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Nanotechnology and Cancer Treatment

Om Pal Singh and R. M. Nehru
Atomic Energy Regulatory Board
Niyamak Bhavan, Anushakti Nagar
Mumbai - 400 049, India

Abstracts : Cancer is caused by damage of genes which control the growth and division of cells. Detection/diagnose/treatment is possible by confirming the growth of the cells and treated by rectifying the damaging mechanism of the genes or by stopping the blood supply to the cells or by destroying it. Conventional detection of the 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. However, the limitation of these methods is that these are not very sensitive and the detection is possible only after substantial growth of the cancerous cells. Nano Particles (NP) being of a few of nano meters size and the cells being of the size of few microns, NP can enter inside the cells and can access the DNA molecules/Genes and therefore, there is a possibility that the defect in the genes can be detected. The conventional treatment options of cancer are surgery, radiation therapy and chemo therapy. However, all the these methods have their own limitations (in surgery one loses the organ and the cancer may appear again, in radiation therapy even the healthy cells get burnt, cancerous cells burning is not uniform and the burnt part may become dead and non functional, in chemotherapy treatment is harmful to healthy cells, approach is gross and rarely successful if the cancer is in advanced stage). In the nanotechnology methods, certain NP can be designed to absorb preferentially certain wave length of radiation and if they enters in the cancerous cells, they will burn them. Nanotechnology can be used to create therapeutic agents that target specific cells and deliver toxin to kill them. The NP will circulate through the body, detect cancer associated molecular changes, assist with imaging, release a therapeutic agent and then monitor the effectiveness of the intervention. In this paper, the details of these possible detection/ diagnose/ treatment methods of nanotechnology are presented. In addition the toxic effects of NP and their regulatory aspects are also discussed.

Key word : Cancer, Nanotechnology, Cantilevers, Nanopores, Nanoshells, Quantum Dotes, Health and Environmental Effects, Nanotechnology and Toxicity, Nanotechnology and Regulatory Aspects.

Introduction

The theme of nanotechnology is the control of material on a scale of 1 to 100 nanometers and fabricates the devices on this scale of length. On nano scale, there is vastly increase in ratio of surface area to volume. Due to this, materials at nano scale show very different properties compared to what they exhibit on a micro scale, enabling unique applications. For instance,

- opaque substances become transparent (copper),
- inert material becomes catalysts (platinum),
- stable material turn combustible (aluminium),
- solids turns into liquids at room temperature (gold),
- insulator become conductors (silicon).

A material such as gold which is inert can become potent chemical catalyst at nano scale. Some of the unique applications of nano materials include,

- titanium dioxide nanoparticles in sunscreen,
- cosmetics and some food products,
- silver nanoparticles in food packing, clothing, disinfectants and house-hold appliances.
- zinc oxide nanoparticles in cosmetics, surface coatings, paints and outdoor furniture varnishes.

However, further applications require actual manipulations or arrangement of nanoscale components await further research.

Cancer : Cancer is caused by damage of genes which control the growth and division of cells. Genes carry the instructions for basic functions 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/diagnose is possible by confirming the growth of the cells.

One nanometer (nm) is one billionth, or 10^{-9} of a meter. For comparison, typical carbon-carbon bond lengths, or the spacing between these atoms in a molecule, are in the range 0.12 - 0.15 nm, and a DNA double-helix has a diameter around 2 nm. On the other hand, the smallest cellular life forms, the bacteria of the genus Mycoplasma, are around 200 nm in length. Many of the cells are of the dimensions of micro meter. This provides the possibility of nanoparticles entering the cells and detect/treat the molecular changes that occur due to cancerous causes, in small percentage of cells. Therefore, the necessary tools must be extremely sensitive. Scientists and researchers hope that nanotechnology can be used to create therapectic agents that target specific cells and deliver the toxin in a controlled, time-release manner. The basic aim is to create single agents that are able to both detect cancer and deliver treatment. The nanoparticles will circulate through the body, detect cancer-associated molecular changes, assist with imaging release a therapeutic agent and then monitor the effectiveness of the intervention.

Cancer Detection

Conventional : Conventional detection of the 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. However the limitation of this method is that it is not very sensitive and the detection is possible only after substantial growth of the cancerous cells. Often the treatment is also not possible once the cancer is in such an advanced stage.

Nano Technology Detection : As mentioned before, nanoparticles (NP) are of a few of nm and the cells are of the size of few microns. So NP can enter inside the cells and can access the DNA molecules/Genes and, there is a possibility that the defect in the genes can be detected. DNA molecules can be detected in their incipient stage. This could be possible in vivo or in vitro. It will be shown latter that NP do show potential of cancer detection in its incipient stage.

Cancer Treatment

Conventional : One of the treatment option is surgery. That is, remove the cancerous part. However, the limitation is that one loses the organ and the cancer may appear again. Further, the surgery is not possible for all types of cases of the cancer. Second option is radiation therapy. In this the cancerous cells are burnt by radiation of specific frequency band and the intensity. The limitation of this method is that even the healthy cells get burnt, cancerous cells burning is not uniform and the burnt part may become dead and non functional. The third option is chemotherapy. That is, cancerous cells are killed by drugs toxic to cells or by stopping cells from taking nutrients needed to divide the cells or stop the mechanism responsible for division of the cell. Normally a combination of drugs is given so that drugs affect all the three aspects of the cancer treatment. The limitation of this approach is that treatment is harmful to healthy cells, approach is gross and rarely successful if the cancer is in advanced stage.

Nanotechnology : Certain nano particles can be designed to absorb preferentially certain wave length of radiation and gets heated. Such a NP if enters in the cancerous cell will burn it if irradiated by suitable wavelength radiation. This is kind of the analogue of radiation therapy. As mentioned before, nanotechnology can be used to create therapeutic agents that target specific cells and deliver toxin to kill them. The NP will circulate through the body, detect cancer associated molecular changes, assist with imaging release a therapeutic agent and then monitor the effectiveness of the intervention.

Tools of Nanotechnology

Some of the tools of nanotechnology having applications in cancer detection and treatment are the following :

(i) Cantilevers : Tiny bars anchored at one end can be engineered to bind to molecules associated with cancer. These molecules may bind to altered DNA proteins that are present in certain types of cancer (Fig.1). This will change the surface tension and cause the cantilevers to bend. By

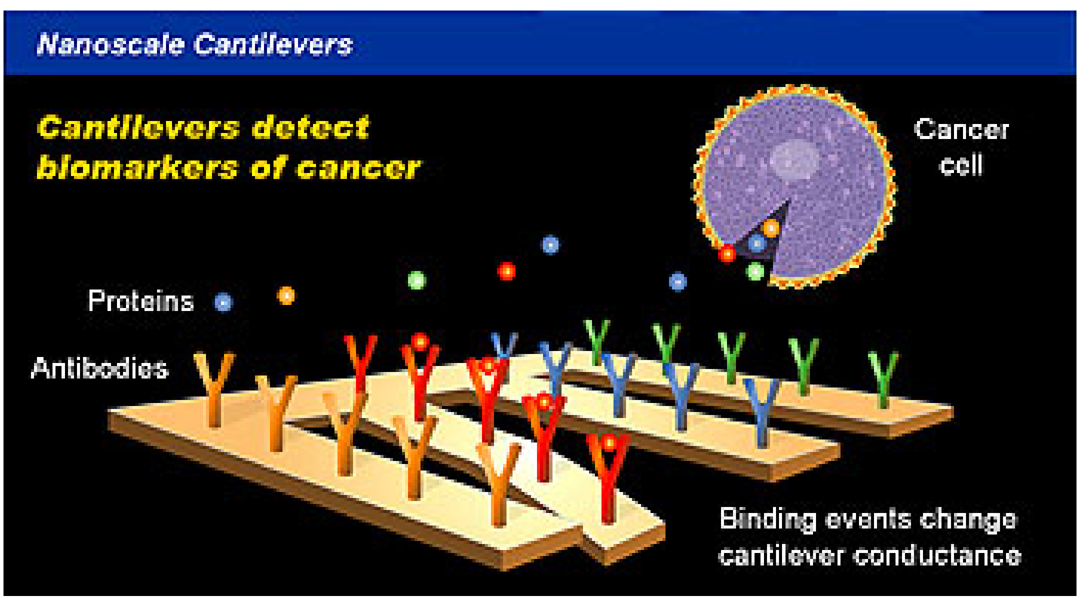

Fig.1 : Schematic diagram showing Cantilevers (Source: National Cancer Institute, USA)

monitoring the bending of cantilevers, it would be possible to tell whether the cancer molecules are present and hence detect early molecular events in the development of cancer.

(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. 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 Nano pores. Nanotubes & carbon rods, about half the diameter of a molecule of DNA, will also help identify DNA changes associated with cancer (Fig. 2). It helps to exactly pin point location of the changes. Mutated regions associated with cancer are first tagged with bulky molecules. Using a nano tube tip, resembling the needle on a record player, the physical shape of the DNA can be traced. A computer translates this information into topographical map. The bulky molecules identify the regions on the map where mutations are present. Since the location of mutations can influence the effects they have on a cell, these techniques will be important in predicting disease.

Fig. 2 : Schematic diagram showing Nanotubes (Source: National Cancer Institute, USA)

(iv) Quantum Dotes (QD) : These are tiny crystals that glow when these are stimulated by ultraviolet light. The latex beads filled with these crystals when stimulated by light, the colors they emit act as dyes that light up the sequence of interest. By combining different sized quantum dotes within a single bead, probes can be created that release a distinct spectrum of various colors and intensities of lights, serving as sort of spectral bar code.

(v) Nanoshells (NS) : These are another recent invention. NS are miniscule beads coated with gold. By manipulating the thickness of the layers making up the NS, the beads can be designed that absorb specific wavelength of light. The most useful nanoshells are those that absorb near-infrared light that can easily penetrate several centimeters in human tissues. Absorption of light by nanoshells creates an intense heat that is lethal to cells. Nanoshells can be linked to antibodies that recognize cancer cells. In laboratory cultures, the heat generated by the light-absorbing nanoshells has successfully killed tumor cells while leaving neighbouring cells intact.

(vi) Dendrimer : A number of nanoparticles that will facilitate drug delivery are being developed. One such molecule that has potential to link treatment with detection and diagnostic is known as dendrimer. These have branching shape which gives them vast amounts of surface area to which therapeutic agents or other biologically active molecules can be attached. 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. It is hoped that dendrimers can be manipulated to release their contents only in the presence of certain trigger molecules associated with cancer. Following drug releases, the dendrimers may also report back whether they are successfully killing their targets.

The technologies mentioned above are in the various stages of discovery and development. Some of the technologies like quantum dots, nano pores and other devices may be available for detection and diagnosis and for clinical use within next ten years.

Challenges of Technology

Today, much of the science on the nanoscale is basic research, designed to reach a better understanding of how matter behaves on this small scale. The surface area of nano-materials being large, the phenomena like friction and sticking are more important then they are in large systems. These factors will affect the use of nanomaterials both inside and outside the body. Nanostructures being so small; the body may clear them too rapidly to be effective in detection or imaging. Larger nanoparticles may accumulate in vital organs, creating a toxicity problem.

Some Important Developments

- Carbon Nano Tubes (CNT) have a novel and useful properties and their manufacturing will increase. The available knowledge indicates that CNT may have unusual toxicity properties.
- Chitosom nanoparticles with enccapslated quantum dots have been synthesized and used to deliver of HERZ SiRNA. Using such a construct, the delivery and transfection of the SiRNA can be monitored by the presence of fluorescent QDs in the Chitosan NPs. Targeted delivery of HERZ SiRNA to HER2 – over expressing SKBR3 breast cancer cells has been shown to be specific with chetosen/QD NP surface labled with HERz antibody targeting the HERz receptors on SkBR3 cells. Gene silencing effects of the conjugated SiRNA has also been established using the luciferase and HER2ELISA assays. These self tracking SiRNA delivery NP will aid in the monitoring of future gene silencing studies in vivo.
- By the use of quantum dots which are powerful tools used for simultaneous imaging of multiple proteins, the minute differences in the subcellular niche of these two proteins in normal and cancer cells has been visualized.

Health and Environmental Effects

There is a growing body of scientific evidence which demonstrates the potential for some nanomaterials to be toxic to humans or the environment. The smaller a particle, the greater its surface area to volume ratio and the higher its chemical reactivity and biological activity. The greater chemical reactivity of nanomaterials results in increased production of reactive oxygen species (ROS), including free radicals. ROS production has been found in a diverse range of nanomaterials including carbon fullerenes, carbon nanotubes and nanoparticle metal oxides. ROS and free radical production is one of the primary mechanisms of nanoparticle toxicity; it may result in oxidative stress, inflammation, and consequent damage to proteins, membranes and DNA. The extremely small size of nanomaterials also means that they are much more readily taken up by the human body than larger sized particles. Nanomaterials are able to cross biological membranes and access cells, tissues and organs that larger-sized particles normally cannot. Nanomaterials can gain access to the blood stream following inhalation or ingestion. At least some nanomaterials can penetrate the skin; even larger microparticles may penetrate skin when it is flexed. Broken skin is an ineffective particle barrier, suggesting that acne, eczema, shaving wounds or severe sunburn may enable skin uptake of nanomaterials more readily. Once in the blood stream, nanomaterials can be transported around the body and are taken up by organs and tissues including the brain, heart, liver, kidneys, spleen, bone marrow and nervous system. Studies demonstrate the potential for nanomaterials to cause DNA mutation and induce major structural damage to mitochondria, even resulting in cell death.

Size is therefore a key factor in determining the potential toxicity of a particle. However it is not the only important factor. Other properties of nanomaterials that influence toxicity include: chemical composition, shape, surface structure, surface charge, aggregation and solubility, and the presence or absence of functional groups of other chemicals. The large number of variables influencing toxicity means that it is difficult to generalise about health risks associated with exposure to nanomaterials – each new nanomaterial must be assessed individually and all material properties must be taken into account.

Regulatory Aspects

In a report of seminar in 2004, Nanoscience and naotechnologies: Opportunities and Uncertaintities, the United Kingdom's Royal Society recommended that nanomaterials be regulated as new chemicals. Research laboratories and factories should treat nanomaterials "as if they were hazardous". That release of nanomaterials into the environment be avoided as far as possible, and that products containing nanomaterials be subject to new safety testing requirements prior to their commercial release. Yet regulations world-wide still fail to distinguish between materials in their nanoscale and bulk form.This means that nanomaterials remain effectively unregulated. There is no regulatory requirement for nanomaterials to face new health and safety testing or environmental impact assessment prior to their use in commercial products, if these materials have already been approved in bulk form.

Summary

- Nanotechnology has large potential in detection and treatment of cancer in its incipient stage.
- The potential arises due to the ability of NP entering inside the cells and access to the chromosomes/FNA molecules.
- Certain nano structures like nanocantilevers, nanopores, nanotubes, nanoshells and quantum dotes are prospective structures that would help in detecting and treatment of cancers.
- Dendrimers are to serve detection, treatment and signaling that the cells are killed.
- Still there are many challenges that are to be met before use of NT becomes a reality.
- Toxicity of the NP is an issue that is to be resolved through legislative and regulatory means.

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