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ADVANCEMENT OF NANOTECHNOLOGY IN CANCER BIOMARKER SCREENING

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ABSTRACT

Cancer is an extremely complicated disease that spreads through a multi-step process that involves angiogenesis, resistance to apoptosis, unchecked cell growth, changes in cellular signalling, tissue invasion, and metastasis. The present review paper was based on the advancements of nanotechnology in cancer biomarker screening through MDPI, PubMed, and Scopus journals. After 2030, it is anticipated that 30 million individuals will succumb to cancer annually. A cancer biomarker is a biological molecule that can be found in the living tissues, bodily fluids, including saliva and urine, and can be used to identify the cancer cells. Quantum Dots, gold nanoparticles and polymer dots are the three most often used nanoparticle probes in the diagnosis of cancer. The presence of genome methylation patterns, known as Methylscape, has been observed in various forms of malignancies, indicating its potential utility as a cancer biomarker. EpCAM has been demonstrated to have considerable expression on circulating tumour cells (CTCs) derived from several types of human malignancies, making it a suitable candidate for use as a cell surface biomarker. The findings from the molecular analysis indicated that there was an elevation in Cas2 mRNA levels in the cancer cells that were subjected to treatment with carboxyl-functionalized carbon nanotubes. It concluded that cancer biomarker screening is one of the main factors in the detection of various subtypes. It is highly likely that cancer nanotechnology will soon provide a comprehensive, efficient, dependable, and secure approach to cancer detection and therapy.

KEYWORDS: Cancer, biomarker, nanotechnology, mRNA, genes.

INTRODUCTION

Cancer is an extremely complicated disease that spreads through a multi-step process that involves angiogenesis, resistance to apoptosis, unchecked cell growth, changes in cellular signalling, tissue invasion, and metastasis.[1] Cancer typically starts as a localised tumour that has the potential to spread to other parts of the body, making care challenging. The incidence and death of cancer are rising globally. Global cancer incidence, mortality, and prevalence (GLOBOCAN) 2018 data showed ≥18.1 million new cancer cases were anticipated, along with 9.6 million deaths due to cancer.[2] After 2030, it is anticipated that 30 million individuals will succumb to cancer annually.[3,4]

Rising pollution, radiation, sedentary lifestyles, unbalanced diets, infections with carcinogenic bacteria, and other factors (such as inheritance) that are also growing more prevalent in developing nations all contribute to the onset of cancer.[5,6] Any one of these factors has the potential to harm the oncogenes, or DNA genes that cause cancer, in host cells.[7]

Nanotechnology is the study of molecules at the atomic, molecular, and supramolecular levels (1-100nm) in order to determine their properties and how they might be used to improve human health. As modern biology and medicine develop, nanotechnology is being developed to produce which can be utilized in biological system.[8,9] Nanoparticles find utility in medical applications due to their unique attributes, such as quantum characteristics, a notably elevated surface to mass ratio compared to other particles and tendecy to adsorb and transport various compounds, including probes, proteins, and drugs.[10]

Nanoscale devices exhibit dimensions that are approximately 100-10000 times smaller than human cells. These entities exhibit a significant resemblance to large biomolecules (enzymes, receptors) in terms of their size.[11] The utilisation of nanotechnology facilitates expeditious and precise detection of cancer-associated substances, so enabling researchers to discern molecular modifications, even in cases where they impact only a little fraction of cells. Furthermore, it is worth noting that nanotechnology possesses the potential to generate novel and potent pharmaceutical drugs.[12]

Ultimately, the utilisation of nanoscale materials in cancer applications hinges on their capacity for rapid functionalization and facile tuning. These materials serve the dual purpose of delivering therapeutic, diagnostic, or combined functionalities. Moreover, their

effectiveness is contingent upon their passive accumulation at the tumour site, active targeting of cancer cells, and successful traversal of conventional biological barriers within the body, including the highly impervious blood-brain barrier that poses challenges for nanoparticle penetration.[13]

The most popular cancer treatment options now are chemotherapy, surgery, radiation, and combinations of these. However, these techniques have serious flaws, such as non-specificity and toxicity, among others.[14,15] Modern medicine aims to maximise drug pharmacological activity and reduce any potential negative effects. The medicine must have a high local concentration at the site of the tumour and a low local concentration in healthy tissues in order to prevent any unintended reactions.[16] The use of nanotechnology in cancer treatment has the potential to get beyond the limitations of current treatments. The amount of drug needed to have a therapeutic effect can be greatly reduced by using nanotechnology, and the concentration of medicine at the cancer location can be increased without harming healthy cells.[17,18]

Several drug delivery strategies utilising nanoparticles, such as viral nanoparticles, HDL nanostructures etc. in care of cancer. Nanodrugs possess unique attributes that make them highly promising in the field of cancer treatment. These attributes include their ability to minimise damage to healthy cells, their effectiveness in multidrug resistance, and their capacity to enhance the solubility of anti-cancer medications.[19]

Applications of nanotechnology in diagnosis of cancer

Different sizes, forms, and architectures can be found in nanoparticles.[20] As well as being multifunctional and capable of delivering hydrophobic compounds, nanoparticles also have the ability to target disease cells, increase the rate at which drugs enter and accumulate in tumour sites, subside drug resistance, facilitate the safety and tolerability.[21]

Nanoparticles are employed in the field of cancer diagnosis owing to their expeditious detection capabilities and cost-effectiveness. Moreover, natural remedies exhibit a reduced incidence of adverse effects compared to chemical-based therapies and radiotherapy. Electrochemical biosensors have been identified as a straightforward, cost-effective, and highly efficient approach, making them a promising modality for the diagnosis of cancer. The enhancement of cancer detection skills in nanoparticles can be achieved by means of their

functionalization. As an illustration, in the identification of breast adenocarcinoma cells, polyethylene glycol was utilised to conjugate antibodies specific to malignancy.[22]

Nanotechnology in cancer biomarkers

A cancer biomarker is a biomolecule and can be used to identify cancer cells.[23] Carbohydrates, nucleic acids (ctDNA, micro-RNA, etc.), proteins.[24] Quantum dots, gold nanoparticles and polymer dots are the three most often used nanoparticle probes in the diagnosis of cancer.[25] In nanotechnology, various cancer indicators can be used.

These biomarkers include as below.

Protein detection

Several protein markers have been authorised for the purpose of detecting cancer. These include CEA, which is used for identifying colorectal cancer,[27] AFP, which is employed for liver cancer detection, PSA, which is utilised for prostate cancer screening,[28,29] and CA-125, which is employed for identifying ovarian cancer. The identification of traits can be facilitated through targeted interactions with probes.[30] The interaction event will be subsequently transformed into a measurable signal.

Quantum dots possess a wide range of applications, encompassing the fields of nanocomposite creation, solar cell technology, and the labelling of biological entities with fluorescent properties.[31] Significant advancements have been made in the field of cancer diagnosis through the utilisation of high-resolution cellular imaging techniques. The alteration of fluorescence characteristics of quantum dots has been seen in response to various chemical stimuli. Furthermore, QDs possess a passive site located on their surface, which allows for the straightforward conjugation of particular antibodies.[32] Numerous applications of quantum dots in the field of bioimaging have been observed. Furthermore, quantum dots have been employed in the field of medication delivery and cancer therapy, specifically in the treatment of lung cancer, as well as in combating bacterial infections. Furthermore, previous studies have demonstrated that conjugated quantum dots (QDs) have the ability to suppress the expression of the P-glycoprotein gene and protein in lung cancer cells through the induction of miR-185 and miR-34b. The potential targets for the therapy of lung cancer are miR-185 and miR-34b. In addition, it was demonstrated that quantum dots (QDs) coupled with an extract derived from Camellia sinensis leaves exhibited the potential to impede the cell cycle of lung tumour cells and reduce the viability of cancer cells.[33,34] In a separate investigation, the administration of uncapped CdTe nanoparticles resulted in the

initiation of oxidative stress within lung tumours and human bronchial epithelial cells. Nevertheless, it was shown that the impact of 730Q was discernible just during extended periods of exposure, while shorter exposure intervals did not yield any noticeable effects.[35] In addition to their numerous advantages, quantum dots include heavy metal which is a well-documented hazardous substance and carcinogen.[36] This characteristic raises potential concerns regarding the safety and suitability of QDs for clinical use.

Circulating tumor DNA detection

The composition of this entity consists of DNA fragments with a length ranging from 100 to 200 base pairs, which are obtained from neoplastic tissues. The release of ctDNA from primary tumours or the utilisation of circulating tumour cells can facilitate the identification of cancer-specific genetic alterations.[37,38] The identification of genetic abnormalities in circulating tumour DNA (ctDNA) enables the detection of cancer even in the absence of clinical manifestations. The use of nucleic acid probes with complementary sequences using a highly selective hybridization process can be employed for the identification of genetic abnormalities associated with cancer. In this study, a novel fluorescent probe based on DNA silver nanoclusters was devised for the purpose of detecting a solitary exon within the BRCA1 gene, specifically in cases of breast cancer. In optimal conditions, this probe significantly enhanced the detection limit. The identification of significant deletion mutations in BRCA1 was facilitated through the utilisation of nanocluster fluorescence for hybridization recognition.[39]

MicroRNA Detection (MiRNAs)

MicroRNAs are a class of endogenous single-stranded RNAs (ssRNAs) that possess a length of 20-22 nucleotides. These molecules possess the ability to form complementary base pairs with messenger RNA (mRNA) and therefore inhibit its translation process. One microRNA has the ability to modulate several gene expressions, while a single messenger RNA can be subject to regulation by multiple microRNAs. These regulatory molecules, which are encoded in the genetic material, play a crucial role in governing gene expression that regulates many cellular processes such as cell proliferation, growth, and apoptosis.[40] Cancer can arise when the normal cellular function is disrupted due to dysregulation in the synthesis of microRNAs (miRNAs). Oncogenic viruses induce carcinogenesis by modulating the regulation of microRNAs through various mechanisms.[41]

DNA methylation detection

The presence of genome methylation patterns, known as Methylscape, has been observed in various forms of malignancies, indicating its potential utility as a cancer biomarker. The scientists employed DNA-gold affinity and DNA solvation techniques in their investigation to discern disparities between cancerous and normal genomes. Subsequently, they were able to devise straightforward, expeditious, specific, and highly sensitive electrochemical or colorimetric assays that enable the diagnosis of cancer in a single step.[42]

Extracellular vesicle detection

It refer to small vesicles ranging in size from 30nm-1µm that carry molecular cargo derived from parent cells. This cargo typically includes miRNA, DNA, protein, and mRNA, enabling the identification of tumour cells at a molecular level that is typically challenging to attain.[19]

Table 1: Specific ligands in different cancer.

Nanoparticle	Specific ligand	Cancer	Reference
QDs	PTK-7	Blood cancer	[44]
PDs	Ep-CAM	Breast cancer	[45]
AuNP	Her-2	Breast cancer	[46]
	Cd-2 Cd-3	Blood cancer	[47]
Carbon nanotubes	Ep-CAM	Liver cancer	[48,49]
Nanorod arrays	Ep-CAM	Breast cancer	[50]
Silicon bead	Ep-CAM CD-146	Breast cancer Colorectal cancer	[51]
Nano-fibers	Ep-CAM	Breast cancer	[52]
Magnetic nanoparticle	Ep-CAM	Colon/Liver/Lung Breast cancer	[43]

Identification of circulating tumor cells

Metastasis accounts for approx. 90% of mortality associated with solid tumours. A cancer cell originating from the main tumour initially infiltrates the adjacent tissue, subsequently gaining access to the microvasculature of the blood and lymph systems (a process known as intravasation). This is followed by the cell's ability to survive and migrate through the bloodstream, ultimately reaching micro-vessels located in distant tissues. Ultimately, these cells undergo extravasation from the bloodstream and manage to persist in a remote milieu, so creating a conducive foreign microenvironment for the formation and growth of secondary tumours.[53] The timely detection of circulating tumour cells which are cancer cells that have spread to other parts of the body through the bloodstream, can exert a substantial influence on the prognosis and diagnosis of cancer. CTCs have undergone comprehensive investigation as

a component of liquid biopsy owing to their potential applications. The detection of circulating tumour cells (CTCs) is a minimally invasive approach that enables the elucidation of the molecular architecture of tumours. However, circulating tumour cells (CTCs) exhibit limited number and heterogeneity, hence presenting significant technological challenges in terms of isolating and characterising them. In recent years, scholars have directed their attention towards the application of nanotechnologies in the precise identification of circulating tumour cells (CTCs). These advanced technologies have the potential to effectively analyse cellular and molecular components, thereby offering a diverse array of clinical applications. These applications include the early detection of diseases, treatment efficacy and disease advancement.[19]

mRNA-Based Detection

In addition to exterior nucleic acids, nanoparticles have been developed for the purpose of detecting intracellular nucleic acids as well. Seferos and colleagues (1998) demonstrated the utilisation of transfection agents and cellular "nanoflares" for the purpose of mRNA detection in viable cells. This was achieved by employing innovative gold nanoparticle probes that were modified with oligonucleotides, which were in turn hybridised to complements labelled with a fluorophore. Nanoflares have the ability to surmount numerous challenges encountered in the advancement of intracellular probes that are both efficient and highly responsive. Nanoflares exhibit efficacy in the detection of intracellular mRNA due to their high orientation, rich oligonucleotide coating, and potential for cellular penetration without the need for a potentially dangerous transfection agent.[54]

Detection of cell surface proteins

The primary approach for cancer cell detection involves the binding of nanoparticle probes, which are linked to various moieties i.e., antibodies, aptamers etc. This binding enables the detection of both cancer cells and those that have entered cells, by facilitating the identification of their genetic content. The initial and important stage in the identification of cancerous cells, such as circulating tumour cells (CTCs), is the process of capturing or isolating these cells. While the physical characteristics of cells, like size, deformability, and density, can be utilised to some extent, the primary factor determining cell capture is the affinity between cell surface chemicals and circulating tumour cells (CTCs), which is often assessed using antibodies or aptamers. EpCAM has been demonstrated to have considerable expression on circulating tumour cells (CTCs) derived from several types of human

malignancies, making it a suitable candidate for use as a cell surface biomarker. This observation has been consistently reported in multiple investigations. Consequently, anti-EpCAM drugs are commonly employed in the screening of circulating tumour cells (CTCs).[19]

Platinum nanoparticles

These find extensive application in the field of medicine. Research has demonstrated that platinum nanoparticles (PtNPs) exhibit inherent anticancer properties due to their antioxidant capacities, leading to the suppression of tumour proliferation. Moreover, the use of ligands specifically designed to bind with functionalized metal platinum nanoparticles (PtNPs) has demonstrated enhanced efficacy in tumour targeting. Additionally, PtNPs have been essential in facilitating superior drug release mechanisms and enhancing the effectiveness of drug delivery. Nevertheless, some recent studies have documented the adverse impacts of nanoplatinum, primarily attributed to the size of the nanoparticles.[55]

Gold nanoparticles (AuNPs)

These possess a multitude of distinctive characteristics that render them highly advantageous for diverse biomedical uses.[56] Gold nanoparticles (AuNPs) are little molecules that exhibit numerous distinctive characteristics suitable for imaging methodologies. Gold nanoparticles have been found to exhibit extended circulation durations in the bloodstream and enhanced tumour targeting capabilities in cancer imaging modalities, hence leading to improved diagnostic outcomes. Furthermore, gold nanoparticles (AuNPs) have demonstrated their versatility in numerous applications, including nucleic acid transport, medication administration, photothermal ablation, and radiotherapy. Gold nanoparticles (AuNPs) exhibit a wide range of sizes and forms, providing them with significant versatility in their synthesis.[56] Furthermore, gold nanoparticles (AuNPs) have demonstrated limited cytotoxicity and enhanced biocompatibility, rendering them highly favourable for potential utilisation in therapeutic settings.

Metal oxide nanoparticles

Metals including NiO, ZnO, MnO2, Fe2O3, TiO2, and Co3O4, are a class of mixed-metal oxides that have emerged as promising candidates for electro-analytical applications in the field of biomolecule detection. The utilisation of metal oxides in the detection of biomolecules presents several notable benefits, including enhanced biocompatibility for enzymes, hence potentially enhancing the accuracy of detection. One additional characteristic

exhibited by metal oxide nanoparticles is their capacity to undergo structural modifications, hence influencing the conductivity and chemical attributes of these nanoparticles.[57] Furthermore, transition metal oxides possess the capability to degrade a wide range of colours when exposed to sunshine or UV light irradiation. There is a growing inclination towards the utilisation of sustainable and environmentally friendly synthesis-based materials. The utilisation of low-cost bioconstituents produced from diverse plant sources in the green process offers numerous advantages.[58] One instance of employing zinc oxide nanoparticles as a therapeutic intervention for cardiovascular illness associated with diabetes was the administration of streptozotocin to diabetic rats. It indicates that the administration of a low dosage of ZnO nanoparticles effectively mitigated heart cell damage by decreasing serum cholesterol levels.

Graphene

It is characterised by a planar lattice structure composed of regularly arranged hexagonal rings. The material in question possesses remarkable characteristics such as being exceptionally thin, translucent, lightweight, and exhibiting excellent thermal and electrical conductivity. These properties render it highly appealing for applications in cancer imaging and detection. Graphene exhibits a range of advantageous characteristics, such as its ability to manifest a bipolar transistor effect and display substantial quantum oscillations.[59] These attributes position graphene as a promising contender for the facilitation of efficient cancer diagnosis. Graphene possesses a substantial specific surface area, rendering it advantageous for the loading of anticancer medicines as a result of the existence of π-π stacking and hydrophobic nature. Graphene oxide, an oxidised form of graphene, has been employed in several applications such as cancer therapy, pharmaceutical transport, and cellular visualisation. The utilisation of graphene oxide has been observed to enhance the physicochemical characteristics of advanced functional materials. A study conducted by researchers discovered that the utilisation of isotopic graphene-isolated Au nanocrystals exhibiting cellular Raman-silent signals exhibited potential for the detection of cancer cells.[60] In a separate study, a fluorescent probe that utilises graphene oxide was employed to detect glutathione and facilitate the identification of cancer.

Fullerene

Fullerene is a member of the Buckminsterfullerene family and is classified as an allotrope of carbon. Its molecular structure consists of linked carbon atoms bonded together through

single or double bonds, resulting in a mesh-like arrangement. Fullerene has been employed in chemical applications, wherein medicinal molecules can be encapsulated within the intricate structure of the fullerene lattice, facilitating efficacious drug delivery. The utilisation of fullerene (C60) has been employed in the field of cancer diagnostics and detection. Another work reported the trapping of helium (He) by subjecting C60 to heating in the presence of helium vapour at elevated pressure. According to a recent study, it has been documented that the utilisation of fullerenes and metal nanoparticles exhibits the potential to safeguard the human body from internally and externally generated reactive oxygen species that might cause harm, owing to their inherent reducing characteristics. Recent research has demonstrated that the use of fullerenes and metal-based nanomaterials exhibits a remarkable ability to specifically eliminate pathological cells within tissues, hence effectively impeding the progression of chronic inflammatory disorders. Fullerenes and nanoparticles based on metals exhibit significant promise in the therapeutic management of age-related conditions.[60]

Carbon nanotubes

These consist of a single layer of carbon atoms arranged in a cylindrical structure. The aforementioned materials exhibit exceptional qualities and possess a wide range of practical uses owing to their remarkable electrical and thermal conductivity, exceptional durability, and advantageous lightweight characteristics. It has been shown that single-wall nanotubes possess enhanced characteristics in comparison to multi-wall nanotubes, as well as silver or copper materials. The diameter of the tubes is around 1 nm, and they exhibit significant length. Carbon nanotubes possess significant physical features that render them highly valuable materials. Furthermore, the application of carbon nanotube biosensors has been demonstrated in the detection of organophosphorous substances. For instance, a study employed the deposition of gold nanoparticles and carbon nanotubes onto a gold wire to achieve this objective. To mitigate enzyme leaching and facilitate its function as a sensor electrode, the electrode was subjected to a Nafion coating. The functionality of this nanosensor is based on the mechanism of AChE enzyme inhibition.[61] In a particular investigation, carbon nanotubes that have carboxyl functional groups were subjected to treatment with a cell line derived from human T-cells. This treatment resulted in the activation of gene expression for caspase-2 within the treated cells. The findings indicated a marginal decline in the cellular survival of cancer cells upon exposure to carboxyl-functionalized carbon nanotubes. The findings from the molecular analysis indicated that

there was an elevation in Cas2 mRNA levels in the cancer cells that were subjected to treatment with carboxyl-functionalized carbon nanotubes.[62]

Dendrimers

These exhibit utility as effective delivery or carrier systems for pharmaceutical compounds and genetic material. Furthermore, these substances exhibit solubility, viscosity, and micellar characteristics. Their multifunctional features, stemming from their unique structure, render them highly valuable for the development of advanced nanodevices used in imaging and diagnosis.[63] Dendrimers have demonstrated a wide range of uses and have made substantial contributions to the advancement of materials sciences. Dendrimers have found several uses in the field of medicine, such as drug transport, biosensors etc. Furthermore, the utilisation of nanoparticles in the field of anticancer drug administration has been observed owing to their enhanced stability, solubility in water, and reduced immunogenicity. Furthermore, dendrimers have the capability to induce hypervascularization, enhance the permeability of cancer cells, and impede lymphatic drainage, hence offering advantages for passive targeting. The advantageous impacts of dendrimers may lead to the preferential accumulation of pharmaceutical compounds within tumour tissues. Multiple studies have indicated that the incorporation of dendrimers into therapeutic molecules through encapsulation or conjugation may result in the development of safer and more effective medications. Dendrimers are synthesised by a method known as divergent synthesis. The process entails the sequential incorporation of monomers onto a central nucleus, leading to the formation of a complex and extensively branching configuration. The monomeric units have the potential to undergo modifications, so enabling alterations in the characteristics of the dendrimer, including its dimensions, configuration, and chemical reactivity. The method of synthesising dendrimers is intricate and necessitates meticulous management of the reaction parameters. The properties of dendrimers can be modified by manipulating the choice of monomers, adjusting the reaction conditions, and controlling the amount of monomers incorporated. Dendrimers possess a multitude of distinctive characteristics that render them highly advantageous for a diverse array of applications. These entities exhibit remarkable stability and demonstrate resistance to degradation, rendering them amenable to customization in order to fulfil precise requirements. Moreover, these substances have a remarkable solubility characteristic, rendering them suitable for the targeted transportation of pharmaceutical agents and several other compounds.

NLCs

The utilisation of lipid based nanocarriers has demonstrated encouraging outcomes in the realm of cancer diagnostic. Nanoparticles of polymer origin, which can be produced using different lipid-based chemicals or in conjunction with vectors like liposomes, ethosomes, and transfersomes, have the potential to address challenges associated with medication absorption resistance in biological membranes. The efficiency and precision of polymeric nanoparticles can be enhanced by the combined actions of lipid-based nanocarriers.[64,65]

CONCLUSION

Cancer biomarkers are utilised in the early cancer's detection. However, the utilisation of biomarkers has encountered several challenges, such as the presence of low quantities of biomarkers in bodily fluids, variability in the amount and timing of biomarkers among patients, and the complexities associated with performing prospective research.[66]

The utilisation of nanotechnology has been widely employed in many investigations pertaining to cancer diagnosis and therapeutic interventions, hence potentially offering a viable option for cancer detection and therapy in the near future.[67] Despite the considerable amount of study conducted thus far in the realm of cancer nanotechnology, there remains a need for further inspection in order to achieve a comprehensive understanding of the current state of affairs. Despite the inherent challenges, the potential of nanoparticles in the realm of cancer diagnosis and therapy is unequivocal. Further advancements in the domain of nanomaterials hold the possibility of delivering a substantial approach to identify cancer.[68]

The advancement of nanotechnology in the future hinges upon the progress made in developing multifunctional nanoplatforms that integrate both therapeutic functionalities and multimodal imaging capabilities. In order to address the complexities associated with cancer heterogeneity and adaptive mechanisms, it is imperative to establish a coordinated approach that integrates diagnostic capabilities with therapeutic approaches. The advantageous characteristic of nanocarriers lies in their diminutive dimensions, which facilitate rapid penetration into tumour vasculature and subsequent retention with facilitated permeability. It concluded that cancer biomarker screening is one of the main factors in the detection of various subtypes. It is highly likely that cancer nanotechnology will soon provide a comprehensive, efficient, dependable, and secure approach to cancer detection and therapy.

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Conflict of interest

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REFERENCES

1. Reichert JM, Wenger JB. Development trends for new cancer therapeutics and vaccines. *Drug Discov Today*, 2008; 13(1–2): 30–37.
2. Bray F, Ferlay J, Soerjomataram I, Siegel R, Torre L, Jemal A. Erratum: global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*, 2020; 70(4): 313.
3. Hyuna Sung JF, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. *Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries*. American Cancer Society, 2021; 40.
4. The Lancet. *GLOBOCAN 2018: Counting the Toll of Cancer*. The Lancet, 2018; 985.
5. Anand P, Kunnumakara AB, Sundaram C, et al. Cancer is a preventable disease that requires major lifestyle changes. *Pharm Res*, 2008; 25(9): 2097–2116. doi: 10.1007/s11095-008-9661-9.
6. Sargazi S, Moudi M, Kooshkaki O, Mirinejad S, Saravani R. Hydro-alcoholic extract of *Achillea wilhelmsii* C. Koch reduces the expression of cell death-associated genes while inducing DNA damage in HeLa cervical cancer cells. *Iran J Med Sci*, 2020; 45(5): 359.
7. Sargazi S, Saravani R, Reza JZ, et al. Induction of apoptosis and modulation of homologous recombination DNA repair pathway in prostate cancer cells by the combination of AZD2461 and valproic acid. *Excli J*, 2019; 18: 485.
8. Roco MC, Bainbridge WS. The new world of discovery, invention, and innovation: convergence of knowledge, technology, and society. *J Nanoparticle Res*, 2013; 15(9): 1–17.
9. Surendiran A, Sandhiya S, Pradhan S, Adithan C. Novel applications of nanotechnology in medicine. *Indian J Med Res*, 2009; 130(6): 689–701.
10. Jani P, Subramanian S, Korde A, Rathod L, Sawant KK. Theranostic nanocarriers in cancer: dual capabilities on a single platform. In: *Functional Bionanomaterials*. Springer, 2020; 293–312.

11. Nano delivery Systems and Devices. National Cancer Institute, 2023.
12. Zhu L, Staley C, Kooby D, El-Rays B, Mao H, Yang L: Current status of biomarker and targeted nanoparticle development: The precision oncology approach for pancreatic cancer therapy. *Cancer Lett,* 2016; 388: 139-148.
13. Anchordoquy TJ, Barenholz Y, Boraschi D, Chorny M, Decuzzi P, Dobrovolskaia MA, Farhangrazi ZS, Farrell D, Gabizon A, Ghandehari H *et al*: Mechanisms and Barriers in Cancer Nanomedicine: Addressing Challenges, Looking for Solutions. *ACS Nano,* 2017; 11(1): 12-18.
14. Sargazi S, Laraib U, Barani M, et al. Recent trends in the mesoporous silica nanoparticles with rode-like morphology for cancer theranostics: a review. *J Mol Struct*, 2022; 1261: 132922.
15. Ahmed A, Sarwar S, Hu Y, et al. Surface-modified polymeric nanoparticles for drug delivery to cancer cells. *Expert Opin Drug Deliv*, 2021; 18(1): 1–24.
16. Ho BN, Pfeffer CM, Singh AT. Update on nanotechnology-based drug delivery systems in cancer treatment. *Anticancer Res*, 2017; 37(11): 5975–5981.
17. Vasir JK, Reddy MK, Labhasetwar VD. Nanosystems in drug targeting: opportunities and challenges. *Curr Nanosci*, 2005; 1(1): 47–64.
18. Mollazadeh S, Mackiewicz M, Yazdimamaghani M. Recent advances in the redox-responsive drug delivery nanoplatforms: a chemical structure and physical property perspective. *Mater Sci Engine C*, 2021; 118: 111536.
19. Zhang Y, Li M, Gao X, Chen Y, Liu T. Nanotechnology in cancer diagnosis: progress, challenges and opportunities. *J Hematol Oncol*, 2019; 12(1): 1–13.
20. Machado S, Pacheco J, Nouws H, Albergaria JT, Delerue-Matos C. Characterization of green zero-valent iron nanoparticles produced with tree leaf extracts. *Sci Total Environ*, 2015; 533: 76–81.
21. Yang Q, Jones SW, Parker CL, Zamboni WC, Bear JE, Lai SK. Evading immune cell uptake and clearance requires PEG grafting at densities substantially exceeding the minimum for brush conformation. *Mol Pharm*, 2014; 11(4): 1250–1258.
22. Gardner L, Kostarelos K, Mallick P, Dive C, Hadjidemetriou M. Nano-omics: nanotechnology-based multidimensional harvesting of the blood-circulating cancerome. In: *Nature Reviews Clinical Oncology*. Nature Publishing Group, 2022; 1–11.
23. Borrebaeck CA. Precision diagnostics: moving towards protein biomarker signatures of clinical utility in cancer. *Nat Rev Cancer*, 2017; 17(3): 199–204.

24. Taqui S, Daniels LB. Putting it into perspective: multimarker panels for cardiovascular disease risk assessment. *Biomark Med*, 2013; 7(2): 317–327.
25. Zhang H, Lv J, Jia Z. Efficient fluorescence resonance energy transfer between quantum dots and gold nanoparticles based on porous silicon photonic crystal for DNA detection. *Sensors*, 2017; 17(5): 1078.
26. Campos-da-Paz M, Dórea JG, Galdino AS, Lacava ZG, de Fatima Menezes Almeida Santos M. Carcinoembryonic antigen (CEA) and hepatic metastasis in colorectal cancer: update on biomarker for clinical and biotechnological approaches. *Recent Pat Biotechnol*, 2018; 12(4): 269–279.
27. Tzartzeva K, Singal AG. Testing for AFP in combination with ultrasound improves early liver cancer detection. *Expert Rev Gastroenterol Hepatol*, 2018; 12(10): 947–949.
28. Ilic D, Djulbegovic M, Jung JH, et al. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. *BMJ*, 2018; 362.
29. Moradi A, Srinivasan S, Clements J, Batra J. Beyond the biomarker role: prostate-specific antigen (PSA) in the prostate cancer microenvironment. *Cancer Metastasis Rev*, 2019; 38(3): 333–346.
30. Razmi N, Hasanzadeh M. Current advancement on diagnosis of ovarian cancer using biosensing of CA 125 biomarker: analytical approaches. *Trends Analytical Chem*, 2018; 108: 1–12.
31. Laraib U, Sargazi S, Rahdar A, Khatami M, Pandey S. Nanotechnology-based approaches for effective detection of tumor markers: a comprehensive state-of-The-art review. *Int J Biol Macromol*, 2022; 195: 356–383.
32. Chang P-Y, Kuo Y-B, Wu T-L, et al. Association and prognostic value of serum inflammation markers in patients with leukoplakia and oral cavity cancer. *Clin Chem Lab Med*, 2013; 51(6): 1291–1300.
33. Freeman R, Willner I. Optical molecular sensing with semiconductor quantum dots (QDs). *Chem Soc Rev*, 2012; 41(10): 4067–4085.
34. Fatima I, Rahdar A, Sargazi S, Barani M, Hassanisaadi M, Thakur VK. Quantum dots: synthesis, antibody conjugation, and HER2-receptor targeting for breast cancer therapy. *J Funct Biomater*, 2021; 12(4): 75.
35. Tabish TA, Hayat H, Abbas A, Narayan RJ. Graphene quantum dot–based electrochemical biosensing for early cancer detection. *Curr Opin Electrochem*, 2021; 30: 100786.

36. Bock S, Kim H-M, Kim J, et al. Lateral flow immunoassay with quantum-dot-embedded silica nanoparticles for prostate-specific antigen detection. *Nanomaterials*, 2021; 12(1): 33.
37. Filipska M, Rosell R. Mutated circulating tumor DNA as a liquid biopsy in lung cancer detection and treatment. *Mol Oncol*, 2021; 15(6): 1667–1682.
38. Kurtz DM, Soo J, Co Ting Keh L, et al. Enhanced detection of minimal residual disease by targeted sequencing of phased variants in circulating tumor DNA. *Nat Biotechnol*, 2021; 39(12): 1537–1547.
39. Borghei Y-S, Hosseini M, Ganjali MR. Detection of large deletion in human BRCA1 gene in human breast carcinoma MCF-7 cells by using DNA-silver nanoclusters. *Methods Appl Fluoresc*, 2017; 6(1): 015001.
40. Fiammengo R. Can nanotechnology improve cancer diagnosis through miRNA detection? *Biomark Med*, 2017; 11(1): 69–86.
41. Larrea E, Sole C, Manterola L, et al. New concepts in cancer biomarkers: circulating miRNAs in liquid biopsies. *Int J Mol Sci*, 2016; 17(5): 627.
42. Sina AAI, Carrascosa LG, Liang Z, et al. Epigenetically reprogrammed methylation landscape drives the DNA self-assembly and serves as a universal cancer biomarker. *Nat Commun*, 2018; 9(1): 1–13.
43. Hong W, Lee S, Chang HJ, Lee ES, Cho Y. Multifunctional magnetic nanowires: a novel breakthrough for ultrasensitive detection and isolation of rare cancer cells from non-metastatic early breast cancer patients using small volumes of blood. *Biomaterials*, 2016; 106: 78–86.
44. Pang X, Cui C, Su M, Wang Y, Wei Q, Tan W. Construction of self-powered cytosensing device based on ZnO nanodisks@ g-C3N4 quantum dots and application in the detection of CCRF-CEM cells. *Nano Energy*, 2018; 46: 101–109.
45. Wu C, Schneider T, Zeigler M, et al. Bioconjugation of ultrabright semiconducting polymer dots for specific cellular targeting. *J Am Chem Soc*, 2010; 132(43): 15410–15417.
46. Zhu Y, Chandra P, Shim Y-B. Ultrasensitive and selective electrochemical diagnosis of breast cancer based on a hydrazine–Au nanoparticle–aptamer bioconjugate. *Anal Chem*, 2013; 85(2): 1058–1064.
47. Zhang Y, Chen B, He M, Yang B, Zhang J, Hu B. Immunomagnetic separation combined with inductively coupled plasma mass spectrometry for the detection of tumor cells using gold nanoparticle labeling. *Anal Chem*, 2014; 86(16): 8082–8089.

48. Liu Y, Zhu F, Dan W, Fu Y, Liu S. Construction of carbon nanotube based nanoarchitectures for selective impedimetric detection of cancer cells in whole blood. *Analyst*, 2014; 139(20): 5086–5092.
49. Shen J, Li K, Cheng L, Liu Z, Lee S-T, Liu J. Specific detection and simultaneously localized photothermal treatment of cancer cells using layer-by-layer assembled multifunctional nanoparticles. *ACS Appl Mater Interfaces*, 2014; 6(9): 6443–6452.
50. Sun N, Li X, Wang Z, et al. A multiscale TiO2 nanorod array for ultrasensitive capture of circulating tumor cells. *ACS Appl Mater Interfaces*, 2016; 8(20): 12638–12643.
51. Huang Q, Wang F-B, Yuan C-H, et al. Gelatin nanoparticle-coated silicon beads for density-selective capture and release of heterogeneous circulating tumor cells with high purity. *Theranostics*, 2018; 8(6): 1624.
52. Wu X, Xiao T, Luo Z, et al. A micro-/nano-chip and quantum dots-based 3D cytosensor for quantitative analysis of circulating tumor cells. *J Nanobiotechnology*, 2018; 16(1): 1–9.
53. Gupta GP, Massagué J. Cancer metastasis: building a framework. *Cell*, 2006; 127(4): 679–695.
54. Choi CHJ, Hao L, Narayan SP, Auyeung E, Mirkin CA. Mechanism for the endocytosis of spherical nucleic acid nanoparticle conjugates. *Proc Natl Acad Sci*, 2013; 110(19): 7625–7630.
55. Wang, J.; Cao, F.; He, S.; Xia, Y.; Liu, X.; Jiang, W.; Yu, Y.; Zhang, H.; Chen, W. FRET on lateral flow test strip to enhance sensitivity for detecting cancer biomarker. *Talanta*, 2018; *176*: 444–449.
56. Gurunathan, S.; Jeyaraj, M.; Kang, M.-H.; Kim, J.-H. Anticancer Properties of Platinum Nanoparticles and Retinoic Acid: Combination Therapy for the Treatment of Human Neuroblastoma Cancer. *Int. J. Mol. Sci*, 2020; *21*: 6792.
57. Sharma, M. Chapter 18—Transdermal and Intravenous Nano Drug Delivery Systems: Present and Future. In *Applications of Targeted Nano Drugs and Delivery Systems*; Mohapatra, S.S., Ranjan, S., Dasgupta, N., Mishra, R.K., Thomas, S., Eds.; Elsevier: Amsterdam, The Netherlands, 2019; 499–550.
58. Sankaranarayanan, S.; Hariram, M.; Vivekanandhan, S.; Ngamcharussrivichai, C. Chapter 15—Biosynthesized transition metal oxide nanostructures for photocatalytic degradation of organic dyes. In *Green Functionalized Nanomaterials for Environmental Applications*; Shanker, U., Hussain, C.M., Rani, M., Eds.; Elsevier: Amsterdam, The Netherlands, 2022; 417–460.

59. Abbasi, E.; Akbarzadeh, A.; Kouhi, M.; Milani, M. Graphene: Synthesis, bio-applications, and properties. *Artif. Cells Nanomed. Biotechnol*, 2014; *44*: 150–156.
60. Mao, C.-C. Nanomaterials and Aging. *Curr. Stem Cell Res. Ther,* 2021; *16*: 57–65.
61. Amreddy, N.; Ahmed, R.A.; Munshi, A.; Ramesh, R. Tumor-Targeted Dendrimer Nanoparticles for Combinatorial Delivery of siRNA and Chemotherapy for Cancer Treatment. *Drug Deliv. Syst*, 2019; *2059*: 167–189.
62. Dhull, V. A Nafion/AChE-cSWCNT/MWCNT/Au-based amperometric biosensor for the determination of organophosphorous compounds. *Environ. Technol*, 2018; *41:* 566–576.
63. Zhang, M.; June, S.M.; Long, T.E. Principles of Step-Growth Polymerization (Polycondensation and Polyaddition). In *Polymer Science: A Comprehensive Reference, 10 Volume Set*; Elsevier: Amsterdam, The Netherlands, 2012; 5: 7–47.
64. Cho, H.-Y.; Hossain, K.; Lee, J.-H.; Han, J.; Lee, H.J.; Kim, K.-J.; Kim, J.-H.; Lee, K.-B.; Choi, J.-W. Selective isolation and noninvasive analysis of circulating cancer stem cells through Raman imaging. *Biosens. Bioelectron*, 2018; *102*: 372–382.
65. Duarte, M.; Subedi, P.; Yilmaz, E.; Marcus, K.; Laurell, T.; Ekström, S. Molecularly imprinted polymers synthesized via template immobilization on fumed silica nanoparticles for the enrichment of phosphopeptides. *J. Mol. Recognit*, 2017; *31*: e2677.
66. Hull L, Farrell D, Grodzinski P. Highlights of recent developments and trends in cancer nanotechnology research—view from NCI alliance for nanotechnology in cancer. *Biotechnol Adv*, 2014; 32(4): 666–678.
67. Barani M, Hosseinikhah SM, Rahdar A, et al. Nanotechnology in bladder cancer: diagnosis and treatment. *Cancers*, 2021; 13(9): 2214.
68. Roma-Rodrigues C, Pombo I, Raposo L, Pedrosa P, Fernandes AR, Baptista PV. Nanotheranostics targeting the tumor microenvironment. *Front Bioengine Biotechnol*, 2019; 7: 197.