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Current Approaches of Nanotechnology in Cancer Therapy

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Abstract: ***Nanotechnology is a multidisciplinary field which combines engineering, biology, physics and chemistry. This field has evolved over the past half century and most scientists now agree that it has truly come of age. Nanotechnology is well placed in the diagnosis and treatment of cancer as it enables doctors and scientists to operate at a molecular and cellular level. This allows treatment to be focussed on specific areas without impacting surrounding organs and systems. Using nanotechnology, it is possible that cancer cells could be targeted and destroyed with almost no damage to surrounding healthy tissue. The purpose of this paper is to investigate the developments and future uses of nanotechnology in diagnosing and treating cancer. In addition, we will explain how the advances in the uses of nanotechnology, combined with other developments in medicine, have led scientists to predict that cancer will be eradicated in less than ten years***

Index Terms- Cancer, Tumour Necrosis Factor (TNF), Nano Particles (NP), Radiation Therapy.

I. INTRODUCTION

Cancer is a highly heterogeneous complex disease that encompasses a group of disorders characterized by continuous indefinite growth [1]. Through the annals of history, the malaise of cancer has ailed humans. Despite impressive advances in cancer biology, it is the leading cause of death worldwide and remains a challenge. There are over 200 different types of cancer reported all over the globe[2]. In 2008, approximately 12.7 million cancer cases were reported, causing approximately 7.6 million cancer deaths, out of which 64% of the deaths were reported from economically developing countries[3]. The complexity of this disease at genetic and phenotypic levels clarifies its clinical diversity and therapeutic resistance. There is a 5-year relative survival rate of cancer patients[4], which provides potential opportunities for early diagnosis and improved treatment, which in turn is highly desirable because of widespread occurrence, high death rate, and recurrence after treatment.

II. INTRODUCTION TO NANOTECHNOLOGY

Nanotechnology is an interdisciplinary research field developed with an amalgamation of chemistry, engineering, biology, and medicine, and has various useful applications in cancer biology, such as early detection of tumors, discovery of cancer biomarkers, and development of novel treatments [6].

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It is a rapidly evolving and expanding discipline that has gained public and media interest worldwide. Use of nanotechnology in cancer biology has provided hope within scientific Communities of developing novel cancer therapeutic strategies. Nanotechnology involves the creation and/or manipulation of materials at nanometer scale, either by scaling up from single

To groups of atoms or by refining or reducing bulk materials into nanoparticles (NPs)[7].NPs are typically several hundred nanometers in size and can offer unprecedented interactions with biomolecules present both on the cell surface as well as inside the cell[8].NPs can be engineered as nanoplatforms for effective and targeted delivery of drugs, and imaging labels by overcoming many biological, biophysical, and biomedical barriers. For in vitro and ex vivo applications, the advantages of state-of-the-art nanodevices such as nanochips and nanosensors over traditional methods are quite obvious[9,10]. A variety of NPs are used for diagnosis-cum-therapy of different cancer types, by visualizing tumors and carrying out targeted delivery of drugs with reduced toxic side effects. Cancer related examples of nanodevices include quantum dots (QDs), carbon nanotubes (CNTs), paramagnetic NPs, liposomes, gold NPs (GNPs), magnetic resonance imaging (MRI) contrast agents for intraoperative imaging, and a novel NP-based method for high-specificity detection of DNA and protein[6,11–15].

Recent advances have led to development of bioaffinity NP probes for molecular and cellular imaging, targeted NP drugs for cancer therapy, and integrated nanodevices for early screening and detection of cancer. These developments raise exciting opportunities for personalized oncology in which genetic and protein biomarkers are used to diagnose and treat cancer, based on the molecular profiles of individual patients. However, several barriers do exist for in vivo applications of nanodevices in preclinical and clinical use of nanotechnology. Amongst them are biocompatibility, in vivo kinetics, tumor-targeting efficacy, acute and chronic toxicity, ability to escape the reticuloendothelial system, and cost-effectiveness [6,16]. The development of novel nanotechnology-based approaches towards cancer treatment provides a new ray of hope in the cancer research field. The present review article summarizes the application of various nanotechnology-based approaches towards the diagnostics and therapeutics of cancer.

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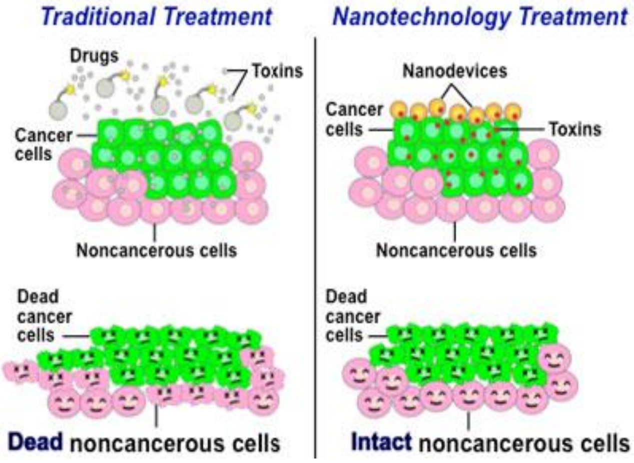


FIG 1. Current research and Medical Uses of Nanotechnology

III. DRUG DELIVERY

One of the most important applications of nanotechnology in medicine which is currently being tested involves employing nanoparticles to deliver drugs or other substances to specific types of cells, in particular to cancer cells. Particles are engineered so that they are attracted to diseased cells, which then allow direct treatment of those cells. This technique reduces damage to healthy cells in the body and allows for earlier detection of disease. One treatment involves targeted chemotherapy that delivers a tumour-killing agent called tumour necrosis factor alpha (TNF) to cancer tumours. One of the major flaws of our body's immune system is that is "oversensitive". It will attack almost anything foreign that enters our body. TNF is attached to a gold nanoparticle along with a chemical (Thiol-derivatised polyethylene glycol) which "hides" the TNF possessing nanoparticle from our immune system. This method to deliver TNF and other chemotherapy drugs to cancer tumours is called cytimmune

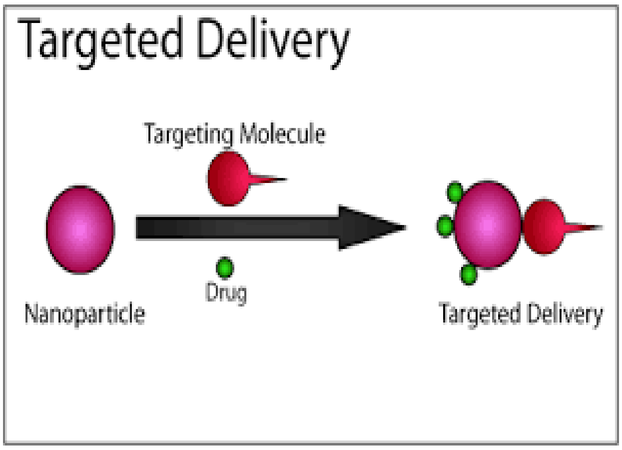


FIG 2

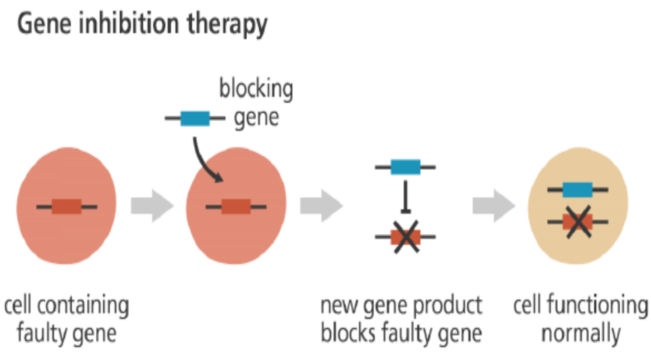
An alternative approach uses nanoparticles constructed from carbon. The value of nanoparticles made of diamond is multifaceted. Very recent studies report that tiny flecks of carbon can shrink tumours in mice by delivering chemotherapy drugs to cancer cells. Made of carbon, they're non-toxic, and the body's immune system doesn't attack them. They can bind tightly to a variety of molecules and deliver them right into a tumour. And because they are only 2 to 8 nanometres in diameter, they are easy for the kidneys to clear from the body before they block up blood vessels, a long-standing problem in nanoparticle therapy. To study the use of nanodiamonds' in cancer treatment, doxorubicin, a standard chemotherapy drug, was injected into mice with drug-resistant breast and liver cancer. With the help of the diamonds, the drug stayed in the bloodstream 10 times longer than usual, making it much more effective. As a result, the tumours shrank significantly, as reported in Science Translational Medicine. This technique also decreased the toxicity of the drug. The researchers were able to inject the mice with doses of doxorubicin that normally would be lethal. But the drug stayed bound to the diamond until it reached the tumour, so it didn't damage cells elsewhere in the body, and the animals survived. It was also interesting to note that the livers of the mice didn't increase enzymatic activity as they normally would in response to high levels of a toxic substance. Most importantly, the doxorubicin-decorated diamonds had no effect on white blood cell count, an indicator of immune system activation that's often the deciding factor in whether a patient can continue chemotherapy[17].

A. Gene Therapy

Gene delivery is another area of current interest; genetic materials (DNA, RNA) have been used as molecular medicine and are delivered to specific cell types to either inhibit some undesirable gene expression or express therapeutic proteins. To date, the majority of gene therapy systems are based on viral vectors delivered by injection to the sites where the therapeutic effect is desired. Viral vectors can have potentially dangerous side effects due to unintended integration of the viral DNA into the host genome, which can potentially affect the expression of essential genes. Gene therapy using nanotechnology does not suffer from this disadvantage.

B. Therapeutic Medicine

The use of infra-red light to target heat on to cancer cells has been well documented. Thus the use of nanoshells to concentrate the heat from infrared light to destroy cancer cells with minimal damage to surrounding healthy cells is likely to prove to be very useful in the near future. The following diagram illustrates the use of nanoshells.



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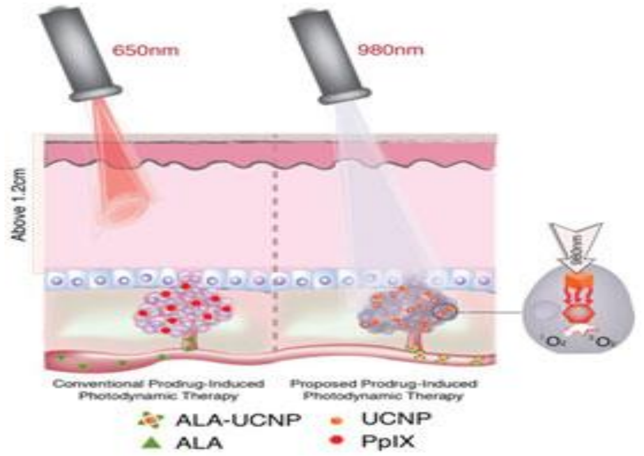
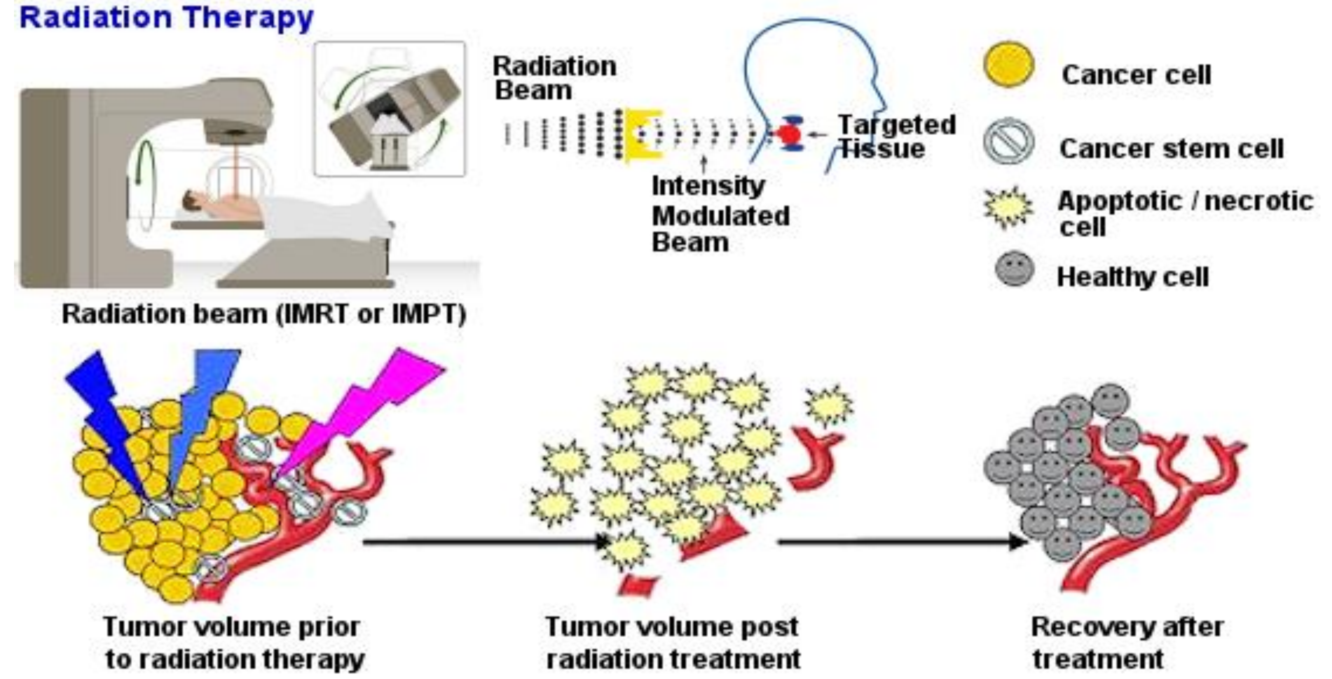


In a similar manner nanoparticles which can be activated by x-rays can be used to generate particles that can cause the destruction of cancer cells to which they have attached themselves. This is a much more focussed approach to radiotherapy than is in use today. A combined chemo-heat therapy method uses not only one nanoparticle to combat a tumour, but two. One nanoparticle is used to deliver the chemotherapy drug and a different nanoparticle is used to guide the drug carrier to the tumour. The guiding nanoparticle would work almost like a magnet, the chemotherapy drug being the metal. The drug would be able to effectively migrate through attraction to the target. The drug carrying nanoparticle attaches to the specific FIGURE 4 FIGURE 3 6 amino acids that bind to this protein, so the increased level of protein at the tumour speeds up the accumulation of the chemotherapy drug. This method if put into practise would be suitable for treating most cancers, even those which are deeper in the body.



C. Diagnostic and Imaging

Nanomaterials are sensitive chemical and biological sensors. They can be integrated into other technologies such as lab-on-a-chip to facilitate molecular diagnostics. Their applications include detection of microorganisms in various samples, monitoring of metabolites in body fluids and detection of tissue pathology such as cancer. Numerous nanodevices and nanosystems for sequencing single molecules of DNA are also feasible. Quantum Dots® (qdots) are nanoparticles that absorb photons of light, then re-emit photons at a different wavelength and can be used in order to search for cancer tumours in the body. However, they exhibit some important differences as compared to traditional fluorophores such as organic fluorescent dyes and naturally fluorescent proteins. Qdot nanocrystals are nanometre-scale (roughly protein-sized) atom clusters, containing from a few hundred to a few thousand atoms of a semiconductor material (cadmium mixed with selenium or tellurium), which has been coated with an additional semiconductor shell (zinc sulphide) to improve the optical properties of the material. These particles fluoresce in a completely different way than do traditional fluorophores. These Qdots may be used in the future to locate cancer tumours and in the short term in performing diagnostic tests. The use of iron oxide nanoparticles to improve MRI images of cancer tumours has also been documented. The nanoparticle is coated with a peptide (polymer coating) that binds to a cancer tumour; once the nanoparticles are attached to the tumour the magnetic property of the iron oxide enhances the images from the Magnetic Resonance Imagining scan. Nanoparticles can also attach to proteins or other molecules, allowing detection of disease indicators in a lab sample at a very early stage. There are several areas of research into nanoparticle disease detection systems. One system uses coated gold nanoparticles for diagnostic purposes.

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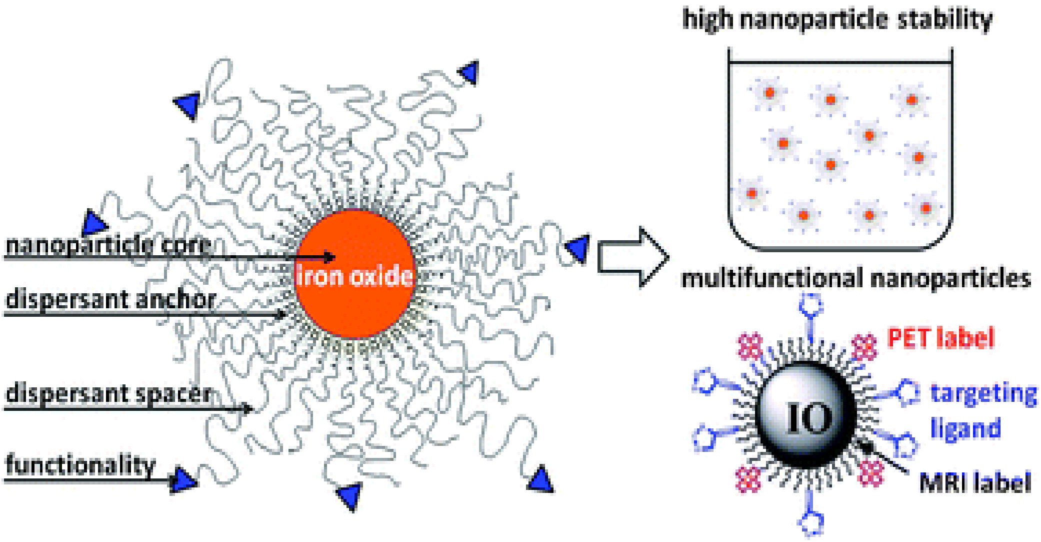
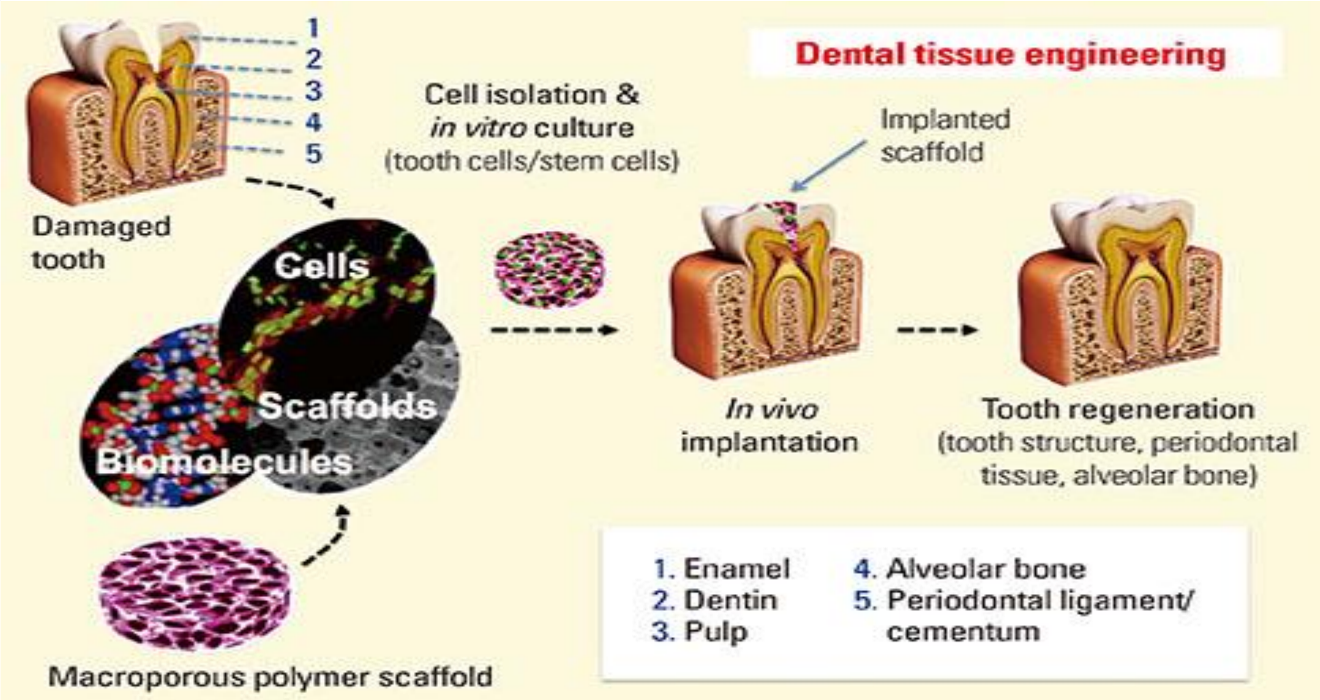


D. Tissue Engineering

Titanium is a well-known bone repairing material widely used in orthopaedics and dentistry. It has a high fracture resistance, ductility and weight to strength ratio. Unfortunately, it suffers from the lack of bioactivity, as it does not support sell adhesion and growth well. Apatite coatings are known to be bioactive and to bond to the bone. Hence, several techniques were used in the past to produce an apatite coating on titanium. Those coatings suffer from thickness non-uniformity, poor adhesion and low mechanical strength. In addition, a stable porous structure is required to support the nutrients transport through the cell growth.

It was shown that using a biomimetic approach – a slow growth of nanostructured apatite film from the simulated body fluid – resulted in the formation of a strongly adherent, uniform nanoporous layer [18]. The layer was found to be built of 60 nm crystallites, and possess a stable nanoporous structure and bioactivity.

An artificial hybrid material was prepared from 15–18 nm ceramic nanoparticles and poly (methyl methacrylate) copolymer [19]. Using tribology approach, a viscoelastic behaviour (healing) of the human teeth was demonstrated. An investigated hybrid material, deposited as a coating on the tooth surface, improved scratch resistance as well as possessed a healing behaviour similar to that of the tooth.



IV. CONCLUSION

Nanotechnology is a rapidly developing field that has given new hope in the treatment of various diseases. Early detection and treatment of cancer remains a challenge to the scientific community. Moreover, different strategies have been explored in recent years for cancer detection and therapy. Application of nanotechnology in cancer treatment seems to solve these limitations, which has given new hope to humanity. Specific targeting of cancer cells was also the major challenge faced by conventional therapeutic approaches of cancer treatment. Recently,

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Various NP-based drug-delivery systems such as liposomes, dendrimers, diamondoids, QDs, viral NPs, and CNTs have shown encouraging results in cancer therapy. Properties like prolonged existence in systemic circulation, enhanced drug localization, and their efficacy make the NP-based model an excellent one. One of the major challenges in cancer treatment, ie, MDR, can also be overcome by these NP formulations the light of our review, we expect that in future, different NP formulations would serve as “Trojan horses” in the field of cancer diagnostics and its treatment. Hereby, we find it pertinent to highlight that toxicity and immune-system induction should be given due consideration before finalizing the use of any NP formulation for diagnostic and treatment purposes

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