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NANOSCIENCE - A REVOLUTION IN TREATING CANCER

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Abstract
The biological application of nano-particles is a rapidly developing area of nanotechnology that raises new possibilities in the diagnosis and treatment of various diseases. Nano-medicine (the application of nanotechnology to health) raises high expectations for millions of patients for better, more efficient and affordable health care and has the potential of delivering promising solutions to many illnesses. The biological application of nano-particles is a rapidly developing area of nanotechnology that raises new promises in the diagnosis and treatment of various cancers. They can also facilitate important advances in detection, diagnosis, and treatment of human cancers and have led to a new discipline of nano-oncology. Nano-particles offer a new method of tumour targeting, already available in clinical practice, which can concomitantly improve the efficacy and decrease the toxicity of existing or novel anticancer agents. This makes them an ideal candidate for precisely targeting cancer cells. Molecular imaging has now considered as a high area in cancer diagnosis. Early assessment of nanotechnologies is also reported by Micro-array Analysis and Photodynamic Therapy implementation, which methodology can be extrapolated to other nanotechnologies in oncology. Current detection methods are restricted with respect to spectrum range, penetration depth, cell targeting, and signal/noise clarity. Focus on the development of quantum dots to improve detection has resulted in the development of dual- functioning beads comprised of quantum dots and iron oxide nanocrystals embedded in silica beads. These particles are able to target specific cells, due to the iron oxide crystals, and have high imaging qualities, due to the quantum dot component. Next- generation contrast agent using carbon nanospheres has been designed to enhance tumor imaging and advance the diagnosis and treatment of cancer by directing nanomolecules to specific biological targets, such as Glioblastoma tumor (one form of aggressive brain cancer). Nanopores (holes) allow DNA to pass through one strand at a time and hence DNA sequencing can be made more efficient. Thus the shape and electrical properties of each base on the strand can be monitored. By combining different sized quantum dots within a single bead, probes can be created that release a distinct spectrum of various colors and intensities of light, serving as a spectral bar code. By using quantum dots for simultaneous imaging of multiple proteins, the minute differences in the sub cellular niche of proteins in both normal and cancer cells can be visualized. If the breakthrough to assembler-based nanotechnology occurs, a huge additional arsenal of medical tools will become available and will include everything from artificial immune systems and cell-herding machines for rapid healing and tissue regeneration to cell-repair machines for cell surgery and gene therapy. The vast knowledge of cancer genomics and proteomics emerging as a result of the Human Genome Project is providing critically important details of how cancer develops, which in turn, creates new opportunities to attack the molecular underpinnings of cancer.

Keywords: Nano-oncology, Glioblastoma tumor, Genomics & proteomics.

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Introduction

Nano-science is well recognized as a revolutionary step in various field of science and a logical field of study for researchers in the coming years as it is, the study of fundamental principles of molecules and structures between one nanometer (one billionth of a meter) and 100 nano meters in size. Nano-materials are structurally and functionally prevalent in the organic, inorganic and biological fields. Their unique size-dependent properties make these materials superior and indispensable in many areas of human activity. The biological application of nano-particles is a rapidly developing area of nanotechnology that raises new possibilities in the diagnosis and treatment of various diseases[1]. Nano-materials are exquisitely sensitive chemical and biological sensors constructed of nano-scale components (e.g., nano-cantilevers, nano-wires, and nano-channels) can recognize genetic and molecular events and have reporting capabilities, thereby offering the potential to detect rare molecular events and have reporting capabilities, there by offering the potential to detect rate molecular signals associated with malignancy. Rapid and sensitive drug screening, one of the limiting factors in combinatorial chemistry for drug discovery and development, is another important application of nano-biosensors[2]. Because of the small dimension, most of the application of nano-biotechnology in molecular diagnostic fall under the broad category of biochips/micro-arrays, but are more correctly termed nano-chips and nano-arrays. As researchers are developing an ever-expanding tool kit of nano- particles for use as drug and imaging agent delivery vehicles, there is a growing need to understand how a given nano-particle's physical and chemical properties affect biological activity and toxicity.

In recent years there has been a rapid increase in nanotechnology applications to medicine in order to prevent and treat diseases in the human body. Nano- medicine (the application of nanotechnology to health) raises high expectations for millions of patients for better, more efficient and affordable health care and has the potential of delivering promising solutions to many illnesses. Nano-medicine, an offshoot of nanotechnology, refers to highly specific medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, nerve chronic pulmonary diseases or coronary artery disease. Nano-crystalline silver products (Acticoat) is effective against most common strains of wound pathogens; can be used as a protective covering over skin grafts; has a broader antibiotic spectrum activity; and is toxic to keratinocytes and fibroblasts[3]. Animal studies suggest a role for nanocrystaline silver in altering wound inflammatory events and facilitation of the early phase of wound inflammatory events and facilitation of the early phase of wound healing. Nano-sized cosmetic or sunscreen ingredients pose no potential risk to human health, whereas their use in sunscreens has large benefits, such as the protection of human skin against skin cancer. It gives the hope of designing new, more efficient drugs with fewer or no side effects.

The development of novel materials and devices operating at the nano-scale range, such as nano-particles, provides new and powerful tools for imaging, diagnosis and therapy. The design of multifunctional nano-particles is suggested as an alternative system for drug and gene delivery, which has great potential for therapy in areas, such as cancer and neuro-pathologies.

New concepts for regenerative medicine give hope to many patients with organ failure or severe injuries. Nano-particle reinforced polymers, orally applicable insulin, artificial joints, made from nano-particulate materials, and low-caloric foods with nano-particulate taste enhancer. Some products are already commercially available. Such as surgical blades and suture needles, contact-enhancing agents for magnetic resonance imaging, bone replacement materials, wound dressings, anti-microbial textiles, chips for in vitro molecular diagnostics, micro-cantilevers and micro-needles. The biological application of nano-particles is a rapidly developing area of nanotechnology that raises new promises in the diagnosis and treatment of various cancers. They can also facilitate important advances in detection, diagnosis, and treatment of human cancers and have led to a new discipline of nano-oncology Nano-particles offer a new method of tumour targeting, already available in clinical practice, which can concomitantly improve the efficacy and decrease the toxicity of existing or novel anticancer agents[4]. This makes them an ideal candidate for precisely targeting cancer cells. Molecular imaging has now considered as a high area in cancer diagnosis. Early assessment of nanotechnologies is also reported by Micro-array Analysis and Photodynamic Therapy implementation, which methodology can be extrapolated to other nanotechnologies in oncology. In the near future, the use of nanotechnology could revolutionize not only oncology, but also the entire discipline of medicine. The development of resistance to variety of chemotherapeutic agents is one of the major challenges in effective cancer treatment. Nanotechnology could enhance the precision of drugs that have one highly specialized mission, like finding and killing cancer cells or tumors.

Cancer[17]

Cancer is a highly complex disease to understand because it entails multiple cellular physiological systems such as cell signaling and apoptosis. Cancer is caused by damage of genes which control the growth and division of cells. Cancerous cell need blood supply to grow. A hormone like molecule causes nearby blood vessel to grow towards the cell to supply the oxygen and other nutrients. Cancer can be cured by rectifying the damaging mechanism of the genes or by stopping the blood supply to the cells or by destroying it. Detection is possible by confirming the growth of the cells. Cytotoxic drugs are effective at killing cancer cells and are the workhorse of most cancer therapy (along with surgery and radiation), but they work by killing neoplastic cells marginally better than they kill other proliferating cells. Nanotechnology could pave the way in solving one of the most challenging problems in medicine, which is elimination of cancer with minimum harm to nounal body tissue. Scientists and researchers hope that nanotechnology can be used to create therapeutic agents that target specific cells and deliver the toxin in a controlled, time- release manner[5]. The aim is to create single agents that detect and treat cancer. The Nano Particles (NP) circulate throughout the body, detect cancer-associated molecular changes, assist with imaging, release a therapeutic agent and then monitor the effectiveness of the intervention.

Conventional cancer detection

Conventional detection of cancer is done by observing the physical growth/changes in the organ by X-rays and/or CT scans and is confirmed by biopsy through cell culture[18]. However the limitation is that it is not very sensitive and detection is possible only after substantial growth of the cancerous cells, by which stage complete cure is almost impossible.

Cancer diagnosis through nanotechnology

Nanotechnology can create a paradigm changing impact on early diagnosis of cancer. Nanotechnology is being used to detect biomarkers, which may help researchers with molecular imaging of malignant lesions and allow doctors to see cells and molecules undetectable through conventional imaging. Photoluminescent NP may aid oncologists to discriminate cancerous and healthy cells[19,].

Current detection methods are restricted with respect to spectrum range, penetration depth, cell targeting, and signal/noise clarity. Focus on the development of quantum dots to improve detection has resulted in the development of dual-functioning beads comprised of quantum dots and iron oxide nanocrystals embedded in silica beads. These particles are able to target specific cells, due to the iron oxide crystals, and have high imaging qualities, due to the quantum dot component. Next-generation contrast agent using carbon nanospheres has been designed to enhance tumor imaging and advance the diagnosis and treatment of cancer by directing nanomolecules to specific biological targets, such as Glioblastoma tumor (one form of aggressive brain cancer). Contrast agent prototype is based on a modification of its trimetasphere carbon nanomaterial known as the hydrochalorone, which significantly enhances relaxivity, a property that provides for better imaging; is extremely stable; is water soluble; and has the potential to be modified to clear from the bloodstream quickly or slowly, depending on the specific application.

The approaches to cancer detection include- *In vitro* (laboratory-based) and *In vivo* diagnostics. Although *in vivo* detection is still a challenge, *in vitro* detection studies have produced impressive breakthroughs.

In vitro **(laboratory-based) diagnostics[20]**

These nanotechnological methods are based on the concept of computer chips similar to the use of nanoarrays. It is possible to detect multiple biomolecular markers at very low concentrations in various biological fluids. There are currently two equally effective nanoarray methods. The first method involves nanowires that are connected to a high-sensitivity electronic ammeter. Each nanowire is designed to be a good binding site for a specific biomolecule. The biofuid under study is passed through a channel where it is allowed to come into direct contact with the wire array. The conductance of the wires changes as the molecules bind, and detection is made possible by measuring the conductance in real time.

The second method involves a nanoarray of Atomic Force Microscope (AFM) cantilevers which are equipped with antibodies specific to selected molecules. The array is submerged in a biofluid where the molecules that are present are allowed to bind to the antibodies. As they bind, they cause the levers to deflect which is measured by a combination of a highly focused laser beam and sensitive photodetectors, with a technique similar to that used in AFM. Both methods can yield data that are highly accurate, even with concentrations in the range of parts per million.

In vivo diagnostics

Some promising *in vivo* techniques are currently under development. One method is to use nanoarrays similar to that described above. However, due to conditions that are much more adverse in a living patient, significantly higher concentrations of the desired molecules are necessary for accurate detection. Another method is to implant biosensors directly into the patient and to have them relay, gathered information to an external data collector.

Conventional cancer treatment

One of the treatment options is surgery, which involves the removal of the cancerous part. However, the limitation is that one looses the organ and the cancer may reappear. The second option is radiation therapy where the cancerous cells are burnt by radiation of specific frequency band and intensity. The third option is chemotherapy where cancerous cells are killed by drugs toxic to cells or by stopping cells from taking nutrients needed to divide or stop the mechanism responsible for cell division.

Drug targeting strategies used in cancer therapy[6-10]

Drug targeting strategies in cancer therapy includes both active and passive targeting. Passive targeting is based on the leaky vasculature of the tumor; the NP surface chemistry promotes phagocytosis by macrophages and then delivery to sites of inflammation or sentinel lymph nodes.

In active targeting, the NP includes a ligand for an extra cellular receptor, like folate and transferrin receptors that is over expressed on the cancer cell surface compared to the non proliferating cells[11,12].

In addition to NP made of gold, iron oxide, titanium oxide, and zinc oxide other nanostructures hold promise for novel nanotechnology-based cancer treatments.

i. **Cantilevers:** The cantilever arrays have been reported to be used for studying the mechanism of action of antibiotics like vancomyin that affect bacterial cell wall. This has been modified accordingly to study the change brought about by the binding to the cantilever array of certain specific proteins associated with different types of cancer[7]. The binding is indicated by the bending of levers, as illustrated in the diagram below, thereby helping in the early diagnosis of cancer associated protein.

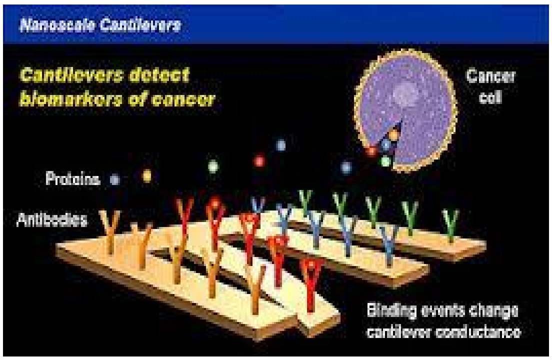

Fig. No. 01: Schematic diagram showing Cantilevers (Source: National Cancer Institute, USA)

ii. **Nanopores:** Nanopores (holes) allow DNA to pass through one strand at a time and hence DNA sequencing can be made more efficient. Thus the shape and electrical properties of each base on the strand can be monitored[8]. As these properties are unique for each of the four bases that make up the genetic code, the passage of DNA through a nanopore can be used to decipher the encoded information, including errors in the code known to be associated with cancer.

iii. **Nanotubes:** Nanotubes are smaller than Nanopores and have been used after coating with polyethylene glycol (PEG) to increase solubility, improve biocompatibility and to help the drug in the body for longer duration, there by reaching the target site.

iv. **Quantum Dots (QD):** QD are non organic semiconductors with electrons confined in 3Dimension.These are tiny crystals that glow when stimulated by ultraviolet light. By combining different sized quantum dots within a single bead, probes can be created that release a distinct spectrum of various colors and intensities of light, serving as a spectral bar code. By using quantum dots for simultaneous imaging of multiple proteins, the minute differences in the sub cellular niche of proteins in both normal and cancer cells can be visualized[9].The advantages of QD are the possibility of attaching hydrophilic ligand making it water soluble and the attachment of upto 15-20 biomolecules (Protein, DNA) to a 6nm QD.

v. **Dendrimer:** Dendrimers are precisely defined, synthetic nano-size tree like macromolecules with branching emanating from a central core (branched nanoparticles). A single dendrimer can carry a molecule that recognizes cancer cells, a therapeutic agent to kill those cells and a molecule that recognizes the signals of cell death[13-16] . Nanotechnology can help diagnose cancer using dendrimers and kill tumor cells without harming normal healthy cells by tumor selective delivery of genes using nanovectors.

Conclusion

Nanotechnology has had a significant impact in many areas of medicine and engineering especially in drug delivery. Today, we have crossed the period of what was called the "bionic convergence"- The convergence of biotechnology with information revolution or the amalgamation of biology with electronics. Today it has expanded to become a synergistic combination of four major "NBIC" provinces of science and technology namely nanotechnology, biotechnology, information technology and cognitive sciences. Everything that is important to health care professionals and patients, diagnostic techniques, prevention, cause and treatment modalities of diseases, medical education, legal and ethical issues will change due to the revolutions currently underway. Nanotechnology and biotechnology are interrelated. Biotechnology (protein engineering in particular) is one of the key components of the technology base of assembler-based nanotechnology; The effects that the "NBIC" convergence may have on the world, society and health care system is very promising yet threatening and likely to go through a comprehensive paradigm change. This change is already underway. The "forecast, prevent, and manage" paradigm that seems likely to emerge and dominate in the coming years integrates many of the developments. If the breakthrough to assembler-based nanotechnology occurs, a huge additional arsenal of medical tools will become available and will include everything from artificial immune systems and cell-herding machines for rapid healing and tissue regeneration to cell-repair machines for cell surgery and gene therapy. The ability to direct events in a controlled fashion at the cellular level is the key that will unlock the indefinite extension of human health and the expansion of human abilities.

Nanotechnology must be allowed to proceed at its own pace and in its own direction. Regulations that address specific identified risks should not delay the advancement of a broad range of products that will surely bring large social and economic benefits. The world in which our children would live will surely be a different one. Continued technological advancement, including on the nanoscale, will not automatically make the world any better or safer, but will increase the resources available to those who want to ensure that it is.

The challenges to this rapidly developing technology include safety and toxicity issues of NP that have to be resolved through legislative and regulatory means. In future many NP will have novel structures that neither our immune systems nor the environment would have ever come into contact with before. The fear is that an engineered particle that is widely used could turn out to be like asbestos or PCBs and have serious long-term health consequences that are recognized only after thousands of people have suffered or large costs have been incurred. In fact, some scientists claim that carbon nanotubes exhibit properties similar to asbestos fibers at the nanoscale. Nanomedicine will help eliminate virtually all common diseases of the 21.st century, all medical pain and suffering, and allow the extension of human capabilities, especially our mental abilities. Nanotechnology will make possible the realization of mankind's noblest aspirations and his darkest nightmares. Effective handling or mishandling of this technology will determine the fate of this planet and destiny of mankind. **Albert Einstein** once said of atomic energy, ***"there is no secret and there is no defense; there is no possibility of control except through the aroused understanding and insistence of the people of the world. ... In this lies our only security and our only hope - we believe that an informed citizenry will act for life and not death".***

"Nanotechnology is going to shape the future of cancer therapy". Nanomedicine, especially as it applies to cancer therapeutics and diagnostics, has a complex developmental pathway, yet the payoffs will be appreciable. The advent of nanotechnology in cancer research has come at an opportune time. The vast knowledge of cancer genomics and proteomics emerging as a result of the Human Genome Project is providing critically important details of how cancer develops, which in turn, creates new opportunities to attack the molecular underpinnings of cancer. However, scientists lack the technological innovations to turn promising molecular discoveries into benefits for cancer patients. It is here that nanotechnology can play a pivotal role, providing the technological power and tools aiding those developing new diagnostics, therapeutics, and preventives to keep pace with today's explosion in knowledge especially in the field of medicine involving cancer therapeutics.

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