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Review

A Review Article On Nanotechnology In Cancer Therapy

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Abstract

Cancer is one of the major causes of mortality worldwide and advanced techniques for therapy are urgently needed. The development of novel nanomaterials and nanocarriers has allowed a major drive to improve drug delivery in cancer. The major aim of most nanocarrier applications has been to protect the drug from rapid degradation after systemic delivery and allowing it to reach tumor site at therapeutic concentrations, meanwhile avoiding drug delivery to normal sites as much as possible to reduce adverse effects. Nanocarriers preferentially accumulate in the tumor through passive targeting due to a leaky vasculature and defective lymphatic drainage in solid tumors. The permeability of a chaotic vasculature and tumor microenvironment (TME) and retention can lead to the accumulation of macromolecules in TME by 70-fold.The rational design of nanoparticles plays a critical role since structural and physical characteristics, such as size, charge, shape, and surface characteristics determine the biodistribution, pharmacokinetics, internalization and safety of the drugs. In this review, we focus on several novel and improved strategies in nanocarrier design for cancer therapy.

Keywords: nanoparticles, nanomedicine, drug delivery, cancer therapy

INTRODUCTION

Nanotechnology

The word "Nano" is derived from the greek word nanos for dwarf. A nanometer is a billionth of a meter, that is, about 1/80,000 of the diameter of a human hair, or 10 times the diameter of a hydrogen atom. When the physicist and Nobel laureate Richard Feynman challenged the science community to think small in his 1959 lecture 'There's Plenty of Room at the Bottom', he planted the seeds of a new era in science and technology that is today’s Nanotechnology. Nanotechnology is defined as the study and use of structures between 1 nanometer and 100 nsanometers in size. Nanotechnology is the synergy of mechanical, electrical, chemical engineering, material sciences, microelectronics, and biological screening. Nanotechnologies are the design, production, characterization, and application of structures, devices and systems by controlling shape and size at nanometer scale. There are more than 300 claimed nanotechnology products already on the market.

Nanotechnology, introduced almost half century ago, is one of the most active research areas with both novel science and useful applications that has gradually established itselfin the past two decades.Not surprisingly, it is observed that expenditure on nanotechnology research is significant. The U.S. National Nanotechnology Initiative (NNI) expenditures exceed $1 billion each year, with the President's 2008 budget for NNI at $1.5 billion. However, the research is mainly moving forward motivated by immediate profitable return generated by high value commercial products .According to a study by the Canadian Program on Genomics and Global Health (CPGGH), nanotechnology in construction ranked 8 of 10 applications that most likely have impact in the developing world.

Nanotechnology basics

Nanotechnology is the creation of materials and devices by controlling of matter at the levels of atoms, molecules, and supramolecular (nanoscale) structures. It is the use of very small particles of materials to create new large scale materials.

Nanotechnology is not a new science or technology. It was believed first introduced by Richard P. Feynman in his lecture at the California Institute of Technology in 1959. However, the research on this has been very active only in recent two decades. This is because the development and application of nanotechnology are relying on the development of other related science and technology such as physics and chemistry that are commonly new to break through at that time.Most promising developments of nanotechnology are fullerene (a new form of carbon, C60) and carbon nanotubes. In some figures are "a grapheme sheet rolled into a cylinder with specific alignment of hexagonal rings."

CANCER THERAPY ADVANCES USING NANOTECHNOLOGY

Cancer is leading cause of death in the United State among people younger than 85 years. Statistics have revealed that the number of cancer related death has remained about the same. It is universally accepted that early detection of cancer is essential even before anatomic anomalies are visible. A major challenge in cancer diagnostic in the 21stcentury is to able to determine the exact relationship between cancer biomarkers and the clinical pathology, as well as to be able to non-invasively detect tumour at an early stage for maximum therapeutic benefit.

In cancer therapy, targeting and localized delivery are the key challenges. To wage an effective war against cancer, we have the ability to selectively attack the cancer cells, while saving the normal tissue from excessive burdens of drug toxicity. There is the need for a new generation of new therapies for cancer.

Nanotechnology has the potential to have a revolutionary impact on cancer diagnosis and therapy. The use of nanotechnology in cancer treatment offers the possibility of destroying cancer tumours with minimal damage to healthy tissue and organs. Most efforts to improve cancer treatment through nanotechnology is at the research or development, stage; a few methods, however, have reached the pre-clinical or clinical trial stage.One treatment involves targeted chemotherapy that delivers a tumor-killing agent called tumour necrosis factor alpha (TNF) to cancer tumors. TNF is attached to a gold nanoparticle along with Thiol-derivatized polyethylene glycol (PEG-THIOL), which hides the TNF bearing nanoparticle from the immune system. This allows the nanoparticle to flow through the blood stream without being attacked. This targeted chemotherapy method to deliver TNF and other chemotherapy drugs to cancer tumours is developed by CytImmune company.

One heat therapy to destroy cancer tumors using nanoparticles is called AuroShell. It was developed by Drs. Naomi Halas and Jennifer West of Rice University in the 1990s.The AuroShell nanoparticles circulate through a patients bloodstream, exiting where the blood vessels are leaking at the site of cancer tumors. Once the nanoparticles accumulate at the tumour the AuroShell nanoparticles are used to concentrate the heat from infrared light to destroy cancer cells with minimal damage to surrounding healthy cells. Nanospectra Biosciences has developed such a treatment using AuroShell that has been approved for a pilot trial with human patients.Targeted heat therapy is being developed to destroy breast cancer tumours also. In this method antibodies that are strongly attracted to proteins produced in one type of breast cancer cell are attached to nanotubes, causing the nanotubes to accumulate at the tumour. Infrared light from a laser is absorbed by the nanotubes and produces heat that incinerates the tumour.

X-ray therapy may be able to destroy cancer tumours using a nanoparticle called NBTXR3. The NBTXR3 nanoparticles, when activated by x-rays, generate electrons that cause the destruction of cancer tumors to which they have attached themselves. This is intended to be used in place of radiation therapy with much less damage to healthy tissue. Nanobiotix has released preclinical results for this technique.

There are efforts underway to develop oral administration of several different drugs using a variety of nanoparticles.The drug is encapsulated in a nanoparticle which helps it pass through the stomach to deliver the drug into the bloodstream. BioDelivery Sciences company has progressed to the clinical testing stage with a drug for treating systemic fungal diseases using a nanoparticle called a cochleate.

An intriguing targeted chemotherapy method uses one nanoparticle to deliver the chemotherapy drug and a separate nanoparticle to guide the drug carrier to the tumor. Another method that targets individual cancer cells inserts gold nanoparticles into the cells, then shines a laser on the nanoparticles. The heat explodes the cancer cells. Using gold nanoparticles to deliver platinum to cancer tumors may reduce the side effects of platinum cancer therapy. The toxicity level of platinum depends upon the molecule it is bonded to (the oxidation state of the platinum). So the researchers chose a platinum containing molecule that has low toxicity to attach to the gold nanoparticles. When the platinum bearing nanoparticle reaches a cancer tumor it encounters an acidic solution which changes the platinum to it's toxic state, in which it can kill cancer cells.

Iron (III) oxide nanoparticles can be used to improve MRI images of cancer tumors. The nanoparticle is coated with a peptide that binds to a cancer tumor. Once the nanoparticles are attached to the tumor, the magnetic property of the iron oxide enhances the images from the Magnetic Resonance Imagining scan. Magnetic nanoparticles that attach to cancer cells in the blood stream may allow the cancer cells to be removed before they establish new tumors.

In another technique, the drug carrying nanoparticle (a liposome) is attached to amino acids that bind to this protein, so the increased level of protein at the tumor speeds up the accumulation of the chemotherapy drug carrying liposome at the tumor. Sensors based upon nanoparticles or nanowires can detect proteins related to specific types of cancer cells in blood samples. This could allow early detection of cancer. T2 Biosystems uses superparamagnetic nanoparticles that bind to the cancer indicating protein and cluster together. These clusters provide a magnetic resonance signal indicating the presence of the cancer related protein. Abraxis BioScience, Incorporation Abraxane is an albumin-bound nanoparticle formulation of the widely used anticancer drug, Paclitaxel (Taxol). It is the only albumin-bound solvent-free taxane nanoparticulate formulation (~130 nm) that takes advantage of albumin to transport Paclitaxel into tumor cells. It was approved by the FDA in 2005 for use in patients with metastatic breast cancer who have failed combination therapy.

Also delivery of short interfering RNAs (siRNA) is interesting because siRNA simply stops the cancer tumor from growing and there is the potential to tailor synthetic siRNA to the version of cancer in an individual patient. Calando Pharmaceuticals, Inc. is a privately held biopharmaceutical company funded by Arrowhead Research Corporation. The company has developed proprietary therapeutic cyclodextrin-containing polymer RNA interference (RNAi) delivery technology and demonstrated the first clear in vivo sequence-specific gene inhibition in tumors. Calando's technology for RNAi is called RONDEL. Specifically, it employs small interfering RNA (siRNA) as the therapeutic RNA. Calando's nanoparticle delivery system is designed for IV injection. According to the company, upon delivery of the RNA-containing nanoparticles, the targeting ligand binds to membrane receptors on the targeted cell surface enabling the nanoparticles to be taken up into the cell via endocytosis.

A new approach to cancer treatment has been through a combination of radiation and photodynamic therapies.The assumption is that supplementing conventional radiation therapy wit photodynamic therapy (PDT) will enable the use of lower doses of radiation. Under this concept, scintillating or persistent luminescence nanoparticles with attached photosensitizers such as pyrophyrins are used as as an in vivo agent for photodynamic therapy. The nanoparticle PDT agents are delivered to the treatment site. Upon exposure to ionozing radiation such as X-rays, the naonparticles emit scintillation or persistent luminescence ,which in turn activates the photosensitizers ; as a consequences, singlet oxygen (O2) is produced. Studies has shown that O2 can be effective in killing of cancer cells. This is the conventional innovation involves the use of in vivo luminescenct nanoparticle so that an external light source is not required to support PDT. Consequently, application of the therapycanbe more localized and the potential of damaged of the healthy cell is reduced. This new modality will provide an efficient low cost approach to PDT while still offering the benefits of augememted radiation therapy at lower doses.

CONCLUSION

The nanotechnology development at present is in its initial stages in India. In an area such as tuberculosis and rural health, clean water, renewable energy food packaging and agricultue fertilizers. There is also a danger in viewing nanotechnology as a solution to developing country challenges. Therefore, it is necessary to develop responsible nanotechnology governance, encourage the development of appropriate products targeted to help meet critical human development needs, and include methods for addressing the safety, appropriateness; accessibility and sustainability of nanotechnology meet the developing countries like India.

Nanotechnology has brought a revolution in manufacturing materials, creating a vast number of new devices, drug delivery systems and monitoring and diagnosing systems. but the implications if this technology are very diverse, impacting consumers, clinicians and the practice of informatics. A major area of concern for health care providers is the ethical use of nanomaterials. Nanotechnology has brought a new era in healthcare but the challenges is to develop it by overcoming various difficulties and implications. New opportunities have provide us with a powerful tool in the field of genomics, proteomics, molecular diagnostics and high throughout screening. Nanoparticles have the properties to become the most versatile materials for developing diagnostics. Advances in nanotechnology will provide a good inside view of our human systems. It has a bright future with the emergence of several promising approaches for delivery of therapeutics agent and imaging using the advantage of nanoscale carriers. Future studies will now be addressing a no. of challenges faced in nanomedicine application. Greater funds are being allocated for clinical and preclinical studies but still are studies are lacking in safety data that includes toxicity studies. Also the cost of nanomedicine should be in acceptable range so that it is successful in clinics. Nanotechnology is being applied at all stages of drug development, from formulations for optimal delivery to diagnostic applications in clinical trials. Actual utilization of nanotechnology novel drug delivery techniques lag behind because of perception that such technologies could delay products due to technical or regulatory reasons. So, oral drug delivery remains a prefered option. Further the cost factor becomes a hinderance in its daily use.

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