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# Nanoparticles technology promoting strategies for cancer therapy: Review

**Ihssin Abdalsamed [a,*], Ibrahim Amar[a], Mohammed Ahwidi[a], Omar Abrika[b], Masood A G Ali[c]**

[a]*Department of Chemistry, Faculty of Sciences, University of Sebha, Sebha-Libya*

[b] *Faculty of Pharmacy, University of Sebha, Sebha-Libya*

[c]*Department of Geology and Environment, Faculty of Sciences, University of Bani Waleed, Bani Waleed-Libya*

## Highlights

- **Nano treatment is used to cure a number of cancer cases, which have shown significantly to fight cancer.**
- **Nanodevices become one of the greatest medical healthcare sittings named, as nanoparticles (NPs) are Quantum dots (QDs), Nanogold shell (AuNPs), Dendrimers, Nanopore, and Nanotubes.**
- **Nanodevices provide potential benefits for diagnosing and treating metastatic cancer such as a tumour, while the ability to deliver drugs to the major sites of metastasis and enrichment of target tumor cells without effecting noncancerous cells.**

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* Corresponding author:

*E-mail address*:
ihs.abdalsamed@sebhau.edu.ly
I. Abdalsamed

ABSTRACT

Cancer is the most serious disease in the world and has been considered as the first fatal disease to the humankind as its incidence rates continue to increase rapidly worldwide. Chemotherapy, Radiation therapy, Immunotherapy and Hyperthermia are the most common treatments for cancer in developed countries, while surgical operations are used in undeveloped countries, which have been found to cause negative side effect on human health.

Recently, Nano treatment is used to cure a number of cancer cases, which have shown significant results than surgical operations. Such success has encouraged scientists and researchers to develop Nanotechnological devices named as nanoparticles (NPs) which have become one of the greatest medical healthcare settings as they provide potential benefits for diagnosing and treating metastatic cancer, such as a tumor. On other hand, nanoparticles improved the ability to delivery drugs to the major sites of metastasis without effecting noncancerous cells. Moreover, beside reported nanoparticles (NPs) have significant to escape antibody and extravasate into the tumor cells.

In this review, we focus and outline on Nanodevice types: Quantum dots (QDs), Nanogold shell (AuNPs), Dendrimers, Nanopore, and Nanotubes for their principles, applications, operation processes and their recent highlights in cancer research area are also considered in this paper. Finally, we provide some perspectives on the future challenges and development of drug delivery systems.

## 1. Introduction

Cancer is defined as the uncontrolled proliferation of cells. Most human cancers arise from a single clone of cells affected by a genetic mutation. Additionally, larger proportions of cells are actively dividing with a rapid growth rate over other normal cells (Fig. 1). Globally, a huge number of people all over the world are diagnosed with various types of cancer, accounting for a yearly 8 million cancer-related deaths, and such number is apparently on the rise (Torre *et al.*, 2015, Siegel *et al.*, 2016, McGuire, 2016, Bray *et al.*, 2018). World Health Organization (WHO) demonstrated that cancer could be correlated with several risk factors such as smoking, dietary habits, age, exposure to UV-radiation and consuming vegetables treated with pesticides, in addition to work-related factors that involve hydrocarbon pollution, etc. The wider scientific community believes that those factors are responsible for growing specific categories of cancer (Parrón *et al.*, 2014; Ramírez *et al.*, 2014; Cuadras *et al.*, 2016; Stewart and Wild, 2017; Valcke *et al.*, 2017; Lee *et al.*, 2019). Presently, multimodal therapies are available against cancer, which include chemotherapy, radiation therapy, surgical operations, hyperthermia as well as immunotherapy.

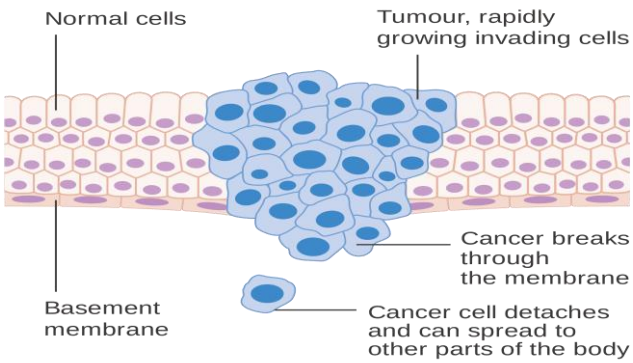


**Fig. 1**. Normal tissue and cancer cells (Singh *et al.*, 2015)

***Chemotherapy*** is the main treatment used to manage cancer in different countries. Doxorubicin is a synthetic drug having a wide

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use to combat cancer. It is able to destroy or/and control the proliferation of cancer cells. Chemotherapy is usually given through intravenous injection, subcutaneous or orally depending on the cancer type and patient situation. Nowadays, several chemotherapy strategies have been applied to the treatment of different types of cancer. Chemotherapy can be used alone or combined with other treatments such as radiotherapy, which could be followed by surgery for controlled mass removal. Although chemotherapy is the most common treatment for cancer management it may cause undesirable side effects such as the need of the patient to be frequently hospitalized for treatment dose administration. More important, chemotherapy may have an unsuccessful outcome for many patients. Further, it could have diverse effective for different individuals (Von Minckwitz *et al*., 2012; Buch *et al*., 2019).

***Radiation therapy*** is therapeutic treatment is applicable to many types of cancers. It uses high-energy rays emitted from instruments used specifically to target cancer cell to reduce the tumor mass. The machines emit short wavelength rays (high-energy radiation). There are different types of radiations that are suitable for cancer treatment including X-rays, gamma rays and other sources such as neutrons and protons. Although radiation therapy is an improved treatment for cancer, it has a number of drawbacks. Firstly, it is normally used for inpatients required to spend a few days in the hospital or clinic. Secondly, long rest is needed for the patients that have been exposed to high levels of radiation. Further, depending on their immune system function status they may have to see visitors for a short time only to avoid picking infections. Thirdly, once the treatment is finished, the amount of residual radiation must be checked in a patient body, and a safe level can be reached before he/she can leave the hospital. Lastly, Radiotherapy can sometimes damage organs that are closely related to the site of rays' targets such as the stomach, bowel, liver and kidneys. This drawback may result in serious side effects (Kratochwil *et al*., 2016; Chang *et al*., 2016; Lin *et al*., 2019).

***Immunotherapy*** is an advanced strategy used against cancer. Indeed, it is a supporting method used to stimulate the immune system to enhance its ability to fight diseases such as microbial infections and cancer. Recently, immunotherapy has become more effective for the treatment of many types of cancer, since it allows the immune system to identify and target cancer cells more effectively compared to other methods, which have a deteriorating effect on the immune system itself. Immunotherapy approach has various modules including vaccines, checkpoint inhibitors, cytokines, monoclonal antibodies (MABs), and the more advanced adoptive cell transfer immunotherapy strategy. Immunotherapy is also known as biological therapy. The substances that modify the immune response or the so-called biological response are referred to as the Biological Response Modifiers (BRMs). Indeed, the body naturally produces small amounts of (BRMs) in response to infection and disease. Therefore, large amounts of BRMs can be made in the laboratory and used for the treatment of a wide range of diseases such as rheumatoid arthritis and cancer. In comparison to chemotherapy and radiotherapy, other cancer treatment methods, immunotherapy appears to improve the strength of the patient's own immune system, with fewer side effects. Furthermore, several investigations showed that combining immunotherapy with chemotherapy treatment decreased the side effect risks. In addition, it improves long-term survival. However, there are some drawbacks of immunotherapy treatment as it sometimes causes unfavorable symptoms, which include fever, chills, nausea, diarrhea and vomiting, besides generalized pain particularly in the bones joints and legs, weakness or fatigue, headaches and rashes in some patients (Smith *et al.,* 2014; Frankel *et al*., 2017; Riley *et al*., 2019).

***Hyperthermia*** is the first clinical method improved for the goals of regional cancerous- directed therapies. In addition, to stopping bleeding, early, it has been used for a long time as the process of raising the patient's body temperature either locally or in general for medicinal purposes. Currently, hyperthermia has the potential to eliminate cancer from the body. The goals of hyperthermia technique include the significant increase in apoptosis of cancer cells or/ and the inhibition cancer cells division. Notably, this is accomplished neither through using medicine (Chemotherapy) nor through using high-energy rays (Radiotherapy) in treating the affected area, but rather by localized high temperature in the tumor area. The mechanism used to achieve hyperthermia is by means of burring or cauterizing the cancerous area with a hot metal such iron. Currently, more sophisticated Hyperthermia treatments have appeared as a new system for cancer treatment such as using a hot liquid including water. By this method, the affected area will cure faster, hence decreasing the side effects (Cabuy, 2011, Bedge *et al*., 2019).

***Surgical Operation*** is the preliminary method for fighting cancer diseases. It involves the surgical operation to remove the primary solid tumor disease from the patient. The ancient physicians used a surgical operation to inhibit the spread of metastatic cancer cells. (Van Gijn *et al*., 2010; Tohme *et al*., 2017; Tsagozis *et al*., 2019). Although several treatment strategies have been applied for cancer treatment, these traditional strategies have various drawbacks through local or systemic effect. In addition, the low specificity of some treatments leads to similar effects in both rapidly dividing normal cells and tumor cells. Additionally to diagnostic strategies problems they are time-consuming with low sensitivity to a specific area and may cause kidney complications while suffering senior people and children practically on surgery operations. Nowadays, several researchers have become interested in further related investigations, which have a new or improved treatment method to treat large panels of cancer disease.

## 2. The significance of nanoparticles in cancer therapy?

Scientist found that most animal cells are 10000 nm to 20000 nm in diameter while nanoparticles have dimensions that equal 100 nm or less (Fig. 2). This enables nanoparticles to enter animal cells (Fig. 3). Moreover, nanoparticles have a greater surface area per weight than conventionally made material, which causes them to be more reactive to some other molecules. The difference between the surface atoms to total atoms of the molecule increases with the decrease in molecular size. This, in fact, can be an important property when NPs interact with biological systems. This, in addition, represents an important property for many biomedical applications (Soliman *et al*., 2012; Douba *et al*., 2017). For instance, zinc oxide has been found in Nano size to have superior UV blocking properties compared to its bulk substitute, silicon has been found at approximately the size 1nm can emit blue color and at approximately 3 nm size can emit red color with no color on material size (Zong *et al*., 2011; Chen and Ma, 2019). The properties of materials change in their size in nanoscale leading the surface of materials to become significant for nanotechnology. Over the past decade, several Nanomaterials were designed based on differences, such as: Quantum dots (QDs), Nanogold shell (AuNPs), Dendrimers, Nanopore, and Nanotubes.

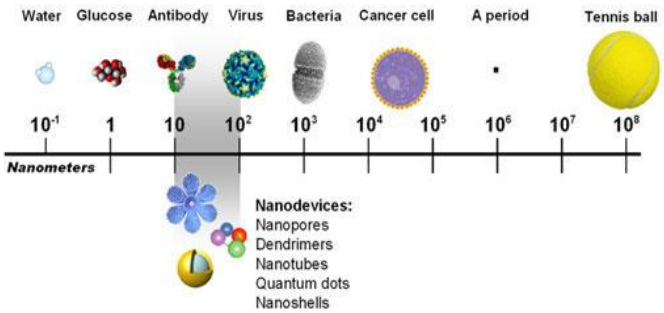


**Fig. 2.** Nanodevices scale (Mewara and Rathore, 2016)

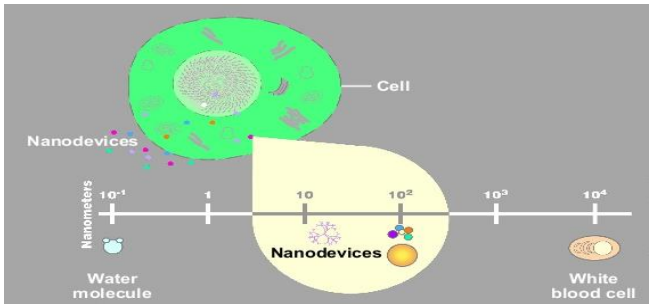


**Fig. 3.** Nanodevices are small enough to enter the cell (Ahmed, 2006)

Nanoparticles have multifunctional systems for cancer disease such as tumor targeting, drug delivery, diagnostics and imaging. Targeting tumor cells by nanoparticles depending on mechanism reaction upon external motivation through the functionality of tumor cells, peptides, polymers and antibodies that can be used to improve NPs circulation, effectiveness and selectivity. This exploration has opened the relatively a new field of Nanomedicine dealing with the detection, control, construction, repair, defence and improvement of all human biological systems. Nanoparticles (NPs) can be synthesised to a size compatible with biological molecules such as proteins, nucleic acids and can appropriately develop for use as potential probes, delivery platforms, carriers and devices giving unique opportunities for improvements in disease detection, therapy and prevention. For all that depending to their Nanoscale size and unique properties allowing nanoparticles to cross and interact with biomolecules in the blood, organs, tissues and cells (Fig. 4) (Conde *et al.*, 2012, Oh and Park, 2014; Wang *et al.*, 2019).

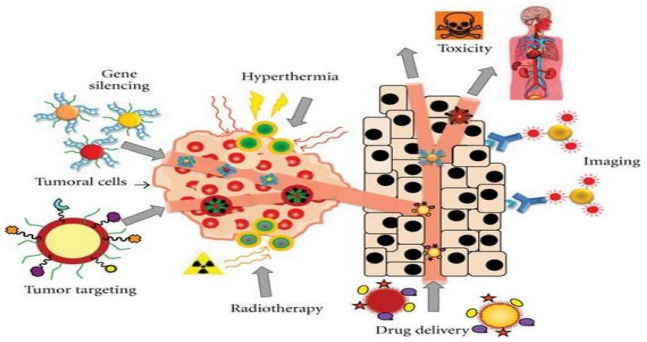


**Fig. 4.** Schematic illustration of potential applications of nanoparticles in cancer cells (Conde *et al.*, 2012; Mercado *et al.*, 2019)

Nanoparticles (NPs) may be organic or inorganic in nature and there are many methods for synthesis and development nanoparticles (Wang and Wang, 2014; Badi'ah *et al.*, 2019) for example synthesis citrate gold nanoparticles and silica-gold nanoparticles(Fig. 5). Recently a new method for the synthesis of eco-friendly nanoparticles have been introduced (Divakaran *et al.*, 2019; Kooshki *et al.*, 2019).

## 3. Quantum dots (QDs)

Quantum dots are inorganic nanoparticles of semiconductors, which had been theorized in the 1970s and were initially created in the early 1980s. Quantum dots are semiconductor nanoparticles that can glow a specific color after absorbing light. The glow of color depends on the size of the nanoparticle. Many semicon-ductor substances on Nano size can use as quantum dots. Semi-conductor substances nanoparticles or other semiconductor substances have high properties of a quantum dot. Quantum dots (QDs) can be great values fluorescent given good photochemical stability and high photoluminescent quantum yields (Chinen *et al.*, 2015; Lu *et al.*, 2019).

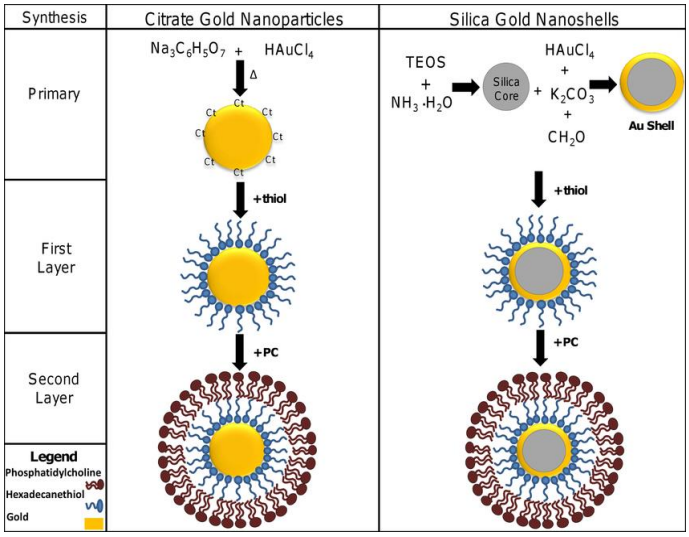


**Fig. 5.** Synthesis of gold nanoparticles (England *et al.*, 2015; Kumar *et al.*, 2019)

Quantum dots (QDs) with properties absorb and emits different wavelengths are becoming a useful tool in many biological applications (Igweh *et al.*, 2018). QDs consist of a core made of heavy metal responsible for fluorescence properties surrounded by an external coating generally an amphiphilic polymer that to increase solubility in a biologically compatible medium. The core/shell QDs usually have a layer (or "shell") of zinc sulphide (ZnS) between the core and the coating that can reduce the leaching of metals from the core and improving photo-stability (Fig. 6A). Nanoscientist found that many types of the quantum dot would emit light when applied UV light and those lights can be different in color due the QDs size, shape and material. For example, larger QDs at radius from 5 nm to 6 nm can emit longer wavelengths resulting in emission colors like orange or red while smaller QDs at radius from 2 nm to 3 nm can emit shorter wavelengths resulting in colors such as green or blue, although the specific colors and sizes vary depending on the exact composition of the QDs. Semiconductor quantum dots (QDs) have attracted the attention of many research groups because of their scientific and technological significance in microelectronics, optoelectronics and cellular imaging several groups have reported that with biocompatible surface coatings, such as PEG-silica, QDs can be well tolerated by cells in vitro as they can be conjugated to a legends by coating a polymeric layer onto it. For further QDs is a critical issue application as diagnostic and imaging tools for the human body. Moreover the applications of QDs for imaging are inside the cell are in the cytoplasm, endosomes and lysosome this can make QDs have got unique properties which make them ideal for detecting specific tumor cells (Fig. 6B) (Di Corato *et al.*, 2011; Yanover *et al.*, 2014; Lim *et al.*, 2015; Cai *et al.*, 2016; Lee *et al.*, 2017).

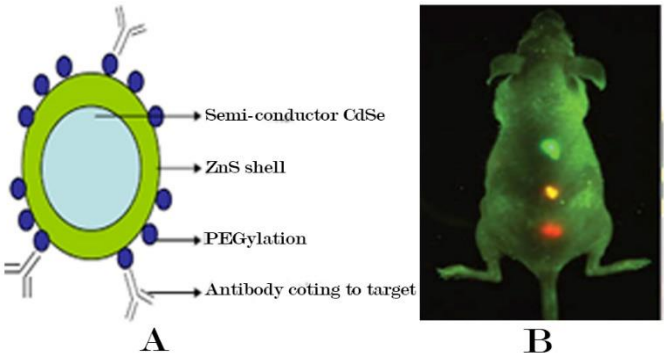


**Fig. 6.** (A) Quantum dots, (B) Quantum dots significant to glow by UV light targeting tumor cells

## 4. Gold nanoparticles (GNPs) drug delivery

Doxorubicin (Dox) is a popular anticancer drug commonly used in chemotherapy. In recent years, gold nanoparticles have been investigated for using them as drug or gene delivery carriers and as diagnostic agents. Having such delivery ability of various payloads into their specific targets they can extravasate (escape) into the tumor tissues. The surfaces of GNPs can be further functionalized to allow for increasing biocompatibility, targeting and uptake by cell (Fig. 7). The gold nanoparticles (Au NPs) have an advantage compared to other agents as they provide nontoxic carriers for drug and gene delivery applications. Furthermore, they can be used to deliver medicine explicitly to cancer cells without affecting normal cells. Gold nanoparticles are shaped so that the gold core imparts stability to the assembly while the monolayer allows tuning of surface properties such as charge and hydrophobicity (Kanapathipillai *et al.*, 2014; Muddineti *et al.*, 2015; Daraee *et al.*, 2016; Mugaka *et al.*, 2019). Significant studies have revealed that Gold Nanoparticles (GNPs) exhibit unique physicochemical properties including Surface Plasmon Resonance (SPR) and the ability to bind amine and thiol groups allowing surface modification and use in biomedical applications. Lately, the synthesis of Gold Nanoparticles (AuNPs) became possible in the laboratory (Guo *et al.*, 2016; Chen *et al.*, 2019).

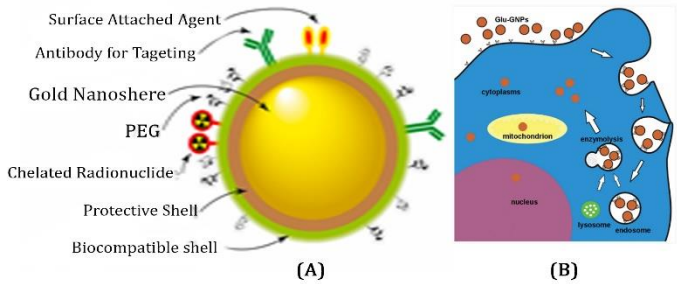


**Fig. 7.** (A) Gold nanoparticles, (B) Gold nanoparticles attached in and out of a cancer cell (Song *et al.*, 2013; Singh and Mitragotri, 2019)

## 5. Gold nanoparticles (GNPs) thermal therapy

Generally, cancer cells die at 47°C and this can be through apoptotic pathways. In fact, hyperthermia method typically involves an external heating source that generates temperature gradients from the external source to the tumor with the maximum heat dissipated on the body's surface, which may affect normal cells. Gold NPs can improve thermal therapy efficiency through absorption of infrared (IR) light, this will exhibit low toxicity, ease of functionalization, suitable biocompatibility and uptake into cells with less exposure of light. Moreover, gold NPs can transform absorbed light into heat giving lower temperature and thus have the high potential for infrared phototherapy (Dorsey *et al.*, 2013; Wang and Wang, 2014; Hainfeld *et al.*, 2014; Baffou, 2018). Extensive studies strongly support the notion that gold nanoparticles at lower wavelength produce heat that can kill cancer cells (Fig. 8). GNP tunable optical properties have propelled them to the forefront of cancer hyperthermia as photothermal agents. Photothermal therapy is a method of killing off cancer cells carried out by changing optical energy to thermal energy upon irradiation with light (Chithrani *et al.*, 2010; Yuan *et al.*, 2012; Yu *et al.*, 2012; Zhang *et al.*, 2019).

GNPs are efficient converters of light energy into heat, making them promising agents for targeted photothermal effects. They have also been investigated for cancer hyperthermia due to their unique optical properties when exposed to visible-near infrared (NIR) wavelengths where they are capable of efficient conversion of light energy into heat, which is quickly dissipated into the environment. Over the past decade, researchers have concentrated on improving GNPs design for hyperthermic treatments focusing on varying particle shapes such as rods, cubes, stars, and prisms to promote GNPs light absorption and thus heat generation (Khlebtsov and Dykman, 2011; Joseph *et al.*, 2019).

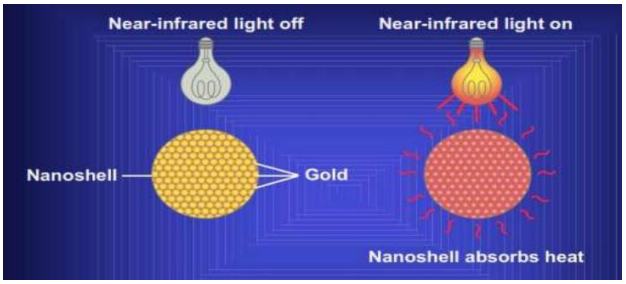


**Fig. 8.** Effective IR light to melt nanogold particles (Ahmed, 2006)

## 6. Dendrimers

Dendrimers are an organic nano type repetitively branched molecules. The name of dendrimers comes from the Greek word (Dendron) which translates to "tree". They have wider uses in a biological system. Dendrimers chemically is typically symmetric around the core and often adopts a spherical three-dimensional morphology; this is means that dendrimers consist of a series of chemicals. They are a branch of the dendritic family as illustrated in (Fig. 9). Applications of dendrimers typically involve conjugating other chemical species to the surface of dendrimers that can function as detecting agents (Zhou *et al.*, 2014; Wei *et al.*, 2015; Caminade, 2019).

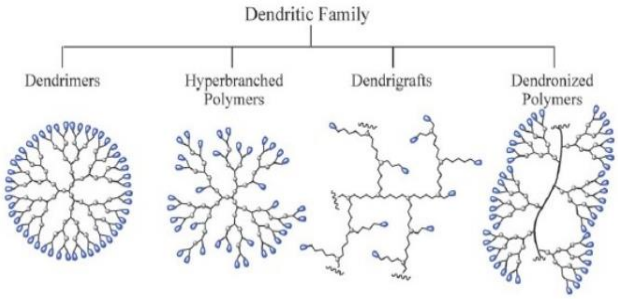


**Fig. 9.** Schematic of dendritic family

In recent years, the application of dendrimers has successfully proved themselves as useful in advanced technology and medicine due to their small size, which is not more than 15 nm, and has very high molecular weight. With this size, dendrimers are easy uptake by the cell through endocytosis. Notably, Dendrimers have advantages over other applications, as they have become an ideal carrier for drug delivery and chemical catalysts.

Dendrimers grow from core to periphery. The core molecular reacts with monomer molecular having two dormant and one reactive group. The small molecular comes together and the reaction proceeds inward and eventually the molecular become attached to the core (Fig. 10). Therefore, the structure of dendrimers from a simple mono molecule compound of the more complex molecule compounds is the key to dendrimers plays multifunction, especially in biosystem. In spite that dendrimers are advantageous for highly specialized applications such as drug delivery along with molecular carrier for chemical catalysts (Fig. 11), they have several disadvantages such as positively charged surface groups prone to destabilize cell membranes and cause cell lysis. Secondly, the degree of substitution, type of amine functionality is important as primary amines being more toxic than secondary or tertiary amines while the fourth generation is the most toxic (Somani and Dufès, 2014; Hughes, 2017; Ho *et al.*, 2019).

Recently, Nanoscientist developed dendrimers that can conjugation with DNA/RNA and have become a new revolution in manipulating cancer cells (Kalomiraki *et al.*, 2016; Gorzkiewicz *et al.*, 2019).

There are several types of dendrimers, which involve Pamam dendrimers, Pamamosdendrirners, Tecto dendrimers, PPI dendrimers, Chiral dendrimers, Hybrid dendrimers Linear Polymers, Amphiphilic dendrimers, and also Micellar dendrimers.

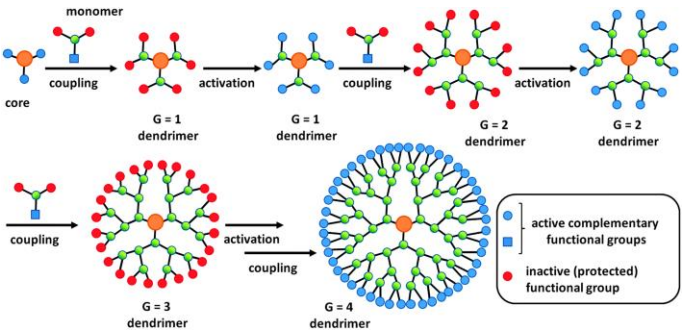


**Fig. 10.** Synthesis of dendrimers according to the divergent method (Sowinska and Urbanczyk-Lipkowska, 2014).

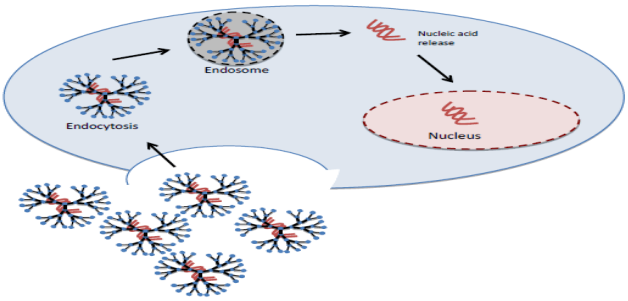


**Fig. 11.** Dendrimers mediated gene delivery to a cancer cell (Ahmed *et al.*, 2016)

## 7. Nanopore

Previously published studies have defined the Nanopore as a very small hole on the instruction of 1 nanometer in internal diameter; hence, electrical current can pass flow through this hole. Nowadays, diverse types of nanopore are available such as Alpha-Hemolysin nanopore, MspA nanopore and Graphene nanopore (Deamer *et al.*, 2016; Jain *et al.*, 2016; Jeck *et al.*, 2019). DNA sequencing is the process of determining the precise order of nucleotides within a DNA molecule. DNA molecules consist of four nitrogen bases. Cytosine (C), Guanine (G), Adenine (A), and Thymine (T). Nanopore can electrically thread DNA electrically through nanometer-sized pores. The pore is submerged in a salt solution while an electrical current is applied. Eventually, the DNA molecule through the pore has detecting and sequencing DNA. In the same time, a low potential (voltage) is applied across the membrane with an ion flux through the pore (Fig. 12). The ion flux is measured by an application specific integrated circuit. The ion flux is partially blocked by the Trans locating DNA strand. Scientific works established the DNA sequencing method has been classified in four generations; first Sanger sequencing, second amplification based massively parallel sequencing, third single molecule sequencing, and fourth nanopore sequencing, it is advantages inexpensive, reliable and high throughput sequencing (Ozsolak and Milos, 2011; Norris *et al.*, 2016). A graphene Nanopore platform using electric fields is improved to tiny DNA strands will pushed through Nanoscale sized, atomically thin pores in a that ultimately may be important for fast electronic sequencing of the four chemical bases of DNA based on their unique electrical (Tian *et al.*, 2013; Craig *et al.*, 2019).

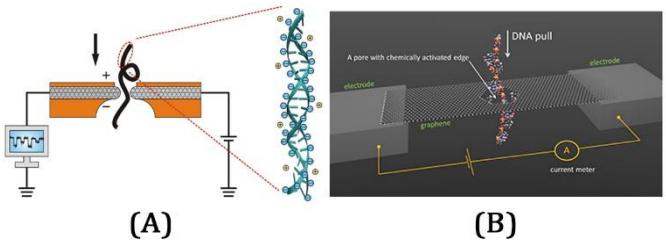


**Fig. 12.** ( A) Nanopore sequencing of DNA, (B) DNA sequencing by graphing nanopore platform (Yang and Jiang, 2017).

## 8. Nanotubes

Several lines of investigation detail that nanotubes found as two types; single-walled nanotubes and multi-walled nanotubes. For instance, carbon nanotubes (CNTs) are hexagonally shaped arrangements of carbon atoms that roll into tubes**.** In this regard, Mittal and his colleagues demonstrated that the (CNTs) are a tubular form of carbon with small diameters; it has a nanometer scale with a hollow tubular structure and atomic arrangement that differ from other carbon allotropes as graphite (Mittal *et al.*, 2015; Kaur *et al.*, 2019). Accumulating data of published studies has identified that carbon nanotubes are cylindrical carbon molecules having novel properties. Their unique surface area with stiffness matrix, strength and resilience has led to much excitement in the field of pharmacy. In addition, CNTs have distinctive electronic and chemical features, which make them suitable for a wide variety of applications, including drug transporters, delivery systems, and diagnostics. Extensive research conducted on anticancer drugs described doxorubicin (Dox) as one of the most efficient anticancer drugs improved for cancer control. However, it can cause the death of non-cancer cells too. In this regard, the nanotubes can successfully deliver Doxorubicin (Dox) only to cancer cells fallow cancer cell marker signatures. Moreover, they are able to enter cells by themselves without obvious toxicity. The cellular uptake mechanism differs depending on the properties and the size of the CNTs (Fig. 13). Recently carbon nanotubes (CNTs) were revealed to have unique advantages over other nano delivery systems such as biological drug delivery and protein delivery (Elhissi *et al.*, 2012; Yu *et al.*, 2012; Yu-Cheng *et al.*, 2013; Sanginario *et al.*, 2017; Kaur *et al.*, 2019; Hosnedlova et al., 2019).

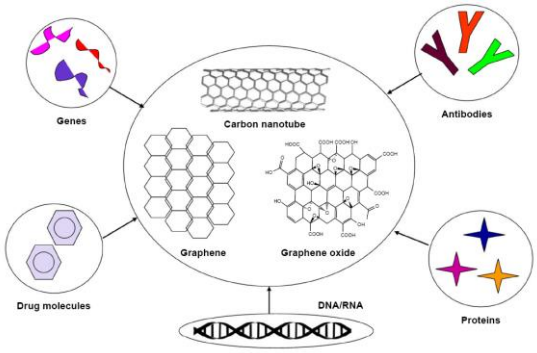


Fig. 13. Schematic of carbon nanotubes delivery system (Yu-Cheng *et al.*, 2013; John *et al.*, 2015; Hosnedlova *et al.*, 2019; Sharma *et al.*, 2019).

## 9. Conclusion

Recently, a mounting body of evidence confirming that nanotechnology has interesting applications in biological and medical sciences. Several publications concerning nanotechnology revealed that devices have many benefits over other modules of nanoparticles. Devices characterized by the simplicity of design in shapes and sizes. Due to the chemistry of their surface, they have the ability to allow more use of properties of matter when used with various biologically useful molecules. The multi-modules of treatment such as chemotherapy, radiotherapy, immunotherapy, hyperthermia and surgical operations techniques are the major treatments for cancer management. However, most of these techniques have various drawbacks. Therefore, the development of Nanodevices has offered a great opportunity to combat cancer, at the same time minimizing the side effect risk in both cancer diagnostic and therapy. More importantly, such devices can control cancer cells without affecting non-cancerous cells. Moreover, Nano devices could prevent or/and regulate cancer from recurrence besides destroying any cancer cells following other treatments. The Quantum dots are described as tiny particles of semiconductor nanocrystal with the size range from 2-10 nm with fluorescent lighting ability. Further, Quantum dots Nanodevices are the perfect devices to reach a good diagnosis compared to rays methods. On this basis, Quantum dots Nanodevices have the potential to be used

to diagnose specific areas of the tumor mass. Additionally, Quantum dots also can glow when stimulated by ultraviolet light, which has less energy than X-rays. Gold nanoparticle can be an effective delivery system for regional cancer-directed therapies. The gold nanoparticles containing drugs coated with targeting agents conjugated antibodies. Therefore, gold nanoparticles circulate through the blood vessels could reach the target cells and thus drugs will be released directly into the cancer cells. Hence, the gold nanoparticles module could be more beneficial than Chemotherapy treatment. Moreover, gold nanoparticle by using IR light, which has less energy than UV and X-ray, is considered a promising method with selective property to fighting cancer cell.

Dendrimers have many properties including macromolecules, high solubility, and miscibility, molecular mass increases, viscosity increase up to a 4th generation, interior layer encapsulates drug molecule, low compressibility. Dendrimers with hydrophilic groups are soluble in polar solvents whilst those with hydrophobic groups are soluble in non-polar solvents. It is important to note that the major advantages of dendrimers are drug delivery and they have the ability to conjugate with DNA/RNA.

Nanopore refers to as a nanoscale hole. Biologically, it is a pore-forming protein in a membrane such as a lipid two layers, while solid-state is formed from synthetic materials such as silicon nitride or graphene. On the other hand, the hybrid type is formed by a pore-forming protein set in synthetic material. Significant research showed that Nanopore allows single-stranded DNA to pass through them, which may help to manipulate defect DNA. Recently, published studies stated that carbon nanotubes are formed by having axis's graphite sheets (<100 nm) rolling into cylinders demonstrating excellent strength with electrical properties, In addition to efficient heat conduction due to carbon nanotubes, which allows carbon conjugation with other molecules, thus could be used in drug delivery. Although efficient, applications of nanotechnology in biology specifically in the biomedical field, it has various disadvantages. Firstly, the safety of nanotechnology has not been well approved. In addition, few investigations have been done *in vivo* to address their safety. Secondly, based on several studies the toxicity of nanodevices remains to be a big problem. Lastly, the Nanodevices functions rely on a targeting agent.

## 10. Future work

The scientists related to nanotechnology are trying developing and regulating the process in Nanochips that can be injected into the human body to control blood pressure. Furthermore, they are trying to invent the Nanorobot machine that could be used in medical applications such as controlling blood sugar, killing bacteria as well as repairing damaged tissues.

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## References

Ahmed, M. (2006) An Overview of Nanomedicine, *Journal of Medical Research Institute*, 27, 4, pp. 248-254

Ahmed, S., Vepuri, S. B., Kalhapure, R. S. & Govender, T. (2016) 'Interactions of dendrimers with biological drug targets: reality or mystery - a gap in drug delivery and development research', *Biomaterials Science*, 4, pp. 1032-1050.

Badi'ah, H., Seedeh, F., Supriyanto, G. Zaidan, A. (2019) Synthesis of Silver Nanoparticles and the Development in Analysis Method. In: IOP Conference Series: *Earth and Environmental Science*, 27, 1, pp. 1-8. IOP Publishing, 012005.

Baffou, G. (2018)'Gold nanoparticles as nanosources of heat', *Photoniques*, pp. 42-47.

Bedge, P. A., Bohara, R. A., Patil, P. M., Joshi, M. G., Bohara, D. A. (2019) 'Current Cancer Therapies: Focus on Hyperthermia and Immunotherapy', Hybrid Nanostructures for Cancer Theranostics, Elsevier.

Bray, F., Ferlay, J., Soerjmataram, I., Siege, R. L., Torre, L. A., Jemal, A. (2018) 'Global cancer statistics 2018: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer', *Journal for clinicians*, 68, pp. 394-424

Buch, K., Gunmalam, V., Andersson, M., Schwarz, P., Brons, C. (2019) 'Effect of chemotherapy and aromatase inhibitors in the adjuvant treatment of breast cancer on glucose and insulin metabolism—A systematic review', *Cancer medicine*, 8, pp. 238-245

Cabuy, E. (2011) 'Hyperthermia in Cancer Treatment', *Reliable Cancer Therapies Energy-based therapies*, 1, pp. 1-48.

Cai, X., Luo, Y., Zhang, W., DU, D., LIN, Y. (2016) 'pH-Sensitive ZnO quantum dots–doxorubicin nanoparticles for lung cancer targeted drug delivery', *ACS applied materials & interfaces*, 8, pp. 22442-22450.

Caminade, A. M. (2019) 'Inorganic Dendrimers and Their Applications', *Smart Inorganic Polymers: Synthesis, Properties, and Emerging Applications in Materials and Life Sciences*, pp. 277-315.

Chang, J. Y., Jabbour, S. K., De Ruysscher, D., Schild, S. E., Simone II, C. B., Rengan, R., Feigenberg, S., Khan, A. J., Choi, N. C.,Bradley, J. D. (2016) 'Consensus statement on proton therapy in early-stage and locally advanced non–small cell lung cancer', *International Journal of Radiation Oncology, Biology, Physics*, 95, pp. 505-516.

Chen, W., Ma, L. (2019) Nanophosphors for visible light enhancement. Google Patents.

Chen, X., Zhu, L., Huang, M., Yang, C. (2019) Synthesis of gold nanoparticles and functionalization with DNA for bioanalytical applications, *Novel Nanomaterials for Biomedical, Environmental and Energy Applications*. Elsevier.

Chinen, A. B., Guan, C. M., Ferrer, J. R., Barnaby, S. N., Merkel, T. J., Mirkin, C. A. (2015) 'Nanoparticle probes for the detection of cancer biomarkers, cells, and tissues by fluorescence', *Chemical reviews*, 115, pp. 10530-10574.

Chithrani, D. B., Jelveh, S., Jalali, F., Van Proijeno, M., Allen, C., Bristow, R. G., Hill, R. P., Jaffray, D. A. (2010) 'Gold nanoparticles as radiation sensitizers in cancer therapy', *Radiation research*, 173, pp. 719-728.

Conde, J., Doria, G., Baptista, P. (2012) 'Noble metal nanoparticles applications in cancer', *Journal of drug delivery*, pp. 1-12. doi:10.1155/2012/751075, Craig, J. M., Laszlo, A. H., Nova, I. C., Brinkerhoff, H., Noakes, M. T., Baker, K. S., Bowman, J. L., Higinbotham, H. R., Mount, J. W., Gundlach, J. H. (2019) 'Determining the effects of DNA sequence on Hel308 helicase translocation along single-stranded DNA using nanopore tweezers', *Nucleic acids research*,95, 1, pp. 505-516.

Cuadras, A., Rovira, E., Marce, R. M., Borrull, F. (2016) 'Lung cancer risk by polycyclic aromatic hydrocarbons in a Mediterranean industrialized area', *Environmental Science and Pollution Research*, 23, pp. 23215-23227.

Daraee, H., Eatemadi, A., Abbasi, E., Fekri Aval, S., Kouhi, M., Akbarzadeh, A. (2016) 'Application of gold nanoparticles in biomedical and drug delivery', *Artificial cells, nanomedicine, and biotechnology*, 44, pp. 410-422.

Deamer, D., Akeson, M., Branton, D. (2016) 'Three decades of nanopore sequencing', *Nature biotechnology*, 34, pp. 518-524.

Di Corato, R., BigallI, N. C., Ragusa, A., Dorfs, D., Genovese, A., Marottaa, R., Manna, L., Pellegrino, T. (2011) 'Multifunctional Nanobeads Based on Quantum Dots and Magnetic Nanoparticles: Synthesis and Cancer Cell Targeting and Sorting', *ACS Nano*, 5, pp. 1109-1121.

Divakaran, D., Lakkakula, J. R., Thakur, M., Kumawat, M. K., Srivastava, R. (2019) 'Dragon fruit extract capped gold nanoparticles: Synthesis and their differential cytotoxicity effect on breast cancer cells', *Materials Letters*, 236, pp. 498-502

Dorsey, J. F., Sun, L., Joh, D. Y., Witztum, A., Zaki, A. A., Kao, G. D., Alonso-Basanta, M., Avery, S., Tsourkas, A., Hahn, S. M. (2013) 'Gold nanoparticles in radiation research: potential applications for imaging and radiosensitization', *Translational Cancer Research*, 2, pp. 280-291.

Douba, A., Genedy, M., Matteo, E., Kandil, U., Stormont, J., Taha, M. R. (2017) 'The significance of nanoparticles on bond strength of polymer concrete to steel', *International Journal of Adhesion and Adhesives*, 74, pp. 77-85.

Elhissi, A., Ahmed, W., Dhanak, V., Subramani, K. (2012) Carbon nanotubes in cancer therapy and drug delivery, Emerging Nanotechnologies in Dentistry. Elsevier.

England, C., S Huang, J., James, K., Zhang, G., Gobin, A., Frieboes, H. (2015) Detection of Phosphatidylcholine-Coated Gold Nanoparticles in Orthotopic Pancreatic Adenocarcinoma using Hyperspectral Imagin', *PLoS ONE*, 10, 6, e0129172. https://doi.org/10.1371/

Frankel, T., Lanfranca, M. P., ZOU, W. (2017) The Role of Tumor Microenvironment in Cancer Immunotherapy. Tumor Immune Microenvironment in Cancer Progression and Cancer Therapy. Springer.

Gorzkiewicz, M., Deriu, M. A., Studzian, M., Janaszewska, A., Grasso, G., Pulaski, Ł., Appelhans, D., Danani, A. & Klajnert-Maculewicz, B. (2019) 'Fludarabine-Specific Molecular Interactions with Maltose-Modified Poly(propyleneimine) Dendrimer Enable Effective Cell Entry of the Active Drug Form: Comparison with Clofarabine', *Biomacromolecules*, 20, pp. pp. 1429-1442.

Guo, M., He, J., Li, Y., Ma, S., Sun, X. (2016) 'One-step synthesis of hollow porous gold nanoparticles with tunable particle size for the reduction of 4-nitrophenol', *Journal of hazardous materials*, 310, pp. 89-97.

Hainfeld, J. F., Lin, L., Slatkin, D. N., Avraham Dilmanian, F., Vadas, T. M., Smilowitz, H. M. (2014) 'Gold nanoparticle hyperthermia reduces radiotherapy dose', *Nanomedicine: Nanotechnology, Biology and Medicine*, 10, pp. 1609-1617.

Ho, M. N., Bach, L. G., Nguyen, T. H., Ho, M. H., Nguyen, D. H., Nguyen, C. K., Nguyen, C. H., Nguyen, N. V., Thi, T. T. H. (2019) 'PEGylated poly (amidoamine) dendrimers-based drug loading vehicles for delivering carboplatin in treatment of various cancerous cells', *Journal of Nanoparticle Research*, 9, 214, pp. 2-17

Hosnedlova, B., Kepinska, M., Fernandez, C., Peng, Q., Ruttkay-Nedecky, B., Milnerowicz, H., Kizek, R. (2019) 'Carbon nanomaterials for targeted cancer therapy drugs: A critical review', *The Chemical Record*, 19, pp. 502-522.

Hughes, G. A. (2017) 'Nanostructure-mediated drug delivery', *Nanomedicine in Cancer*, 1, Pan Stanford.

Jain, M., Olsen, H. E., Paten, B., Akeson, M. (2016) The Oxford Nanopore MinION: delivery of nanopore sequencing to the genomics community. *Genome biology*, 17, 1, pp. 239-250

Jeck, W. R., Lee, J., Robinson, H., Le, L. P., Iafrate, A. J., Naradi, V. (2019) 'A Nanopore Sequencing–Based Assay for Rapid Detection of Gene Fusions', *The Journal of Molecular Diagnostics*, 21, pp. 58-69.

John, A. A., Subramanian, A. P., Vellayappan, M. V., Balajl, A., Mohandas, H., Jaganathan, S. K. (2015) 'Carbon nanotubes and graphene as emerging candidates in neuroregeneration and neurodrug delivery', *International journal of nanomedicine*, 10, 4267-4277.

Joseph, D., Baskaran, R., Yang, S. G., Huh, Y. S., Han, Y.-K. (2019) 'Multifunctional spiky branched gold-silver nanostars with near-infrared and short-wavelength infrared localized surface plasmon resonances', *Journal of Colloid and Interface Science*, 542, pp. 308-316

Kalomiraki, M., Theros, K., Chaniotakis, N. A. (2016) 'Dendrimers as tunable vectors of drug delivery systems and biomedical and ocular applications', *International journal of nanomedicine*, 11, pp. 1-12.

Kalluri, A., Debnath, D., Dharmadhikari, B. & Patra, P. (2018) 'Graphene Quantum Dots: Synthesis and Applications', *Methods in enzymology*, 609, pp. 335-354

Kanapathipillai, M., Brock, A., Ingeber, D. E. (2014) 'Nanoparticle targeting of anti-cancer drugs that alter intracellular signaling or influence the tumor microenvironment', *Advanced drug delivery reviews*, 79, pp. 107-118.

Kaur, J., Gill, G. S., Jeet, K. (2019) Applications of Carbon Nanotubes in Drug Delivery: A Comprehensive Review. Characterization and Biology of Nanomaterials for Drug Delivery. Elsevier.

Khlebtsov, N., Dykman, L. (2011) 'Bio distribution and toxicity of engineered gold nanoparticles: a review of in vitro and in vivo studies', *Chemical Society Reviews*, 40, pp. 1647-1671.

Kooshki, H., Sobhani-Nasab, A., Eghbali-Arani, M., Ahmadi, F., Ameri, V., Rahimi-Nasrabadi, M. (2019) 'Eco-friendly synthesis of PbTiO3 nanoparticles and PbTiO3/carbon quantum dots binary nano-hybrids for enhanced photocatalytic performance under visible light', *Separation and Purification Technology*, 211, pp. 873-881.

Kratochwil, C., Bruchertseifer, F., Giesel, F. L., Weis, M., Verburg, F. A., Mottaghy, F., Kopka, K., Apostolidis, C., Haberkorn, U., Morgenstern, A. (2016) '225Ac-PSMA-617 for PSMA-targeted a-radiation therapy of metastatic castration-resistant prostate cancer', *J Nucl Med*, 57, pp. 1941-1944.

Kumar, P. V., Kala, S. M. J., Prakash, K. (2019) 'Green synthesis of gold nanoparticles using Croton Caudatus Geisel leaf extract and their biological studies', *Materials Letters*, 236, pp. 19-22.

Lee, H., Kim, C., Lee, D., Park, J. H., Searson, P. C., Lee, K. H. (2017) 'Optical coding of fusion genes using multicolor quantum dots for prostate cancer diagnosis', *International journal of nanomedicine*, 12, pp. 4397-4407.

Lee, Y. C. A., LI, S., Chen, Y., LI, Q., Chen, C. J., Hsu, W. L., Lou, P. J., Zhu, C., Pan, J., Shen, H. (2019) 'Tobacco smoking, alcohol drinking, betel quid chewing, and the risk of head and neck cancer in an East Asian population', *Head & neck*, 41, pp. 92-102.

Lim, S. Y., Shen, W., GAO, Z. (2015) 'Carbon quantum dots and their applications', *Chemical Society Reviews*, 44, pp. 362-381.

Lin, A. J., Kidd, E., Dehdashti, F., Siegel, B. A., Mutic, S., Thaker, P. H., Massad, L. S., Powell, M. A., Mutch, D. G., Markovina, S. (2019) 'Intensity modulated radiation therapy and image-guided adapted brachytherapy for cervix cancer', *International Journal of Radiation Oncology, Biology, Physics*, 103, pp. 1088-1097.

Lu, J., Tang, M., Zhang, T. (2019) 'Review of toxicological effect of quantum dots on the liver', *Journal of Applied Toxicology*, 39, pp. 72-86.

Mcguire, S. (2016) World cancer report 2014. Geneva, Switzerland: World Health Organization, international agency for research on cancer, WHO Press, 2015. Oxford University Press.

Mercado, N., Bhatt, P., Sutariya, V., Florez, F. L. E., Pathak, Y. V. (2019) Application of Nanoparticles in Treating Periodontitis: Preclinical and Clinical Overview. Surface Modification of Nanoparticles for Targeted Drug Delivery. Springer.

Mewara, D., Rathore, B. P. S. (2016) 'A Study of Appoaches of Nanotechnology in Biomedical Nanotechnology', *International Journal Of Applied Research In Science And Engineering* (International Conference on Emerging Technologies in Engineering, Biomedical, Medical and Science (ETEBMS-November 2016)), pp. 53-5.

Mittal, G., Dhand, V., Rhee, K. Y., Park, S.-J., Lee, W. R. (2015) 'A review on carbon nanotubes and graphene as fillers in reinforced polymer nanocomposites', *Journal of Industrial and Engineering Chemistry*, 21, pp. 11-25.

Muddineti, O. S., Ghosh, B., Biswas, S. (2015) 'Current trends in using polymer coated gold nanoparticles for cancer therapy', *International journal of pharmaceutics*, 484, pp. 252-267.

Mugaka, B. P., Hu, Y., Ma, Y. & Ding, Y. (2019) Surface Modification of Gold Nanoparticles for Targeted Drug Delivery. Surface Modification of Nanoparticles for Targeted Drug Delivery. Springer.

Norris, A. L., Workman, R. E., Fan, Y., Eshleman, J. R., Timp, W. (2016) 'Nanopore sequencing detects structural variants in cancer', *Cancer biology & therapy*, 17, pp. 246-253.

Oh, N., Park, J.-H. (2014) 'Endocytosis and exocytosis of nanoparticles in mammalian cells', *International journal of nanomedicine*, 9, 1, pp. 51-63.

Ozsolak, F., Milos, P. M. (2011) 'RNA sequencing: advances, challenges and opportunities', *Nature reviews genetics*, 12, 87-98.

Parro'n, T., Requena, M., Herna'ndez, A. F., Alarco'n, R. (2014) 'Environmental exposure to pesticides and cancer risk in multiple human organ systems', *Toxicology Letters*, 230, pp. 157-165.

Rami'rez, N., Özel, M. Z., Lewis, A. C., Marce', R. M., Borruli, F., Hamilton, J. F. (2014) 'Exposure to nitrosamines in third hand tobacco smoke increases cancer risk in non-smokers', *Environment international*, 71, pp. 139-147.

Riley, R. S., June, C. H., Langer, R., Mitchell, M. J. (2019) 'Delivery technologies for cancer immunotherapy', *Nature Reviews Drug Discovery*, 18, pp. 175-196.

Sanginario, A., Miccoli, B., Demarchi, D. (2017) 'Carbon Nanotubes as an Effective Opportunity for Cancer Diagnosis and Treatment', *Biosensors*, 7, 1, pp. 9-32.

Sharma, S., Naskar, S., Kuotsu, K. (2019) 'A review on carbon nanotubes: Influencing toxicity and emerging carrier for platinum based cytotoxic drug application', *Journal of Drug Delivery Science and Technology*, 51, pp. 708-720

Siegel, R. L., Mille, K. D., Jemal, A. (2016) 'Cancer statistics', *CA: a cancer journal for clinicians*, 66, 1, 7-30.

Singh, B., Mitragotri, S. (2019) 'Harnessing cells to deliver nanoparticle drugs to treat cancer', *Biotechnology advances*, In press. doi:10.1016/j.biotechadv.2019.01.006

Singh, S. D Rai, Praveen, A. (2015) 'DNA Methylation in Cancer: Review', *Indo Global Journal of Pharmaceutical Sciences*, 5(2), pp. 138-148

Smith, A. J., Oertle, J., PRATO, D. (2014) 'Immunotherapy in cancer treatment', *Open Journal of Medical Microbiology*, 4, 178-191.

Soliman, E. M., Kandil, U. F., Taha, M. M. R. (2012) 'The significance of carbon nanotubes on styrene butadiene rubber (SBR) and SBR modified mortar', *Materials and structures*, 45, pp. 803-816.

Somani, S. & Dufe's, C. (2014) 'Applications of dendrimers for brain delivery and cancer therapy', Nanomedicine, 9, pp. 2403-2414.

Song, K., XU, P., Meng, Y., Geng, F., Li, J., Li, Z., Xing, J., Chen, J., Kong, B. (2013) 'Smart gold nanoparticles enhance killing effect on cancer cells', *International journal of oncology*, 42, pp. 597-608.

Sowinska, M., Urbanczyk-Lipkowska, Z. (2014) 'Advances in the chemistry of dendrimers', *New Journal of Chemistry*, 38, pp. 2168-2203.

Stewart, B. & Wild, C. P. (2017) World cancer report 2014. Word Health Organization.

Tian, K., He, Z., Wang, Y., Chen, S.-J., Gu, L.-Q. (2013) 'Designing a Polycationic Probe for Simultaneous Enrichment and Detection of MicroRNAs in a Nanopore', *ACS Nano*, 7, pp. 3962-3969.

Tohme, S., Simmons, R. L., Tsung, A. (2017) 'Surgery for cancer: a trigger for metastases', *Cancer research*, 77, pp. 1548-1552.

Torre, L. A., Bray, F., Siegel, R. L., Ferlay, J., Lortet-Tieulent, J., Jemal, A. (2015) 'Global cancer statistics, 2012', *CA: a cancer journal for clinicians*, 65, pp. 87-108.

Tsagozis, P., Forsberg, J., Bauer, H. C., Wedin, R. (2019) How Expected Survival Influences the Choice of Surgical Procedure in Metastatic Bone Disease. *Management of Bone Metastases*. Springer.

Valcke, M., Bourgault, M.-H., Rochette, L., Normandin, L., Samuel, O., Belleville, D., Blanchet, C., Phaneuf, D. (2017) 'Human health risk assessment on the consumption of fruits and vegetables containing residual pesticides: a cancer and non-cancer risk/benefit perspective', *Environment international*, 108, pp. 63-74.

Vangijn, W., Gooiker, G., Wouters, M., Post, P., Tollenaar, R., Van De VeldeEL, C. (2010) 'Volume and outcome in colorectal cancer surgery', *European Journal of Surgical Oncology (EJSO)*, 36, pp. S55-S63.

Von Minckwitz, G., Untch, M., Blohmer , J.-U., Costa, S. D., Eidtmann, H., Fasching, P. A., Gerber, B., Eiermann, W., Hilfrich, J., Huober, J. (2012) 'Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes', *Journal of clinical oncology*, 30, pp. 1796-1804.

Wang, E. C. & Wang, A. Z. (2014) 'Nanoparticles and their applications in cell and molecular biology', *Integrative Biology*, 6, pp. 9-26.

Wang, Y., Wang, Z., Xu, C., Tian, H., Chen, X. (2019) 'A disassembling strategy overcomes the EPR effect and renal clearance dilemma of the multifunctional theranostic nanoparticles for cancer therapy', Biomaterials, 197, pp. 284-293

Wei, T., Chen, C., Liu, J., Liu, C., Posoco, P., Liu, X., Cheng, Q., Huo, S., Liang, Z., Fermeglia, M., Pricl, S., Liang, X.-J., Rocchi, P., Peng, L. (2015) Anticancer drug nanomicelles formed by self-assembling amphiphilic dendrimer to combat cancer drug resistance. Proceedings of the National Academy of Sciences.

Yang, N., Jiang, X. (2017) 'Nanocarbons for DNA sequencing: A review', *Carbon*, 115, pp. 293-311.

Yanover, D., Vaxenburg, R., TilchinIL, J., Rubin-Brusilovski, A., Zalats, G., Čapek, R. K., Sashchiuk, A., LIFSHITZ, E. (2014) 'Significance of Small-Sized PbSe/PbS Core/Shell Colloidal Quantum Dots for Optoelectronic Applications', *The Journal of Physical Chemistry* C, 118, pp. 17001-17009.

Yu-Cheng, C., Xin-Chun, H., Yun-Ling, L., Yung-Chen, C., You-Zung, H., Hsin-Yun, H. (2013) 'Non-metallic nanomaterials in cancer theranostics: a review of silica- and carbon-based drug delivery systems', *Science and Technology of Advanced Materials*, 14, 4, 044407. doi: 10.1088/1468-6996/14/4/044407

Yu, J.-G., Jiao, F.-P., Chen, X.-Q., Jiang, X.-Y., Peng, Z.-G., Zeng, D.-M., Huang, D.-S. (2012) 'Irradiation-mediated carbon nanotubes' use in cancer therapy', *Journal of Cancer Research and Therapeutics*, 8, pp. 348-354.

Yuan, H., Khoury, C. G., Hwang, H., Wilson, C. M., Grant, G. A., Vo-Dinh, T. (2012) 'Gold nanostars: surfactant-free synthesis, 3D modelling, and two-photon photoluminescence imaging', *Nanotechnology*, 23, 7, 075102. doi: 10.1088/0957-4484/23/7/075102.

Zhang, Z., Wang, F., Xu, G., Liu, X., Cao, Y., Min, W. (2019) 'Design and simulation of optical drive tunable grating based on GNP and PDMS', *Materials Research Express*, 6, 5, 055704. https://doi.org/10.1088/2053-1591/ab0575

Zhou, Z., Ma, X., Murphy, C. J., Jin, E., Sun, Q., Shen, Y., Van Kirk, E. A., Murdoch, W. J. (2014) 'Molecularly precise dendrimer–drug conjugates with tunable drug release for cancer therapy', *Angewandte Chemie International Edition*, 53, pp. 10949-10955.

Zong, C., Ai, K., Zhang, G., Li, H., Lu, L. (2011) 'Dual-Emission Fluorescent Silica Nanoparticle-Based Probe for Ultrasensitive Detection of Cu2+', *Analytical Chemistry*, 83, pp. 3126-3131