Chapter 1
Potential Role of Biomarkers, Biosensors, Technologies, and Computational Methods in Early Detection of Gastrointestinal Cancer

Pallaval Veera Bramhachari and Nageswara Rao Reddy Neelapu

Abstract The current challenge for effective treatment of gastrointestinal cancer is detection of cancer at an early stage. Detection of gastrointestinal cancer at an early stage requires biomarkers expressing at early stage, biosensors, promising technologies, and computational methods. Therefore, this chapter discusses the role of biomarkers, biosensors, promising technologies, and computational methods which can be used for detection of gastrointestinal cancer. This provides information and new insights which can be used for early detection of gastrointestinal cancer.

Keywords Biomarkers · Biosensors · Computational methods for early detection of cancer · Technologies for early detection of cancer

1.1 Introduction

The current challenge for effective treatment of gastrointestinal cancer is detection of cancer at an early stage. Detection of gastrointestinal cancer at an early stage requires biomarkers expressing at early stage, biosensors, promising technologies, and computational methods (Fig. 1.1). Biomarkers provide understanding on features of cancer or tumor and helps in determining the features of cancer or tumor. Biosensors are used to sense or determine the biomarkers (expressed features of cancer or tumor) both qualitatively and quantitatively. The promising technologies are used either to identify biomarkers or develop sensors or devices. Computational methods used

P. Veera Bramhachari
Department of Biotechnology, Krishna University, Machilipatnam, Andhra Pradesh, India

N. R. R. Neelapu (✉)
Department of Biochemistry and Bioinformatics, GITAM Institute of Science, Gandhi Institute of Technology and Management (GITAM) (Deemed-to-be-University), Visakhapatnam, Andhra Pradesh, India

P. Veera Bramhachari, N. R. R. Neelapu (eds.), *Recent Advancements in Biomarkers and Early Detection of Gastrointestinal Cancers*, Diagnostics and Therapeutic Advances in GI Malignancies, https://doi.org/10.1007/978-981-15-4431-6_1

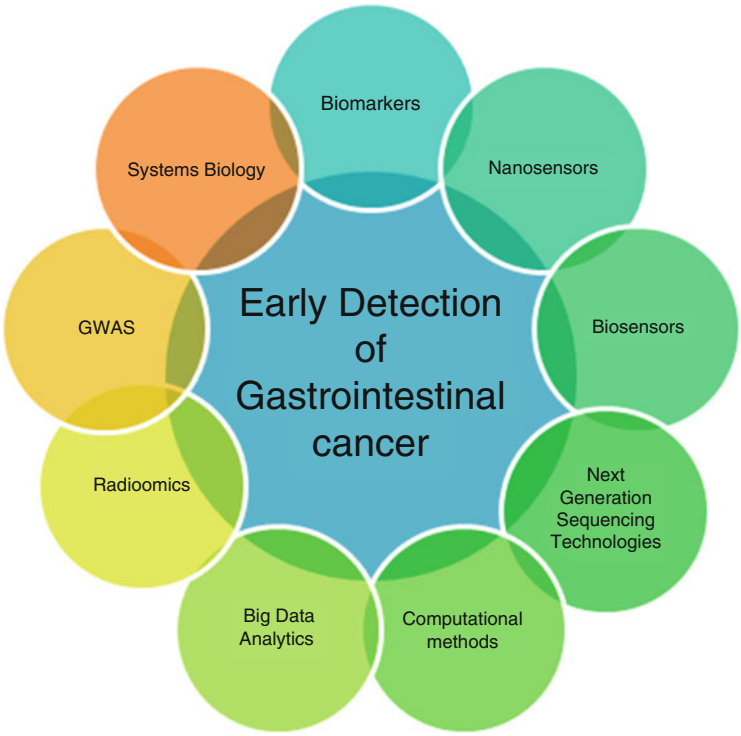

Fig. 1.1 Potential role of biomarkers, biosensors, technologies, and computational methods in early detection of gastrointestinal cancer

mathematical methods or expressions to identify or model or quantify features of cancer or tumor. Thus, this chapter discusses in detail about the role of biomarkers, biosensors, promising technologies, and computational methods which can be used for detection of gastrointestinal cancer. This provides information and new insights which can be used for early detection of gastrointestinal cancer.

1.2 Role of Biomarkers in Early Detection of Gastrointestinal Cancer

Molecular signatures or profiles generated by tumor or cancer due to proteins, microsatellite instability, hypermethylation, single nucleotide polymorphism, volatile compounds, serum, etc. are known as biomarkers. These markers are known as protein markers (if protein profiles are used), microsatellite instability markers (if microsatellite instability signatures are defined), hypermethylation markers (if hypermethylation profiles are identified), single nucleotide polymorphism markers (when SNP profiles are characterized), volatile markers (when volatile

compounds are expressed), and serum markers (if serum profiles are outlined). These markers can be used to diagnose gastrointestinal cancer. Biomarkers are generally classified based on disease state, types of biomolecules, and other criteria (Radhika et al. 2016). The disease state biomarkers available for early detection of cancer are risk assessment biomarkers, screening/detection biomarkers, diagnosis biomarkers, prognosis biomarkers, prediction biomarkers, and monitoring biomarkers. The biomolecule biomarkers are DNA biomarker, RNA biomarker, protein biomarker, glycol biomarkers, metabolite biomarkers, and serum biomarkers (Radhika et al. 2016). The biomarkers in other criteria are imaging biomarkers, pathological biomarker, next-generation biomarkers, and in silico biomarkers (Radhika et al. 2016). Molecular markers like CDH1 gene (Bussemakers et al. 1994), DNMT3A gene (De Carvalho et al. 2012), PTPRCAP gene (Hyoungseok et al. 2009), PSCA gene (Sakamoto et al. 2008), VEGF-A gene (Yancopoulos et al. 2000), XRCC1 gene (Caldecott et al. 1996), IL-1 gene (England et al. 2014), HER-2 gene (Baselga et al. 1996), and MUC1 gene (Bafna et al. 2010) are known as genetically susceptible markers. These genetically susceptible markers are inherited by individual or population leading to cancer, which can be used to diagnose gastrointestinal cancer. The new dimension of cancer diagnosis is use of serum biomarkers in the development of serum biomarker panels which made diagnosis of gastrointestinal cancer simple based on serum profiles. Thus, it can be established that biomarkers have a role in the early diagnosis of gastrointestinal cancer.

1.3 Role of Biosensors in Early Detection of Gastrointestinal Cancer

Biosensors are used in fields like drug discovery (Morris 2013), fermentation industry (Yan et al. 2014), defense (Pohanka 2019), food quality (Torun et al. 2012), environmental monitoring (Arora et al. 2011), metabolic studies, and plant studies (Berens and Suess 2015). Biosensors can now provide key information on cancer for effective and safe treatment. Cost effectiveness, reliability, accuracy, and less time consuming are the important aspects of biosensors. DNA, antibody, antigen, enzyme, whole cell, and cell organelle are used as a biological recognition element for biosensors (Malhotra et al. 2017). The biological sample interacts with the element of the biosensor and forms a product (Malhotra et al. 2017). The product then reaches the transducer, amplifies, records, and displays on the devices (Malhotra et al. 2017). The different types of biosensors are affinity biosensor, catalytic biosensor, metabolism biosensor, DNA biosensor, electrochemical biosensor, optical biosensor, mass change biosensor, graphene-based biosensor, amperometric biosensor, microbial biosensor, miRNA biosensor, and many more (Leech 1994; Freitas et al. 2018; Jainish and Prittesh 2017; Medley et al. 2008; Tothill 2009; Kavita 2017; Lei et al. 2006; D'Souza 2001; Steinberg et al. 1995; Kumar et al. 2006; Choi and Chae 2012; Correia et al. 2017; Morgan et al. 2016; Rogers et al.

2016; Liu et al. 2017; Cheng et al. 2015; Kwon et al. 2018; Zhang et al. 2014; Szunerits and Boukherroub 2018). Biosensors role in early detection and diagnosis of cancer is known. Biosensors improved the diagnostic capability by its sensitivity, specificity, reproducibility, linearity, and high-throughput screening (Bhalla et al. 2016). Thus, biosensors have an important role in early detection of gastrointestinal cancer.

The second and the new dimension in biosensors is the use of nanotechnology for the development of biosensors. This shows how nanotechnology is a powerful and promising technology for early detection of gastrointestinal cancer. Nanobiosensors are developed using nanomaterial's like quantum dots, carbon nanotubes, nanopores, nanorods, nanowires, cantilevers, nanoparticles, and nanomembranes (Madani et al. 2013; de La Zerda and Gambhir 2007; Clarke et al. 2009; Hu et al. 2011; Israelsen et al. 2015; Zang et al. 2012; Daneshpour et al. 2016). Nanobiosensors role in early detection of cancer via carbon nanotube for CEA biomarker is reported (Länge et al. 2008). Nanobiosensors role in early detection of gastrointestinal cancer via electrochemical nanobiosensor for biomarkers miRNA 106A is also reported (Richardson et al. 2001). The different nanobiosensors are nanoparticles-based sensors (acoustic wave biosensors, magnetic biosensors, electrochemical biosensors), nanotube-based sensors, nanowire-based sensors, and ion channel-based sensors (Clark Jr and Lyons 1962; Desai et al. 1999; Cui et al. 2001; Cornell et al. 1997). The immobilization of biomolecules onto nanomaterials develops nanobiosensors for detection of analyte. The different strategies used for immobilization of biomolecules onto nanomaterials are covalent, noncovalent, and linker with covalent (Dubertret et al. 2002; Bruchez et al. 1998; Taton et al. 2001). The different parameters like selectivity, reproducibility, dynamic range, and negligible changes in concentrations of biomolecules indicate the performance of nanobiosensors. Thus, the potential role of nanobiosensors in early detection of gastrointestinal cancer can be materialized in the development of diagnostic devices or healthcare wearables in the near future.

1.4 Role of Technologies in Early Detection of Gastrointestinal Cancer

Expression profiling of microRNA, circulating microRNAs, serum microRNA, and plasma microRNA derive the signatures of the cancer. Expression profiling include RNA sequencing using next-generation sequencing technology or microarray of miRNAs using Affymetrix microarray or real-time reverse transcription PCR (qRT-PCR) to generate expression profile datasets. The analysis of these expression profile datasets between normal and gastric cancer cells would provide the differential expression profiles or patterns. The analysis indicates upregulated and downregulated miRNAs involved in signaling pathways related to environmental

information processing and diseases. Therefore, these set of signature miRNAs may be promising biomarkers for the early diagnosis of gastrointesinal cancer.

In order to fulfill some of our knowledge gaps on cancer, it is essential to continually generate and explore omic's data on cancer. There are five next-generation sequencing technologies available to generate NGS data: first-, second-, third-, fourth-, and fifth-generation sequencing technologies. The first-generation sequencing technologies include Sanger sequencing and Maxam Gilbert sequencing method (Neelapu and Surekha 2016). The second-generation sequencing method includes Roche/454 Sequencing, Ion torrent sequencing, Illumina/Solexa sequencing, and ABI/SOLiD sequencing (Neelapu and Surekha 2016). The third-generation sequencing method includes Single Molecule Real-Time (SMRT) sequencing approach and Oxford Nanopore Technology (ONT) sequencing approach (Neelapu and Surekha 2016). The fourth-generation sequencing method includes Nanopore-based sequencing by biological nanopores and solid-state nanopores (Neelapu and Surekha 2016). The fifth-generation sequencing method includes high-fidelity nanopore sequencing of ultra-short DNA targets and cyclomics: ultra-sensitive nanopore sequencing of cell-free tumor DNA (Neelapu and Surekha 2016). The technologies like Roche/454 Sequencing, Illumina/Solexa sequencing, Single Molecule Real-Time (SMRT) sequencing approach and Nanopore-based sequencing are used to generate whole-genome sequencing (WGS) data (Neelapu and Surekha 2016). WGS of tumor or cancer cell followed by the analysis of WGS data provides genetic information and heterogeneity of tumor or cancer cell when compared with the normal cell (Nakagawa and Fujita 2018).

Whole exome sequencing (WES), is a genomic technique for sequencing all of the protein-coding regions of genes in a genome (known as the exome) (Ng et al. 2009). This information provides insights on understanding nature of tumor or cancer cell. Epigenome sequencing of cancer or tumor cell helps in understanding the epigenetic features regulating cancer cells or tumor. The technologies such as methylation-sensitive restriction enzyme sequencing (MRE-seq), methylated DNA immunoprecipitation sequencing (MeDIP-seq), methyl-CpG-binding domain protein sequencing (MBD-seq), reduced representation bisulfite sequencing (RRBS), whole-genome bisulfite sequencing (WGBS), oxidative bisulfite sequencing (oxBS-seq) generate epigenome data-based methylation patterns (Sarda and Hannenhalli 2014). The other technologies like chromatin immunoprecipitation sequencing (ChIP-seq), and chromatin immunoprecipitation-exonuclease (ChIP-exo) generate epigenome data based on histone modifications (Sarda and Hannenhalli 2014). These technologies helped in understanding epigenetic features regulating cancer cells or tumor. The deep sequencing of mRNA-seq, long-read, direct RNA-seq, and short sequence reads (transcriptomes) by RNA sequencing technologies helps in generating transcriptome data (Stark et al. 2019). The short-read cDNA, long-read c DNA, and long-read RNA are generated using platforms Illumina and Ion Torrent; PacBio and ONT; and Nanopore technology, respectively. This helps in understanding single-cell gene expression, translation (the translatome), RNA structure (the structurome), and spatial transcriptomics (spatialomics) and also aids in understanding nature of tumor or cancer cell (Stark et al. 2019). De novo peptide sequencing via

tandem mass spectrometry is used to generate proteomics data (Dancík et al. 1999). This proteomics approach can be used to understanding nature of tumor or cancer cell. Thus, genomics, epigenomics, transcriptomics, and proteomics approach can be used understanding the nature of tumor or cancer cell.

1.5 Role of Computational Methods in Early Detection of Gastrointestinal Cancer

The role of computational methods like genome-wide association studies (GWAS) (Challa and Neelapu 2018), big data analytics, and systems biology approach is known and can be used for early detection of gastrointestinal cancer. The genome sequencing projects of human led to genome-wide association studies (GWAS) to recognize genes and its respective variants related with any traits or diseases. GWAS was used for prediction of early onset of gastrointestinal cancer and can be utilized as biomarker in the detection and prevention of gastrointestinal cancer. Biomarkers, like carcinoembryonic antigen (Länge et al. 2008) and carbohydrate antigen 19-9 (Perkins et al. 2003), are in clinical use for detection of advanced stage of gastric cancer. Genome studies reported that expression level of CDH1 (Suriano et al. 2003; Bacani et al. 2006), CTNNB1 (Zhou et al. 2002), CDX-2 (Seno et al. 2002; Mizoshita et al. 2003; Fan et al. 2005), HER2 (Moelans et al. 2011), CD44v6 (Carvalho et al. 2006), 5p15 (Du et al. 2013), PRKAA1 (Jiang et al. 2018), and Reprimo (Bernal et al. 2008) predictive biomarker for the early onset of gastric cancer.

Imaging biomarkers, pathological biomarker, next-generation biomarkers generate large amounts of data. Big data analytics help in analyzing the big data to discover diagnostics and therapeutics for gastric cancer. Radiomics is a process of converting digital medical images into mineable high-dimensional data, and radiomics uses machine-learning approach to make clinical decision (Lambin et al. 2012). Radiomics include correlating and integrating omics data with radiomics features extracted from radiological images and integrate them to create a more efficient and robust prognostic model (Lambin et al. 2012). Thus, radiomics helps in early detection of gastrointestinal cancer. In the same way, big data generated by imaging technologies, pathological methods or technologies, and next-generation sequencing technologies can be analyzed by employing various methods in big data analytics for early detection of cancer.

Systems biology approach integrated high-throughput and "omics" data in understanding the disease (Kang et al. 2016). Systems biology is necessary to analyze the complexities of various pathways involving signaling, regulation of the gene, cell metabolism, and alterations in its system caused due to mutations leading to malignancy (Kang et al. 2016). These approaches seem to be complicated with several interlinks connecting pathways, and it is necessary to signify it in the form of a computational model (Kang et al. 2016). And, also in identifying the proteins and

pathways of gastric cancer that can be useful sequentially in identifying major proteins and pathways (Kang et al. 2016). This helps in understanding the functional difference that takes place from a normal and disease cell. Thus, systems biology approach helps in early detection of gastrointestinal cancer. However, these findings require further wet-lab validation.

1.6 Significance

Detection of gastrointestinal cancer at an early stage requires biomarkers expressing at early stage, biosensors, promising technologies, and computational methods. Next-generation sequencing technologies especially the fifth-generation technology like high-fidelity nanopore sequencing of ultra-short DNA targets and cyclomics: ultra-sensitive nanopore sequencing of cell-free tumor DNA can be used to identify biomarkers which are expressed at an early stage of cancer. NGS technologies can also be used to develop gene panels, whole exome sequencing (WES), and whole-genome sequencing for cancer detection. NGS gene panels are already in use for diagnosis of hereditary cancers like breast, ovarian, colon, etc. Biomarkers identified can be integrated into biosensors or nanosensors to develop real-time measurement devices for early detection of gastrointestinal cancer. Healthcare monitoring devices or healthcare wearables are already in market for diagnosing diseases like diabetes. These healthcare wearables may help in early detection of cancer, as well as help in monitoring the cancer patient condition and treatment outcome from time to time. The NGS technologies and omic's technologies may help in understanding the genes, epigenetic features, proteins, and other features responsible for transition of normal cell to cancer state. The computational methods help in developing new methods for analysis, and modeling of the data and also in mining the big data like radioimages. These computational methods may provide novel insights on cancer which can be used for detection of cancer. Thus, this chapter discusses about the potential role of biomarkers, biosensors, promising technologies, and computational methods for early detection of gastrointestinal cancer.

Acknowledgements NNRR is grateful to GITAM (Deemed-to-be-University) for providing necessary facilities to carry out the research work and for extending constant support. PVBC is thankful to Krishna University for providing necessary facilities to carry out the research work.

Conflict of Interest The authors declare that there is no potential conflict of interest.

References

Arora P, Sindhu A, Dilbaghi N, Chaudhury A (2011) Biosensors as innovative tools for the detection of food borne pathogens. Biosens Bioelectron 28(1):1–12

Bacani JT, Soares M, Zwingerman R, Bacani JT, Soares M, Zwingerman R, di Nicola N, Senz J, Riddell R, Huntsman DG, Gallinger S (2006) CDH1/E-cadherin germline mutations in early-onset gastric cancer. J Med Genet 43(11):867–872

Bafna S, Kaur S, Batra SK (2010) Membrane-bound mucins: the mechanistic basis for alterations in the growth and survival of cancer cells. Oncogene 29:2893–2904

Baselga J, Tripathy D, Mendelsohn J, Baughman S, Benz CC, Dantis L, Sklarin NT, Seidman AD, Hudis CA, Moore J, Rosen PP, Twaddell T, Henderson IC, Norton L (1996) Phase II study of weekly intravenous recombinant humanized anti-p185HER2 monoclonal antibody in patients with HER2/neu-overexpressing metastatic breast cancer. J Clin Oncol 14:737–744

Berens C, Suess B (2015) Riboswitch engineering—making the all-important second and third steps. Curr Opin Biotechnol 31:10–15

Bernal C, Aguayo F, Villarroel C, Bernal C, Aguayo F, Villarroel C, Vargas M, Díaz I, Ossandon FJ, Santibáñez E, Palma M, Aravena E, Barrientos C, Corvalan AH (2008) Reprimo as a potential biomarker for early detection in gastric cancer. Clin Cancer Res 14:6264–6269. https://doi.org/10.1158/1078-0432.CCR-07-4522

Bhalla N, Jolly P, Formisano N, Estrela P (2016) Introduction to biosensors. Essays Biochem 60 (1):1–8

Bruchez M, Moronne M, Gin P, Weiss S, Alivisatos AP (1998) Semiconductor nanocrystals as fluorescent biological labels. Science 281(5385):2013–2016

Bussemakers MJG, Van Bokhoven A, Völler M, Smit FP, Schalken JA (1994) The genes for the calcium-dependent cell adhesion molecules P- and E-cadherin are tandemly arranged in the human genome. Biochem Biophys Res Commun 203:291–1294

Caldecott KW, Aoufouchi S, Johnson P, Shall S (1996) XRCC1 polypeptide interacts with DNA polymerase beta and possibly poly (ADP-ribose) polymerase, and DNA ligase III is a novel molecular 'nick-sensor' *in vitro*. Nucleic Acids Res 24:4387–4394

Carvalho R, Milne ANA, Polak M, Offerhaus GJ, Weterman MA (2006) A novel region of amplification at 11p12-13 in gastric cancer, revealed by representational difference analysis, is associated with overexpression of CD44v6, especially in early-onset gastric carcinomas. Genes Chromosomes Cancer 45:967–975

Challa S, Neelapu NRR (2018) Genome-wide association studies (GWAS) for abiotic stress tolerance in plants. In: Biochemical, physiological and molecular avenues for combating abiotic. Academic, Cambridge, pp 135–150

Cheng F, Kardashliev T, Pitzler C, Shehzad A, Lue H, Bernhagen J et al (2015) A competitive flow cytometry screening system for directed evolution of therapeutic enzyme. ACS Synth Biol 4 (7):768–775

Choi S, Chae J (2012) An array of microliter-sized microbial fuel cells generating 100 μW of power. Sensors Actuators A Phys 177:10–15

Clark LC Jr, Lyons C (1962) Electrode systems for continuous monitoring in cardiovascular surgery. Ann N Y Acad Sci 102(1):29–45

Clarke J, Wu HC, Jayasinghe L, Patel A, Reid S, Bayley H (2009) Continuous base identification for single-molecule nanopore DNA sequencing. Nat Nanotechnol 4(4):265–270

Cornell BA, Braach-Maksvytis VLB, King LG, Osman PDJ, Raguse B, Wieczorek L, Pace RJ (1997) A biosensor that uses ion-channel switches. Nature 387(6633):580–583

Correia CN, Nalpas NC, McLoughlin KE, Browne JA, Gordon SV, MacHugh DE, Shaughnessy RG (2017) Circulating microRNAs as potential biomarkers of infectious disease. Front Immunol 8:118

Cui Y, Wei Q, Park H, Lieber CM (2001) Nanowire nanosensors for highly sensitive and selective detection of biological and chemical species. Science 293(5533):1289–1292

D'Souza SF (2001) Microbial biosensors. Biosens Bioelectron 16(6):337–353

Dancík V, Addona TA, Clauser KR, Vath JE, Pevzner PA (1999) De novo peptide sequencing via tandem mass spectrometry. J Comput Biol 6(3–4):327–342

Daneshpour M, Omidfar K, Ghanbarian H (2016) A novel electrochemical nanobiosensor for the ultrasensitive and specific detection of femtomolar level gastric cancer biomarker miRNA-106a. Beilstein J Nanotechnol 7(2016):2023–2036

De Carvalho DD, Sharma S, You JS, Su SF, Taberlay PC, Kelly TK, Yang X, Liang G, Jones PA (2012) DNA methylation screening identifies driver epigenetic events of cancer cell survival. Cancer Cell 21:655–667

de La Zerda A, Gambhir SS (2007) Drug delivery: keeping tabs on nanocarriers. Nat Nanotechnol 2 (12):745–746

Desai T, Hansford D, Ferrari M (1999) Characterization of micromachined silicon membranes for immunoisolation and bioseparation applications. J Membrane Sci 159:221–231

Du J, Xu Y, Dai J, Ren C, Zhu C, Dai N, Ma H, Shi Y, Hu Z, Lin D, Shen H, Jin G (2013) Genetic variants at 5p15 are associated with risk and early onset of gastric cancer in Chinese populations. Carcinogenesis 34:2539–2542

Dubertret B, Skourides P, Norris DJ, Noireaux V, Brivanlou AH, Libchaber A (2002) In vivo imaging of quantum dots encapsulated in phospholipid micelles. Science 298(5599):1759–1762

England H, Summersgill HR, Edye ME et al (2014) Release of interleukin-1α or interleukin-1β depends on mechanism of cell death. J Biol Chem 289(23):15942–15950

Fan Z, Li J, Dong B, Huang X (2005) Expression of Cdx2 and hepatocyte antigen in gastric carcinoma: correlation with histologic type and implications for prognosis. Clin Cancer Res 11:6162–6170

Freitas M, Nouws HP, Delerue-Matos C (2018) Electrochemical biosensing in cancer diagnostics and follow-up. Electroanalysis 30(8):1584–1603

Hu Y, Fine DH, Tasciotti E, Bouamrani A, Ferrari M (2011) Nanodevices in diagnostics. Wiley Interdiscip Rev Nanomed Nanobiotechnol 3(1):11–32

Hyoungseok JU, Lim B, Kim M, Kim YS, Kim WH, Ihm C, Noh S-M, Han DS, Yu H-J, Choi BY, Kang C (2009) A regulatory polymorphism at position −309 in PTPRCAP is associated with susceptibility to diffuse-type gastric cancer and gene expression. Neoplasia 11:1340–1347

Israelsen ND, Hanson C, Vargis E (2015) Nanoparticle properties and synthesis effects on surface-enhanced Raman scattering enhancement factor: an introduction. Sci World J 2015:124582. https://doi.org/10.1155/2015/124582

Jainish P, Prittesh P (2017) Biosensors and biomarkers: promising tools for cancer diagnosis. Int J Biosens Bioelectron 3(4):00072

Jiang Y, Li W, Lu J, Zhao X, Li L (2018) Association between PRKAA1 rs13361707 T>C polymorphism and gastric cancer risk: evidence based on a meta-analysis. Medicine (Baltimore) 97:e0302. https://doi.org/10.1097/MD.0000000000010302

Kang W, Cheng AS, Yu J, To KF (2016) Emerging role of Hippo pathway in gastric and other gastrointestinal cancers. World J Gastroenterol 22(3):1279

Kavita V (2017) DNA biosensors—a review. J Bioeng Biomed Sci 7:2

Kumar J, Jha SK, D'Souza SF (2006) Optical microbial biosensor for detection of methyl parathion pesticide using *Flavobacterium* sp. whole cells adsorbed on glass fiber filters as disposable biocomponent. Biosens Bioelectron 21(11):2100–2105

Kwon KK, Lee DH, Kim SJ, Choi SL, Rha E, Yeom SJ et al (2018) Evolution of enzymes with new specificity by high-throughput screening using DmpR-based genetic circuits and multiple flow cytometry rounds. Sci Rep 8(1):2659

Lambin P, Rios-Velazquez E, Leijenaar R, Carvalho S, van Stiphout RG, Granton P, Zegers CM, Gillies R, Boellard R, Dekker A, Aerts HJ (2012) Radiomics: extracting more information from medical images using advanced feature analysis. Eur J Cancer 48(4):441–446

Länge K, Rapp BE, Rapp M (2008) Surface acoustic wave biosensors: a review. Anal Bioanal Chem 391(5):1509–1519

Leech D (1994) Affinity biosensors. Chem Soc Rev 23(3):205–213

Lei Y, Chen W, Mulchandani A (2006) Microbial biosensors. Anal Chim Acta 568(1-2):200–210

Liu Y, Liu Y, Wang M (2017) Design, optimization and application of small molecule biosensor in metabolic engineering. Front Microbiol 8:2012

Madani SY, Shabani F, Dwek MV, Seifalian AM (2013) Conjugation of quantum dots on carbon nanotubes for medical diagnosis and treatment. Int J Nanomedicine 8:941–950

Malhotra S, Verma A, Tyagi N, Kumar V (2017) Biosensors: principle, types and applications. Int J Adv Res Innov Ideas Educ 3(2):3639–3644

Medley CD, Smith JE, Tang Z, Wu Y, Bamrungsap S, Tan W (2008) Gold nanoparticle-based colorimetric assay for the direct detection of cancerous cells. Anal Chem 80(4):1067–1072

Mizoshita T, Tsukamoto T, Nakanishi H, Inada K, Ogasawara N, Joh T, Itoh M, Yamamura Y, Tatematsu M (2003) Expression of Cdx2 and the phenotype of advanced gastric cancers: relationship with prognosis. J Cancer Res Clin Oncol 129:727–734

Moelans CB, Milne AN, Morsink FH, Offerhaus GJ, van Diest PJ (2011) Low frequency of HER2 amplification and overexpression in early onset gastric cancer. Cell Oncol (Dordr) 34:89–950

Morgan SA, Nadler DC, Yokoo R, Savage DF (2016) Biofuel metabolic engineering with biosensors. Curr Opin Chem Biol 35:150–158

Morris MC (2013) Fluorescent biosensors—probing protein kinase function in cancer and drug discovery. Biochim Biophys Acta 1834(7):1387–1395

Nakagawa H, Fujita M (2018) Whole genome sequencing analysis for cancer genomics and precision medicine. Cancer Sci 109(3):513–522

Neelapu NRR, Surekha C (2016) Next-generation sequencing and metagenomics. In: Wong K-C (ed) Computational biology and bioinformatics: gene regulation. CRC Press, Boca Raton, pp 331–351

Ng SB, Turner EH, Robertson PD, Flygare SD, Bigham AW, Lee C, Shaffer T, Wong M, Bhattacharjee A, Eichler EE, Bamshad M, Nickerson DA, Shendure J (2009) Targeted capture and massively parallel sequencing of 12 human exomes. Nature 461(7261):272–276

Perkins G, Slater E, Sanders G, Prichard J (2003) Serum tumor markers. Am Fam Physician 68 (6):1075–1082

Pohanka M (2019) Current trends in the biosensors for biological warfare agents assay. Materials (Basel) 12(14):2303. https://doi.org/10.3390/ma12142303

Radhika T, Jeddy N, Nithya S, Muthumeenakshi RM (2016) Salivary biomarkers in oral squamous cell carcinoma—an insight. J Oral Biol Craniofac Res 6(Suppl 1):S51–S54

Richardson J, Hawkins P, Luxton R (2001) The use of coated paramagnetic particles as a physical label in a magnetoimmunoassay. Biosens Bioelectron 16(9–12):989–993

Rogers JK, Taylor ND, Church GM (2016) Biosensor-based engineering of biosynthetic pathways. Curr Opin Biotechnol 42:84–91

Sakamoto H, Yoshimura K, Saeki N, Katai H, Shimoda T, Matsuno Y, Saito D, Sugimura H, Tanioka F, Kato S, Matsukura N, Matsuda N, Nakamura T, Hyodo I, Nishina T, Yasui W, Hirose H, Hayashi M, Toshiro E, Ohnami S, Sekine A, Sato Y, Totsuka H, Ando M, Takemura R, Takahashi Y, Ohdaira M, Aoki K, Honmyo I, Chiku S, Aoyagi K, Sasaki H, Ohnami S, Yanagihara K, Yoon KA, Kook MC, Lee YS, Park SR, Kim CG, Choi IJ, Yoshida T, Nakamura Y, Hirohashi S (2008) Genetic variation in PSCA is associated with susceptibility to diffusetype gastric cancer. Nat Genet 40:730–740

Sarda S, Hannenhalli S (2014) Next-generation sequencing and epigenomics research: a hammer in search of nails. Genomics Inform 12(1):2–11. https://doi.org/10.5808/GI.2014.12.1.2

Seno H, Oshima M, Taniguchi M-A, Usami K, Ishikawa TO, Chiba T, Taketo MM (2002) CDX2 expression in the stomach with intestinal metaplasia and intestinal-type cancer: prognostic implications. Int J Oncol 21:769–774

Stark R, Grzelak M, Hadfield J (2019) RNA sequencing: the teenage years. Nat Rev Genet 20:631–656

Steinberg SM, Poziomek EJ, Engelmann WH, Rogers KR (1995) A review of environmental applications of bioluminescence measurements. Chemosphere 30(11):2155–2197

Suriano G, Oliveira C, Ferreira P, Machado JC, Bordin MC, De Wever O, Bruyneel EA, Moguilevsky N, Grehan N, Porter TR, Richards FM, Hruban RH, Roviello F, Huntsman D, Mareel M, Carneiro F, Caldas C, Seruca R (2003) Identification of CDH1 germline missense

mutations associated with functional inactivation of the E-cadherin protein in young gastric cancer probands. Hum Mol Genet 12:575–582
Szunerits S, Boukherroub R (2018) Graphene-based biosensors. Interface Focus 8(3):20160132
Taton TA, Lu G, Mirkin CA (2001) Two-color labeling of oligonucleotide arrays via size-selective scattering of nanoparticle probes. J Am Chem Soc 123(21):5164–5165
Torun Ö, Boyacı İH, Temür E, Tamer U (2012) Comparison of sensing strategies in SPR biosensor for rapid and sensitive enumeration of bacteria. Biosens Bioelectron 37(1):53–60
Tothill IE (2009) Biosensors for cancer markers diagnosis. Semin Cell Dev Biol 20(1):55–62
Yan C, Dong F, Chun-yuan B, Si-rong Z, Jian-guo S (2014) Recent progress of commercially available biosensors in China and their applications in fermentation processes. J Northeast Agric Univ 21(4):73–85
Yancopoulos GD, Davis S, Gale NW, Rudge JS, Wiegand SJ, Holash J (2000) Vascular-specific growth factors and blood vessel formation. Nature 407:242–248
Zang D, Ge L, Yan M, Song X, Yu J (2012) Electrochemical immunoassay on a 3D microfluidic paper-based device. Chem Commun 48:4683–4685
Zhang Y, Gao G, Liu H, Fu H, Fan J, Wang K, Chen Y, Li B, Zhang C, Zhi X, He L (2014) Identification of volatile biomarkers of gastric cancer cells and ultrasensitive electrochemical detection based on sensing interface of Au-Ag alloy coated MWCNTs. Theranostics 4(2):154
Zhou YN, Xu CP, Han B, Li M, Qiao L, Fang DC, Yang JM (2002) Expression of E-cadherin and β-catenin in gastric carcinoma and its correlation with the clinicopathological features and patient survival. World J Gastroenterol 8:987–993