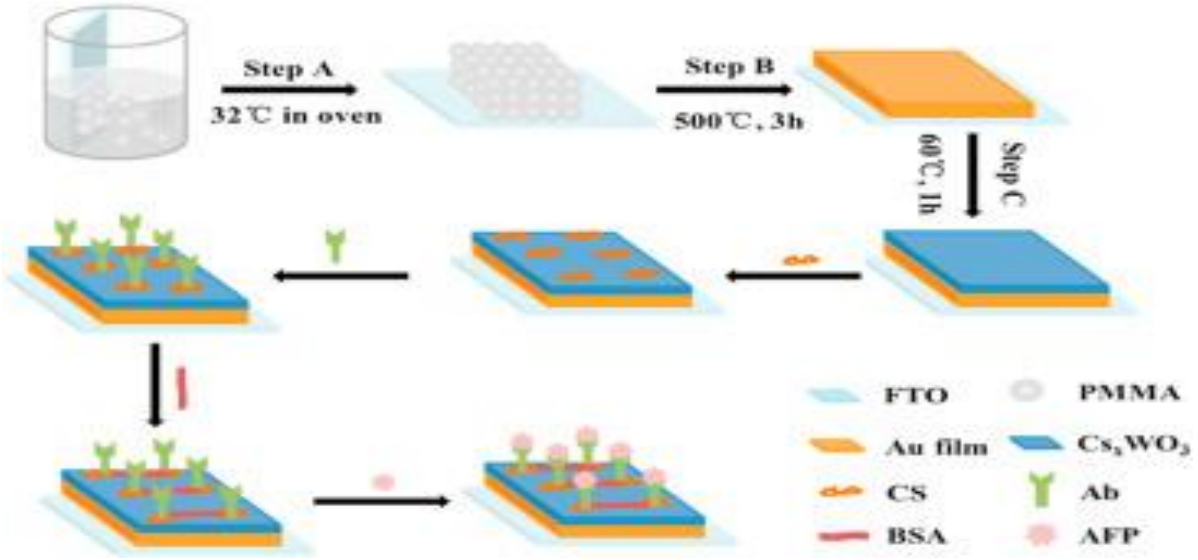


Figure 4. label-free photoelectrochemical (PEC) biosensor constructed on Au/Cs_xWO_3 heterogeneous films https://ars.els-cdn.com/content/image/1-s2.0-S0039914020313655-fx1.jpg

Table: Geno sensor used in breast and lung

Cancer	Biomarker	Nanomaterial	Technique	LOD/linear range	References
Breast cancer	mi RNA-21	AgNPS/PANI/N-graphene	DPV	0.2 fM/10 fM–10 μM	[27]
	BRCA1	polyether sulfone / (RCNFs - MWCNTs)	(EIS)	2.4 Pm/	[30]
	BRCA1	rGO-pyroll3 carboxylic acid	CV DPV EIS	3 fM/10 fM–0.1 μM	[31]
	BRCA1	PEG/TA/pDA	EIS/CV	0.05 fM/0.1 fM 10 pM	[32]
	mi RNA-34a/MCF	Ppy-(PGE)/ Ag/AgCl	EIS	0.2 $\mu g.mL^{-1}$ /5–80 $\mu g.mL^{-1}$	[33]
	Muc-1	MWCNT/PGA	(DPASV)	25 cells/1.0×10^2 to 1.0×10^7 cells·mL^{-1}	[34]
	Small RNAs-221	Bionylated polythiophene/Au	EIS	0.7 Pm	[35]
Lung cancer	mi-RNA21	DNA hydrogel/(ITO/PET)	EDS CV DPV	5 nM/10 nM to 50 μM.	[36]
Lung cancer	CYFRA21-1-DNA	3D GF/Ag NPs	CV	1.0×10^{-14} M/1.0×10^{-14} to 1.0×10^{-7} M.	[37]
Lung cancer	EGFR exon 21	(Ni-OTC NPs)-PGE/(rGO/f-OMC)	DPV	(120 nM)/ 0.1 μM to 3 μM	[38]

Prostate cancer:

The development of simple detection methods aimed at widespread screening and testing is crucial for many infections and diseases, including prostate cancer where early diagnosis increases the chances of cure considerably. In this paper, we report on Geno sensors with different detection principles for a prostate cancer specific DNA sequence (PCA3). The Geno sensors were made with carbon printed electrodes or quartz coated with layer-by-layer (LbL) films containing gold nanoparticles and chondroitin sulfate and a layer of a complementary DNA sequence (PCA3 probe). The highest sensitivity was reached with electrochemical impedance spectroscopy with the detection limit of 83 88.3%, which means that further developments in image analysis are required for this innovative approach. pM in solutions of PCA3, while the limits of detection were 2000 pM and 900 pM for cyclic voltammetry and UV–vis spectroscopy, respectively. That detection could be performed with an optical method is encouraging, as one may envisage extending it to colorimetric tests. Since the morphology of sensing units is known to be affected in detection experiments, we applied machine learning algorithms to classify scanning electron microscopy images of the Geno sensors and managed to distinguish those exposed to PCA3-containing solutions from control measurements with an accuracy of 99.9%. The performance in distinguishing each individual PCA3 concentration in a multiclass task was lower, with an accuracy of

Prostate cancer and neck cancer

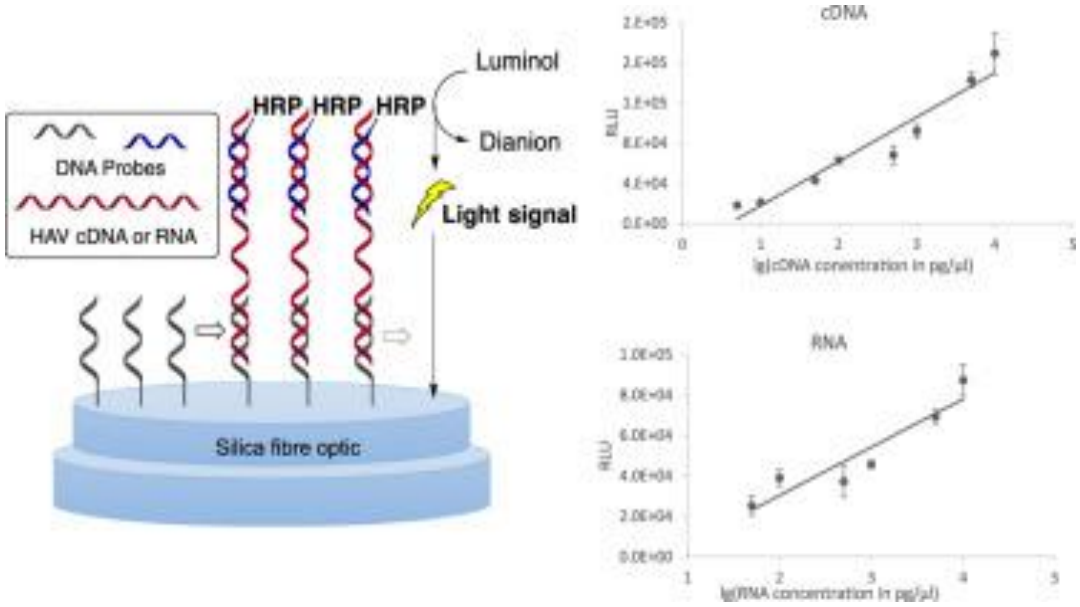
Prostate cancer	Biomarker	Nanomaterial	Technique	LOD/linear range	References
Prostate cancer	PCA3	Au/Chondroitin sulfate	EIS/CV/UV Spectroscopy	83 pM/2000 pM and 900 pM	[39]
	PCA3	MMA/Au	EIS	2.1×10^{-9} mol L^{-1}/1.2×10^{-9} and 1.7×10^{-9} mol L^{-1}	[40]
	mi RNA-21	(SWCNTs) - (FTO)/ (Cd^{2+})	DPV	0.01 fmol L^{-1}/(0.01 fmol L^{-1} to 1 µmol L^{-1})	[41]
	PC DNA	ZnO-PE	CV/EIS	1 pM/50 µM to 1 pM.	[42]
Head and neck	*MGMT* gene	Au- (11-MUA) /SAM	EIS	0.24×10^{-12} mol L^{-1}./	[43]

Viral Infections genosensing

Fast and reliable diagnosis of viral infections biomarkers and timely initiation of treatment are crucial for their fruitful clinical management. There are several reports that genosensors applied to viral infections.

Hepatitis:

Hepatitis A virus (HAV) infection has caused substantial morbidity and economic losses to human society, presenting a major public health problem in many parts of the world. Despite the capability for low-concentration detection, current PCR-based techniques are limited by the requirement of specialized lab equipment, trained personnel and a relatively large time-commitment. The need for a prompt in-field quantitative identification of HAV in real samples has led us to develop a chemiluminescent fibre optic genosensor system. In this study, a two-probe sandwich-type hybridization process was implemented on the tip of a fibre optic with an area of 0.12 mm^2. After optimization of the probes and the working conditions, we showed that the biosensor was able to work for both cDNA and RNA with a relatively large signal/noise ratio and a good sensitivity. Excellent specificity was also confirmed by screening with a broad range of other pathogen samples. The nucleic acid probes method was validated by optimized PCR and qPCR, and may thus be used when field testing would be required.



https://ars.els-cdn.com/content/image/1-s2.0-S0039914017306689-fx1.jpg

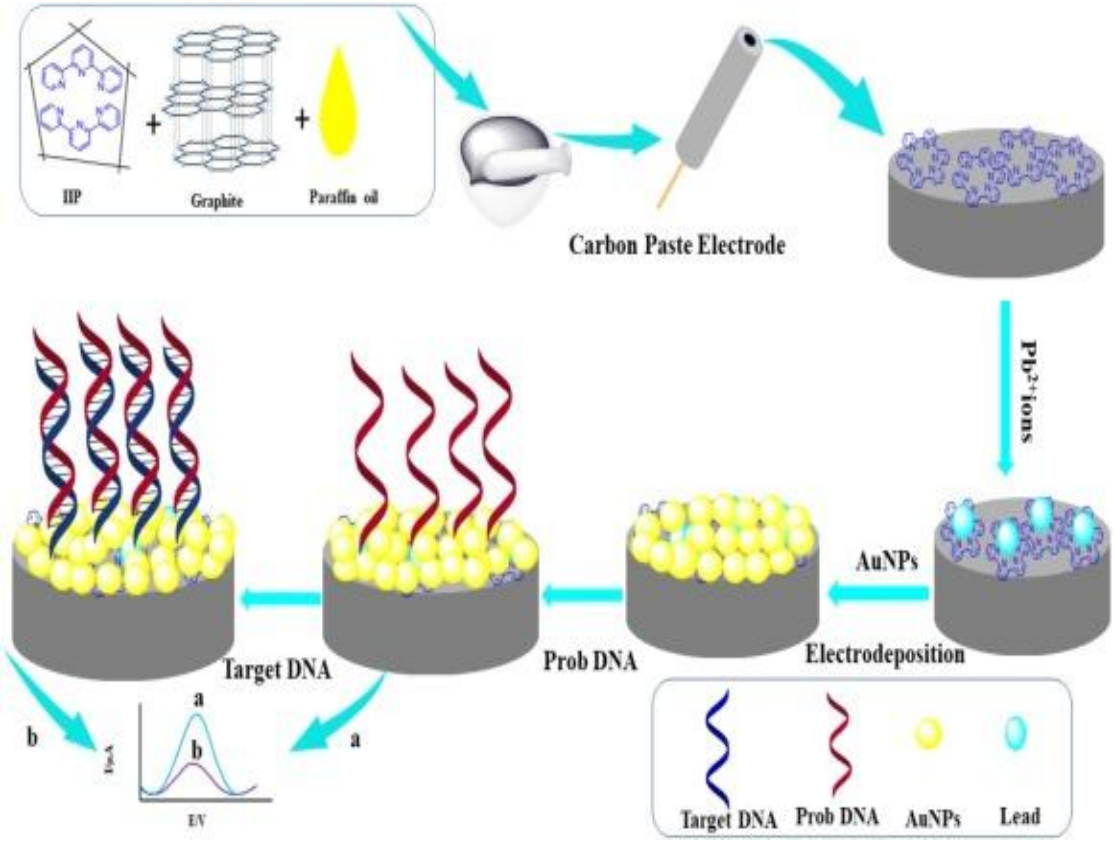
GENOSENSORS FOR HEPATITIS

Hepatitis	Biomarker	Nanomaterial	Technique	LOD	References
	HCV1	MB@SiNPs/FTO	PCR/EIS	90 copies/mL/ 100–10^6 copies/mL,	[44]
	HCV1	Qurecitin/GCE	DPV/EIS	83 pM	[45]
	HCV	GO-ETD	EIS/DPV	1:483 (v/v) or 1.36 nmol·L^{-1}	[46]
	HCV DNA	(mrGO-CuNCs)	EIS	405.0 pM /0.5–10 nM	[47]
	HCV RNA	NG/ Cu_2O/ Au NPs	DPV	1×10^{-15} mol. $L^{-1/}$ (1×10^{-15}– 1×10^{-6} mol. L^{-1})	[48]
HepatitisB	HBV DNA	• ssDNA/Co_3O_4PNCs/GCE	EIS	0.38 pM/	[49]
		(MWCNT)/ (FTO)/Zeolite	CV/DPV/EIS	150 and 10^6 copies/ml.	[50]

Human immunodeficiency virus (HIV):

Human immunodeficiency virus (HIV) spread to humans from chimpanzees (HIV-1 groups M and N), gorillas (HIV-1 groups P and O), and sooty mangabeys (HIV-2). HIV is spread mainly through blood or body fluids. Subjects can become infected with HIV by sexual contact, needle sharing, blood transfusions, or maternal transmissions as a blood-borne virus or via breast-milk. The incubation period of HIV-1 from infection to the development of AIDS ranges from 8 to 11 years. In the past 3 decades, HIV has caused a great burden to global wealth and health. [51]

It is a sort of lentivirus (a subclass of retrovirus), foundations acquired immunodeficiency syndrome (AIDS)for the detection of (HIV)**Mujtaba shamsipur et, al.,** developed a simple and label-free voltametric Geno sensor to determine the HIV-1 pole gene by using lead ion-imprinted polymer (Pb-IIP) nanoparticles as a novel electrochemical probe. For this purpose, a carbon paste electrode (CPE) was impregnated with lead ion-imprinted polymer nanoparticles. Lead ions were reduced and accumulated onto the surface of CPE at − 1.0 V vs. Ag/AgCl and then, Au nanoparticles (AuNPs) were electrochemically deposited on the surface of Pb-IIP-CPE. The modified AuNPs/Pb-IIP-CPE electrode showed a well-defined lead oxidation peak with excellent stability and reproducibility. Finally, the thiol-DNA probe of HIV-1 pole gene was immobilized on the surface of the modified electrode through a self-assembly method. Due to the blocking of lead electron transfer at the electrode surface with the probe DNA immobilization, the Pb oxidation peak current was decreased. In the end, upon the hybridization of probe DNA with the target DNA, the response current of the electrochemical probe was further decreased. Under optimum conditions, the developed genosensor showed a linear detection range from 1 fM to 0.1 nM, with a detection limit of 0.3 fM (S/N = 3).[52]



Schematic representation of genosensor used for HIV -1gene
https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.sciencedirect.com%2Fscience%2Farticle%2Fpii%2FS0026265X20328721%23!&psig=AOvVaw0yMqti2DHoQf1K9lIlhnHt&ust=1616088576855000&source=images&cd=vfe&ved=0CAIQjRxqFwoTCJjU4aDtt-8CFQAAAAAdAAAAABAD

GENOSENSORS FOR HIV And HPV

AIDS	Biomarker	Nanomaterial	Technique	LOD	References
AIDS	HIV DNA	MoS_2 / Exo III,	UV	5.3 pM/ 0.01 nM to 10 nM	
AIDS	HIV-1 pol gene	AuNPs/Pb-IIP-CPE	DPV	f 0.3 fm/ 1 fM to 0.1 nM,	[52]
AIDS	HIV-1	BIOTIN/SAM	SER/CV	$2.5\ 10^{-12}$ $molL^{-1}$	
HEAD AND	HPV-16	Chitosan/ chondroitin sulfate	EIS	10.5 pM	[53]

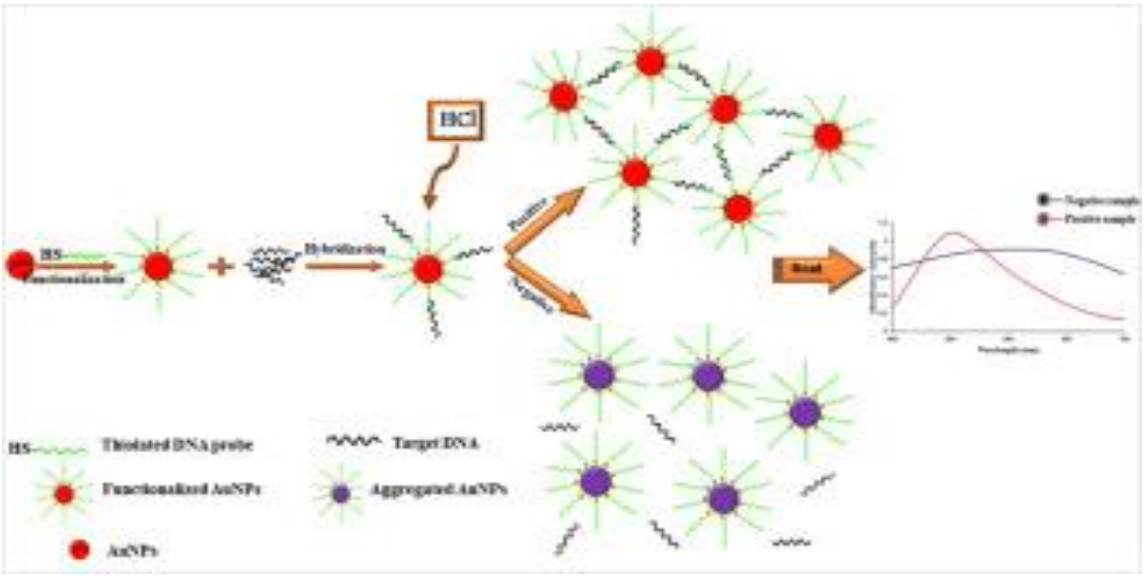
NECK CANCER					
Head and neck cancer	• HPV11/HPV16	PANI) / AuNps)	EIS/AFM	2.74 pg μL^{-1} and 7.43 pg μL^{-1}	[54]
Cervix head ans neck	HPV16	LbL) film of chitosan/c	EIS/UV	18.5 pmol L^{-1} i	[55]
Cervical cancer	HPV subtypes	(PPy) / (AuNPs)/ (PET)/ (ITO).	EIS/CV	0.89 pg μL^{-1}	[56]
corona	Covid 19/ (RdRP)seq	Ag^{+-} (HT18C6)/ (SiQDs@PAMAM)/CPE	DPV	0.3 pM./ 1.0 pM–8.0 nM	[57]
Influenza	L-fuculokinase gene	Zn-based MOF/CMC/Au	CV	/0.1 pM–10 nM	[58]
	Haemophilus influenza genome	(CysA-AuNPs) /Ag-DPA-GQDs / GCE.	SWV	1 pM–1 ZM and 1 ZM	[59]
	Influenza A	Meso/macroporous cobalt (II) oxide/*N*-methylpyrrolidone	Hybridization/PCR	86.4 amol L^{-1} f /[60]1.0 fmol L^{-1} to 1.0 nmol L^{-1}.	[60]
	H1 N1 influenza	(EDC/NHS). /MT	RT/PCR/DPV	0.002 ng/6 µL	
	H-influenza	Cit-AgNPs	DPV	LLOQ) = 1 ZM	[61]
	InflenzaA/influenzaB	GSB/PGE	DPV	35 nM f/ Inf A 21 nM Inf B .	[62]

Bacterial Infections Biomarkers :

Customarily, the revelation and identification of bacteria predominantly depends upon on particular microbiological and biochemical dtection methods, which involve at least 3 and as various as 7 days to produce results.[63] Electrochemical genosensors suggests a fast means for recognition and prognosis, rely on the practice of definite probe for gene of malignancy.

Shigellosis;

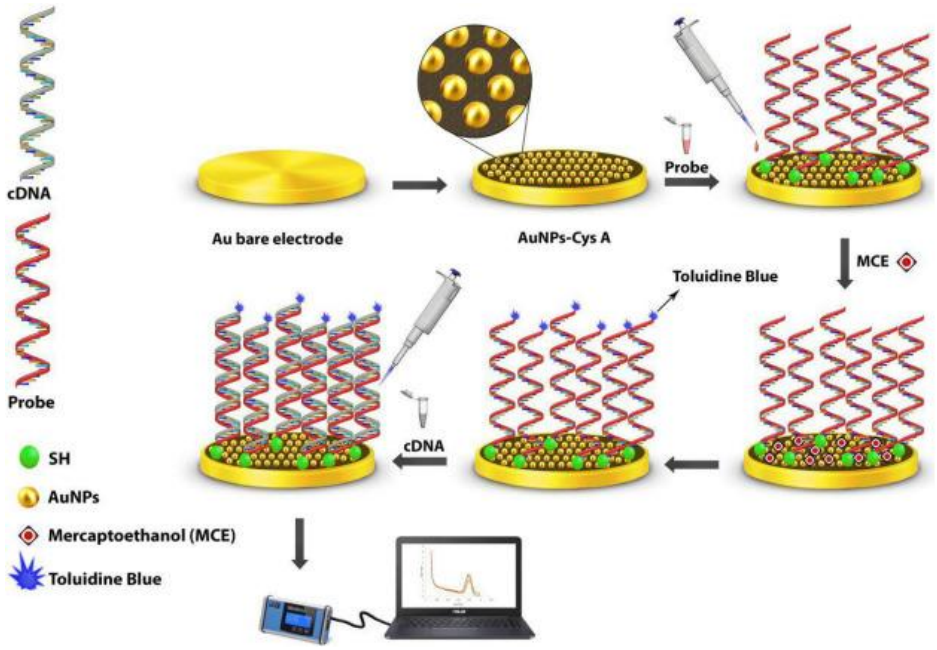
Early detection of infectious bacteria is a necessity for combating infectious diseases. Due to low infectious dose of *Shigella*, rapid and sensitive detection is needed.[64] Compared to the presented genes, *Spa* gene can be introduced as a novel sequence for all species of *Shigella* detection. Herein, the possibility of *Spa* genes for detection of four species of *Shigella* was investigated for the first time by AuNPs-based optical genosensing system. In this method, AuNP–DNA probes were hybridized with *Spa* gene sequence. When the complementary target is present, it prevents the aggregation of the complex under acid environment and the solution remains red whereas in the absence of the specific sequence, it turns to purple. Therefore, visual detection is possible with bare eye. The comparison of this Optical DNA biosensor and PCR-based method showed that the proposed method is simple, cost-effective, rapid operation, with high or comparable detection limit of (LOD and LOQ: 8.14 and 26.6 ng mLl^{-1}, respectively), without need of any expensive techniques, and equipments compared to the conventional methods. In conclusion, the described method may develop into a platform that could be utilized for detection of various bacterial species with high accuracy and prompt screening ofsamples.[65]



https://ars.els-cdn.com/content/image/1-s2.0-S0167701219300739-ga1.jpg

LEGINARIES DISEAS/PONTIAC FEVER:

Legionella pneumophila is a causative agent of Pontiac fever and Legionaries' disease. *L. pneumophila* is a gram-negative, fastidious and hard to grow bacterium. Since severe growth of this pathogen, molecular diagnostics based on DNA can be very important. *Mip* gene is one of the strongest constructed in *Legionella pneumophila* that targeted in several molecular detection methods. Also, *L. pneumophila* is one of the threatening pathogens that has many challenges for its rapid and specific detection. A novel study develop to identify *Legionella pneumophila* specific genes using a DNA-based bioassay. In this work, gold nanostructures supported by cysteamine (Cys A/AuNPs) were deposited on the surface of gold electrode to engineer an innovative DNA based biosensor. The Cys A/AuNPs interface provides a large surface area for the effective immobilization of ssDNA, as well as it ascertains the bioactivity and stability of immobilized pDNA. Field emission scanning electron microscope (FE-SEM), and EDS photoelectron spectroscopies were used to monitor the sensor fabrication. Cyclic voltammetry (CV) and square wave voltammetry (SWV) were used for electrochemical characterization of DNA immobilization and hybridization by cDNA as complementary target sequence. Obtained results showed good sensitivity, selectivity and stability. Finally, target DNA was quantified at a linear range from 1 µM to 1 ZM and low limit of quantification (LLOQ) was 1 Zepto-molar. The results of this study indicate that nucleic acid based bioassay in the near future can be a good alternative to the detection of *L. pneumophila*.[66]



https://ars.els-cdn.com/content/image/1-s2.0-S0026265X19303856-sc1.jpg
https://ars.els-cdn.com/content/image/1-s2.0-S0026265X19303856-gr3.jpg

Disease	Nanomaterial	Biomarker	Technique	LOD	References
Meningococcal meningitis	C/ poly(4amphinophenol)	DNA Neisseria gonhrea	DPV	0.6ng-6ng/µL	[67]
Typhoid	GO/Fe3O4 NPs	Typhoidal Salmonella		3.16×10-18 M /10-17 to 10-9 M	[68]
Shigellosis	AuNPs	Shigella spa gene	PCR	8.4ng/ml	[65]
Cholera	Lyophilized AuPNs	Vibrio cholera		1 fM / 1 aM–1 fM	[69]
Tuberculosis	(SPGE) / (LAMP-EC)	MTB		0.015 ng/µL /: 0.015–150 ng/µL	[70]
Pontiac fever Legionaries' disease.	Poly (dopamine-β-Cyclodextrin) /AuPNs/TB	*Legionella pneumophila*	Swv/cv	1 µM to 1 ZM (LLOQ)= 1 Zepto-molar.	[66]

quality testing, pathogen detection, environmental monitoring and most importantly for single nucleotide polymorphism detection related to various types of cancers . Geno sensors have really been playing a crucial

role in developing point of care diagnostic tools for various infectious agents and diseases. Geno biosensors in particular have been devised in recent past, because of their biocompatible and quite specific detection of diseases like breast cancer, prostate cancer etc.[71]

Conclusion:

DNA because of it's quite robust properties with respect to temperature and pH conditions, along with a very high specificity towards its target had been extensively explored for chemical and biological sensing platforms. A large variety of nucleic acid-based biosensors or Geno sensors have been designed and fabricated for utilizing them in quite versatile applications related to foo

Materials having 2D properties like graphene, graphene oxide etc. have been utilized for devising Geno sensors which may be specifically used as biomarkers for specific cancer detection. Aptamers for biosensing applications have also been quite attractive targets for studying the DNA methylation, breast cancer, hepatitis B virus, and small molecule detection etc. . DNA hairpins having stem and loop structures (called as molecular beacons) have also been utilized for probing even living cancer cells. Despite lots of above-mentioned recent developments in the field of biosensors, still many challenges lie ahead in the fabrication of more sensitive, selective, specific biosensors. Fabrication of more specific geno sensors for their versatile applications is the need of the hour.

References

1. Morales, M.A. and J.M.J.B.c. Halpern, Guide to selecting a biorecognition element for biosensors. 2018. 29(10): p. 3231-3239.
2. Senf, B., W.-H. Yeo, and J.-H.J.B. Kim, Recent Advances in Portable Biosensors for Biomarker Detection in Body Fluids. 2020. 10(9): p. 127.
3. Pacheco, J., et al., Biosensors, in Current Developments in Biotechnology and Bioengineering. 2017, Elsevier. p. 627-648.
4. Sezgintürk, M.K., Introduction to commercial biosensors, in Commercial Biosensors and their Applications. 2020, Elsevier. p. 1-28.
5. Asal, M., et al., An overview of biomolecules, immobilization methods and support materials of biosensors. 2019.
6. Didyuk, O., et al., Continuous glucose monitoring devices: past, present, and future focus on the history and evolution of technological innovation. 2020: p. 1932296819899394.
7. Srushtee, K., P.J.F. Sujata, and A.S. Journal, BIOSENSORS: Introduction and its Applications. 2020. 1(4).
8. Eggins, B.R., Biosensors: an introduction. 2013: Springer-Verlag.
9. Abdulbari, H.A. and E.A.J.C.R. Basheer, Electrochemical biosensors: electrode development, materials, design, and fabrication. 2017. 4(2): p. 92-105.
10. Zhang, Y. and X.J.N. Chen, Nanotechnology and nanomaterial-based no-wash electrochemical biosensors: from design to application. 2019. 11(41): p. 19105-19118.
11. Yazdi, M.K., et al., Nanotechnology-based biosensors in drug delivery, in Nanoengineered Biomaterials for Advanced Drug Delivery. 2020, Elsevier. p. 767-779.
12. Azimzadeh, M., et al., Electrochemical miRNA biosensors: the benefits of nanotechnology. 2017. 2(1): p. 36-48.
13. Saeed, A.A., et al., DNA biosensors based on gold nanoparticles-modified graphene oxide for the detection of breast cancer biomarkers for early diagnosis. 2017. 118: p. 91-99.
14. Cesewski, E., B.N.J.B. Johnson, and Bioelectronics, Electrochemical biosensors for pathogen detection. 2020: p. 112214.
15. Sadighbayan, D., et al., Recent advances on the DNA-based electrochemical biosensing of cancer biomarkers: Analytical approach. 2019. 119: p. 115609.
16. Sardini, E., M. Serpelloni, and S.J.B. Tonello, Printed Electrochemical Biosensors: Opportunities and Metrological Challenges. 2020. 10(11): p. 166.
17. Babaie, P., A. Saadati, and M.J.J.o.B.M.R.P.B.A.B. Hasanzadeh, Recent progress and challenges on the bioassay of pathogenic bacteria. 2021. 109(4): p. 548-571.
18. El Goumi, Y.J.I.J.B.B., Electrochemical genosensors: Definition and fields of application. 2017. 3: p. 353-355.
19. Campuzano, S., P. Yáñez-Sedeño, and J.M.J.S. Pingarrón, Electrochemical genosensing of circulating biomarkers. 2017. 17(4): p. 866.
20. Senel, M., et al., Electrochemical DNA biosensors for label-free breast cancer gene marker detection. 2019. 411(13): p. 2925-2935.
21. Jainish, P. and P.J.I.J.B.B. Prittesh, Biosensors and biomarkers: promising tools for cancer diagnosis. 2017. 3(4): p. 00072.
22. Zugazagoitia, J., et al., Current challenges in cancer treatment. 2016. 38(7): p. 1551-1566.
23. Zheng, R.t., et al., Report of cancer epidemiology in China, 2015. 2019. 41(1): p. 19-28.
24. Cui, F., Z. Zhou, and H.S.J.J.o.T.E.S. Zhou, Measurement and analysis of cancer biomarkers based on electrochemical biosensors. 2019. 167(3): p. 037525.
25. Sadighbayan, D., et al., Development of electrochemical biosensors for tumor marker determination towards cancer diagnosis: Recent progress. 2019. 118: p. 73-88.
26. Koo, K.M., N. Soda, and M.J.J.C.O.i.E. Shiddiky, Magnetic nanomaterial-based electrochemical biosensors for the detection of diverse circulating cancer biomarkers. 2020: p. 100645.
27. Salahandish, R., et al., Label-free ultrasensitive detection of breast cancer miRNA-21 biomarker employing electrochemical nano-genosensor based on sandwiched AgNPs in PANI and N-doped graphene. 2018. 120: p. 129-136.

28. Anwanwan, D., et al., Challenges in liver cancer and possible treatment approaches. 2020. 1873(1): p. 188314.
29. Li, J., et al., Label-free photoelectrochemical biosensor for alpha-fetoprotein detection based on Au/CsxWO3 heterogeneous films. 2021. 225: p. 122074.
30. Ehzari, H., M. Safari, and M.J.M.J. Shahlaei, A simple and label-free genosensor for BRCA1 related sequence based on electrospinned ribbon conductive nanofibers. 2018. 143: p. 118-126.
31. Shahrokhian, S., R.J.S. Salimian, and A.B. Chemical, Ultrasensitive detection of cancer biomarkers using conducting polymer/electrochemically reduced graphene oxide-based biosensor: Application toward BRCA1 sensing. 2018. 266: p. 160-169.
32. Chen, L., X. Liu, and C.J.J.o.E.C. Chen, Impedimetric biosensor modified with hydrophilic material of tannic acid/polyethylene glycol and dopamine-assisted deposition for detection of breast cancer-related BRCA1 gene. 2017. 791: p. 204-210.
33. Mandli, J. and A.J.J.o.S.S.E. Amine, Impedimetric genosensor for miRNA-34a detection in cell lysates using polypyrrole. 2018. 22(4): p. 1007-1014.
34. Yazdanparast, S., et al., Dual-aptamer based electrochemical sandwich biosensor for MCF-7 human breast cancer cells using silver nanoparticle labels and a poly (glutamic acid)/MWNT nanocomposite. 2018. 185(9): p. 1-10.
35. Voccia, D., et al., Direct determination of small RNAs using a biotinylated polythiophene impedimetric genosensor. 2017. 87: p. 1012-1019.
36. Liu, S., et al., Manufacturing of an electrochemical biosensing platform based on hybrid DNA hydrogel: Taking lung cancer-specific miR-21 as an example. 2018. 103: p. 1-5.
37. Chen, M., et al., Three-dimensional electrochemical DNA biosensor based on 3D graphene-Ag nanoparticles for sensitive detection of CYFRA21-1 in non-small cell lung cancer. 2018. 255: p. 2910-2918.
38. Shoja, Y., et al., Diagnosis of EGFR exon21 L858R point mutation as lung cancer biomarker by electrochemical DNA biosensor based on reduced graphene oxide/functionalized ordered mesoporous carbon/Ni-oxytetracycline metallopolymer nanoparticles modified pencil graphite electrode. 2018. 113: p. 108-115.
39. Rodrigues, V.C., et al., Electrochemical and optical detection and machine learning applied to images of genosensors for diagnosis of prostate cancer with the biomarker PCA3. 2021. 222: p. 121444.
40. Raymundo-Pereira, P.A., et al., Influence of the Molecular Orientation and Ionization of Self-Assembled Monolayers in Biosensors: Application to Genosensors of Prostate Cancer Antigen 3. 2020.
41. Sabahi, A., et al., Electrochemical nano-genosensor for highly sensitive detection of miR-21 biomarker based on SWCNT-grafted dendritic Au nanostructure for early detection of prostate cancer. 2020. 209: p. 120595.
42. Gautam, A., et al., Detection of prostate cancer DNA using tetrapods based disposable paper ecofriendly biosensor device. 2020: p. e10122.
43. Carr, O., et al., Genosensor made with a self-assembled monolayer matrix to detect MGMT gene methylation in head and neck cancer cell lines. 2020. 210: p. 120609.
44. Singhal, C., et al., Impedimetric genosensor for detection of hepatitis C virus (HCV1) DNA using viral probe on methylene blue doped silica nanoparticles. 2017. 98: p. 84-93.
45. Alipour, E., S. Norouzi, and S.J.A.M. Moradi, The development of an electrochemical DNA biosensor based on quercetin as a new electroactive indicator for DNA hybridization detection. 2021. 13(5): p. 719-729.
46. Oliveira, D.A., et al., Carbon nanomaterial as platform for electrochemical genosensor: A system for the diagnosis of the hepatitis C in real sample. 2019. 844: p. 6-13.
47. Roohizadeh, A., et al., Label-free RNA-based electrochemical nanobiosensor for detection of Hepatitis C. 2020. 2: p. 187-192.
48. Li, J., et al., Sensitive electrochemical detection of hepatitis C virus subtype based on nucleotides assisted magnetic reduced graphene oxide-copper nano-composite. 2020. 110: p. 106601.
49. Kannan, P., et al., Cobalt oxide porous nanocubes-based electrochemical immunobiosensing of hepatitis B virus DNA in blood serum and urine samples. 2019. 91(9): p. 5824-5833.
50. Narang, J., et al., Impedimetric genosensor for ultratrace detection of hepatitis B virus DNA in patient samples assisted by zeolites and MWCNT nano-composites. 2016. 86: p. 566-574.
51. Yoshimura, K.J.J.o.I. and Chemotherapy, Current status of HIV/AIDS in the ART era. 2017. 23(1): p. 12-16.
52. Shamsipur, M., et al., Development of an ultrasensitive electrochemical genosensor for detection of HIV-1 pol gene using a gold nanoparticles coated carbon paste electrode impregnated with lead ion-imprinted polymer nanomaterials as a novel electrochemical probe. 2021. 160: p. 105714.
53. Soares, A.C., et al., Microfluidic-based genosensor to detect human papillomavirus (HPV16) for head and neck cancer. 2018. 10(43): p. 36757-36763.
54. Avelino, K.Y., et al., Metal-polymer hybrid nanomaterial for impedimetric detection of human papillomavirus in cervical specimens. 2020. 185: p. 113249.
55. Soares, J.C., et al., Detection of HPV16 in cell lines deriving from cervical and head and neck cancer using a genosensor made with a DNA probe on a layer-by-layer matrix. 2020. 4(11): p. 3258-3266.
56. Avelino, K.Y., et al., Flexible sensor based on conducting polymer and gold nanoparticles for electrochemical screening of HPV families in cervical specimens. 2021. 226: p. 122118.
57. Farzin, L., et al., A nanoscale genosensor for early detection of COVID-19 by voltammetric

determination of RNA-dependent RNA polymerase (RdRP) sequence of SARS-CoV-2 virus. 2021. 188(4): p. 1-12.
58. Sohrabi, H., et al., A novel engineered label-free Zn-based MOF/CMC/AuNPs electrochemical genosensor for highly sensitive determination of Haemophilus Influenzae in human plasma samples. 2021. 188(3): p. 1-16.
59. Saadati, A., et al., Binding of pDNA with cDNA using hybridization strategy towards monitoring of Haemophilus influenza genome in human plasma samples. 2020. 150: p. 218-227.
60. Mohammadi, J., et al., Electrochemical biosensing of influenza A subtype genome based on meso/macroporous cobalt (II) oxide nanoflakes-applied to human samples. 2017. 979: p. 51-57.
61. Hassanpour, S., et al., pDNA conjugated with citrate capped silver nanoparticles towards ultrasensitive bio-assay of haemophilus influenza in human biofluids: a novel optical biosensor. 2020. 180: p. 113050.
62. Subak, H., D.J.S. Ozkan-Ariksoysal, and A.B. Chemical, Label-free electrochemical biosensor for the detection of Influenza genes and the solution of guanine-based displaying problem of DNA hybridization. 2018. 263: p. 196-207.
63. Yusa, T., et al., New possible biomarkers for diagnosis of infections and diagnostic distinction between bacterial and viral infections in children. 2017. 23(2): p. 96-100.
64. Bennish, M.L. and S. Ahmed, Shigellosis, in Hunter's Tropical Medicine and Emerging Infectious Diseases. 2020, Elsevier. p. 492-499.
65. Elahi, N., M.H. Baghersad, and M.J.J.o.m.m. Kamali, Precise, direct, and rapid detection of Shigella Spa gene by a novel unmodified AuNPs-based optical genosensing system. 2019. 162: p. 42-49.
66. Mobed, A., et al., An innovative nucleic acid based biosensor toward detection of Legionella pneumophila using DNA immobilization and hybridization: A novel genosensor. 2019. 148: p. 708-716.
67. de Castro, A.C.H., et al., A new genosensor for meningococcal meningitis diagnosis using biological samples. 2018. 22(8): p. 2339-2346.
68. Xu, S., et al., Novel approach to fabrication of DNA Biosensor Based on a Carboxylated Graphene Oxide Decorated with Fe3O4 NPs for the Detection of Typhoidal Salmonella. 2019. 14: p. 1248-1269.
69. Rahman, M., et al., Ultrasensitive biosensor for the detection of Vibrio cholerae DNA with polystyrene-co-acrylic acid composite nanospheres. 2017. 12(1): p. 1-12.
70. Jaroenram, W., et al., Graphene-based electrochemical genosensor incorporated loop-mediated isothermal amplification for rapid on-site detection of Mycobacterium tuberculosis. 2020. 186: p. 113333.
71. Singh, S., et al., Prostate cancer biomarkers detection using nanoparticles based electrochemical biosensors. 2019. 137: p. 213-221.