

## NANOMEDICINE AND CANCER

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The integration of nanotechnology with biology and medicine has given birth to a new field of science called "Nanomedicine". The ultimate goal of nanomedicine is to develop well engineered nanotools for the prevention, diagnosis and treatment of many diseases. The extraordinary growth in nanotechnology has brought us closer to be able to vividly visualize molecular and cellular structures. This technology has ability to differentiate between normal and cancerous cells and to detect as well as quantify minute amounts of signature molecules produced by the cells. Nanomedicines have wide range of applications to treat the cancer. With the use of nanomedicine, targeted drug delivery has been achieved.

**Keywords:** Nanomedicine, cancer, nanoparticles.

**INTRODUCTION**

It is now widely accepted that cancer has a genetic origin. Cancer may be the result of DNA damage due to carcinogens or spontaneously during DNA replication. Inability to correct the DNA damage due to mutated DNA repair genes or absence of functional cell cycle checkpoint genes may give the cell a growth advantage.<sup>1</sup> It has been seen that normal human development and physiologic homeostasis depends on the co-ordinate interactions of the products of many genes working together in the body. Mutations of genes result in the failure to synthesize a particular protein or to the synthesis of a defective protein. These results in abnormalities in genes cause various genetic disorders.

Recent scientific advances have provided a map of the human genome along with a better understanding of the processes that transform healthy cells into diseased cells. This has led to the emergence of a new class of drugs called targeted therapies.<sup>2</sup> The goal of targeted therapy for cancer treatment is to selectively treat cancer cells without harming healthy tissue by acting on pathways that are unique to cancer cells.<sup>3</sup> They achieve their specificity by targeting differences in cancer cells on a molecular level. It also referred to as molecular-targeted drugs or molecularly-targeted therapies.<sup>4</sup> Cancer is a genetic disease involving multiple and sequential genetic changes that affect oncogenes, tumor suppressor genes and modifier genes. In addition, there is interplay of various cells in the body which are important in immune surveillance, responsible for removing abnormal cells from the body. The three conventional modalities of treatment of cancer – surgery, radiotherapy and chemotherapy are often unsuccessful in treating cancer,<sup>5-7</sup> but at the same time having certain limitations. Nanotechnology is thus a new modality to treat cancer. Many of the cells are of dimensions of micrometer. These

provide the possibility of nanoparticles entering the cells and detect/treat the molecular changes that occur due to cancerous cells. Scientists and researchers hope that nanotechnology can be used to create therapeutic agents that target the 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. Approaches to treat cancer with use of nanomedicines are as follow.

**Cantilevers**

Nanoscale cantilevers - microscopic, flexible beams resembling a row of diving boards - are built using semiconductor lithographic techniques. Nanoscale cantilevers are built using semiconductor lithographic techniques.<sup>8</sup> Tiny bars anchored at one end can be engineered to bind two molecules associated with cancer. (Fig 1) These molecules may bind to altered DNA proteins that are present in certain type of cancer. This will change the surface tension and cause the cantilevers to bend. By 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. The nanometer-sized cantilevers are extremely sensitive and can detect single molecules of DNA or protein. Thus providing fast and sensitive detection methods for cancer related molecules.<sup>9</sup>

**Nanopores**

A nanopore is a small hole in an electrically insulating membrane that can be used as a single-molecule detector.<sup>10</sup> It may be considered a coulter counter for much smaller particles. It can be a biological protein channel in a high electrical resistance lipid bilayer, a pore in a solid-state membrane or a protein channel set in a



synthetic membrane. The detection principle is based on monitoring the ionic current passing through the nanopore as a voltage is applied across the membrane. Nanopores 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 four bases that make up the genetic code, the passage of DNA through a nanopore can be used to decipher the encoded information, including the errors in the code known to be associated with cancer.<sup>11</sup>

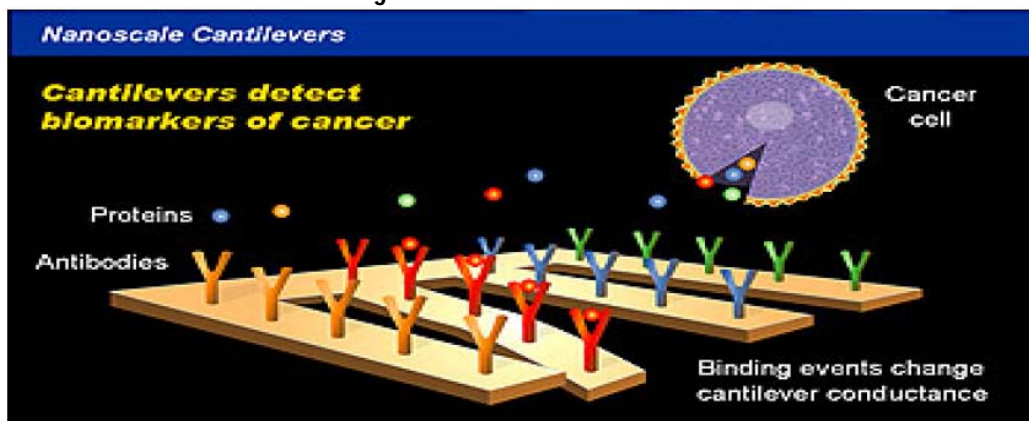
**Nanotubes**

Nanotubes are smaller than nanopores. Nanotubes and carbon rods, about half the diameter of a molecule of DNA, will also help identify DNA changes associated with cancer. It helps to exactly pinpoint location of the changes. Mutated regions associated with cancer are first tagged with bulky molecules.<sup>12</sup> Fig 2. Using a nanotubes 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.<sup>13,14</sup>

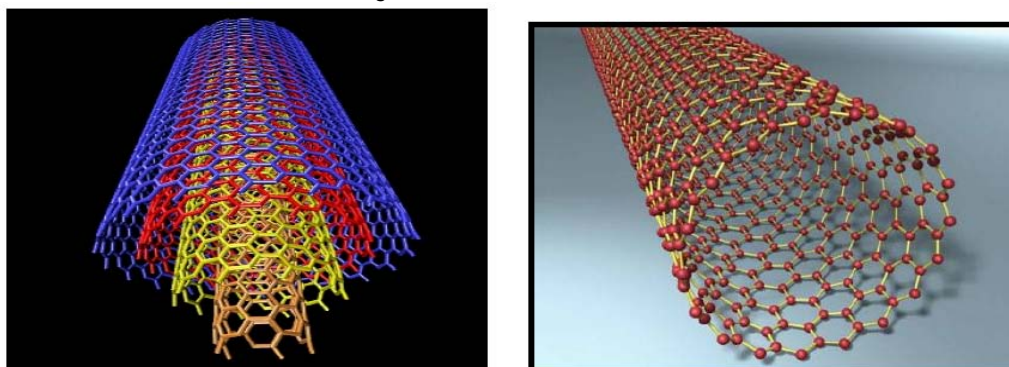
**Table 1: Cancer Treatments using Nanotechnology**

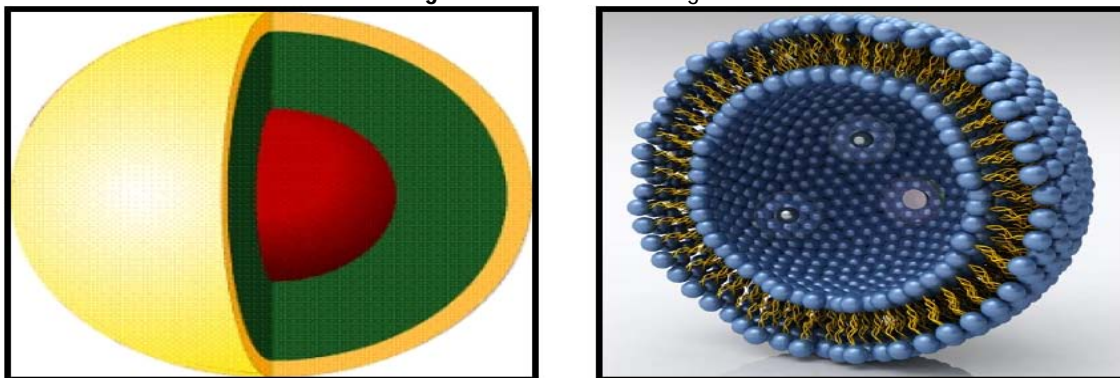
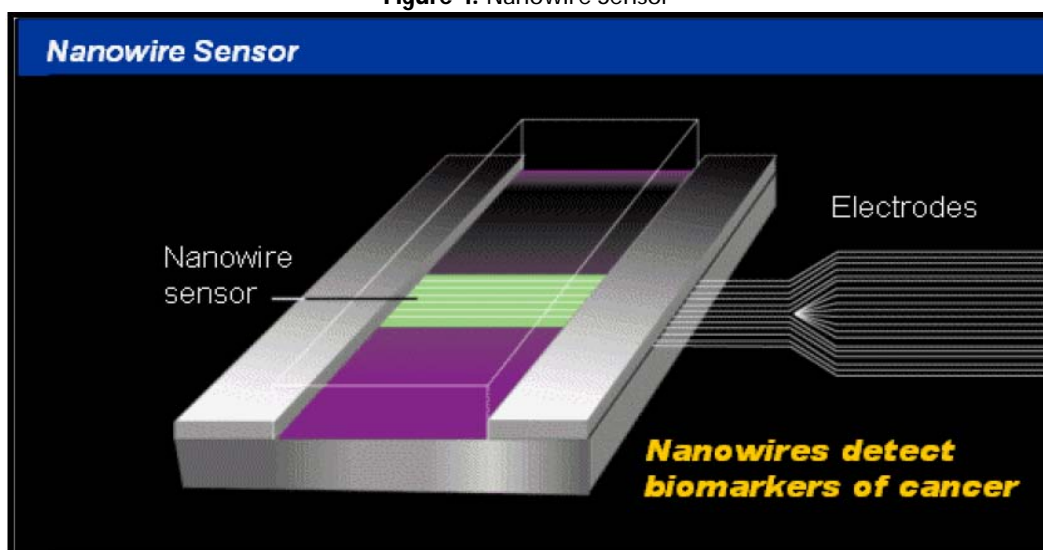
Company	Product
CytImmune	Gold nanoparticles for targeted delivery of drugs to tumors
NanoBioMagnetics	Magnetically responsive nanoparticles for targeted drug delivery and other applications
Abraxis BioScience	Nanoparticles composed of a protein called albumin for targeted delivery of drugs to tumors
Epeius Biotechnologies	Nanoparticles for targeted delivery of drugs to tumors
Nanobiotix	Nanoparticles that target tumor cells, when irradiated by xrays the nanoparticles generate electrons which cause localized destruction of the tumor cells.
Nanospectra	AuroShell particles (nanoshells) for thermal destruction of cancer tissue
Nanosphere	Diagnostic testing using gold nanoparticles to detect low levels of proteins indicating particular diseases
Oxonica	Diagnostic testing using gold nanoparticles (biomarkers)
MagForce	Iron oxide nanoparticles used in heat treatment of solid tumors

**Figure 1: Nanoscale Cantilevers**



**Figure 2: Carbon Nano tubes**



**Figure 3: Nanoshells with gold****Figure 4: Nanowire Sensor**

### Quantum Dots (QD)

A quantum dot is a semiconductor whose excitons are confined in all three spatial dimensions. Consequently, such materials have electronic properties intermediate between those of bulk semiconductors and those of discrete molecules.<sup>15,16</sup> 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 dots within a single bead, probes can be treated that release a distinct spectrum of various colors and intensities of lights, serving as sort of spectral barcode.<sup>17</sup>

### Nanoshells (NS)

These are another recent in invention. NS are miniscule beads coated with gold. (Fig 3)<sup>18</sup> By manipulating the thickness of the layers making up the Nanoshells, the beads can be designed that absorb specific wavelength of light. Nanoshell-assisted photo-thermal therapy (NAPT) is a simple, non invasive procedure for selective photo-thermal tumor removal. They make use of nanoshells those absorb light near infrared that can easily penetrate several centimeters in human tissues. Absorption of light

by nanoshells creates an intense heat that is lethal to cancerous cells. Nanoshells can be linked to antibodies that organize cancer cells. In laboratory cultures, the heat generated by the light absorbing Nanoshells has successfully killer tumor cells while leaving neighbouring cells intact.<sup>19</sup>

### Dendrimers

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.<sup>20</sup> These have branching shape which gives them vast amounts of surface area to which therapeutic agents or other biologically active molecule can be attached. A single dendrimer can carry a molecule that recognize cancer cells, a therapeutic agent to kill those cells and a molecule that recognize the signals of cell death. It is hoped that dendrimers can be manipulated to release their contents only in presence of certain trigger molecules associated with cancer. Following drug release, the dendrimers may also report back whether they are successfully killing their targets.<sup>20</sup>



### Fullerene- based derivatives

Fullerene- based derivatives are recently proposed in nano pharmaceutical formulations and have found various applications in cancer therapy. They are crystalline particles in form of carbon atoms. The most abundant form of Fullerene is Buckminster fullerenes (C<sub>60</sub>) with 60 carbon atoms and arranged in a spherical structure with truncated icosahedron shape, resembles that of a soccer ball (bucky ball), which contains 20 hexagons and 12 pentagons. Other fullerenes are C<sub>70</sub>, C<sub>76</sub>, C<sub>78</sub>, C<sub>84</sub>, C<sub>86</sub>, C<sub>540</sub> etc. Fullerenes cages are about 0.7 to 1.5 nm in diameter and the cage structure of fullerene is ideal for attaching anticancer agents or even radiological agents to increase treatment efficacy for killing as well as diagnosis of cancerous cells. Their good stability makes them unique candidates for safely delivering highly toxic substances to tumors. Both empty and metallofullerenes have shown their potential application in diagnosis. Water solubilized forms of metallofullerenes like M<sub>2</sub>C<sub>82</sub>(OH)<sub>30</sub> are being used as magnetic resonance imaging (MRI) contrast agents, X-Ray contrast agents and radio pharmaceuticals. Another metallofullerenes derivative, 166Ho<sup>3+</sup>2C<sub>82</sub>(OH)<sub>30</sub> has been extensively studied as radioactive tracer for imaging and killing of cancerous cells. The advantage of fullerene based therapies over other targeted therapies is likely to be fullerene potential to carry multiple drug payload – loads such as taxol and other chemotherapeutic agents.<sup>21</sup>

### Solid Lipid Nanoparticles

Solid Lipid Nanoparticles hold significant promise in cancer treatment. They are particles of submicron size (50 to 1000 nm) made from lipids that remain in a solid state at room as well as body temperature. Since early 1990's a number of solid lipid nanoparticles based systems for the delivery of anticancer agents have been successfully formulated and tested. Various anticancer agents like doxorubicin, daunorubicin, idarubicin, paclitaxel, camptothecins, etoposide etc have been encapsulated using this nanotechnological approach. Several obstacles are frequently encountered with anticancer drugs, such as a high incidence of drug resistant tumor cells can be partially overcome by delivering them using solid lipid nanoparticles.<sup>22</sup>

### Magnetic nanoparticles

Magnetic nanoparticles are able to target cancerous cells and have potential use in cancer therapeutics. The magnetic effect of magnetic nanoparticles is due to super paramagnetic iron oxides typically Fe<sub>2</sub>O<sub>3</sub> and Fe<sub>3</sub>O<sub>4</sub> which do not retain their magnetic property when removed from the magnetic field. Their paramagnetic characteristics have made them good candidate for the destruction of tumors in vivo through hypothermia. Polymer coating on the surface of magnetic nanoparticles prevent their cytotoxicity and allows them to move freely in the organism without any reaction or adhesion.

### Nanowires

Nanowires as structures that have a thickness or diameter constrained to tens of nanometers or less and an unconstrained length. They are glowing silica wires in nanoscale, wrapped around single strand of human hairs. They are about five times smaller than virus and several times stronger than spider silk. Nanowires based arrays have significant impact for early diagnosis of cancer and cancer treatment. The nanowire based delivery enables simultaneous detection of multiple analytes such as cancer biomarkers in a single chip, as well as fundamental kinetic studies for biomolecular reactions.<sup>23</sup> Protein coated nanowires have potential applications in cancer imaging like prostate cancer, breast cancer and ovarian malignancies. (Fig 4)

### CONCLUSION

Nanomedicine is a powerful and revolutionary development that is likely to have significant impact on society, the economy and life in general. As quoted from Langdon Winner's Technologies as forms of life, technologies are not merely aids to human activity, but also powerful forces acting to reshape that activity and meaning. A very important area of nanomedicine would be to not only pay attention to the making of the physical instruments and processes, but also to the production of psychological, social and political conditions as a part of any significant technological change.

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