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Nanotech - Big Promise from a Tiny World

Raj Kumar Maloth* *CSE, SLCIET, Hyd-501512* ***India***
L. Kiran Kumar Reddy *Associate Professor, CSE, SLCIET, Hyd-501512* ***India***
Mohammad Zainuddin *CSE, CMRIT, Hyd-501401* ***India***

Abstract— Nanoscale and Nanotechnology are not new to the world because chemists have been making polymers for decades. A polymer is a large macromolecule made up of nanoscale subunits. This paper analyses the brief impact of Nanotechnology in Medicine field which is given a unique name called "Nanomedicine". Nanomedicine can play a vital role in diagnosis, cancer therapy etc. which may help in fighting cancer. Hence, this paper analyses the vast effect of Nano Science in the field of medicine.

Keywords— nanoscale, passive targeting, active targeting, cantilevers, nanopores, quantum dots

I. INTRODUCTION

Richard P. Feynman, the Father of Nanotechnology [1] [2], mentioned in his famous lecture "There is plenty of room at the bottom" the idea of swallowing a surgeon. This "nano-surgeon" would recognize infected cells and remove those brick-by-brick, rather than demolishing an entire wall. It would leave neighbouring normal cells intact, thus neither the toxicities of "chemo" drugs nor surgically produced deformities would result.

Nanomedicine is a new branch of science that tries to find nanotechnology solutions for medical challenges. A "nano" is one thousand millionth of a meter. Imagine the width of a human hair—it is 80,000 nanometre wide, or a human RBC that is 7000 nm in width, while a water molecule is 0.3 nm across. Thus, application of nanoscale materials (usually <100 nm) for diagnosis, treatment of diseases and for repair, control and monitoring of cells and tissues is what nano-medicine is all about. The emerging field of Nanomedicine [3] involves scientists from many different disciplines like physicists, chemists, biologists and metallurgists besides physicians, surgeons and oncologists.

II. IS NANOTECHNOLGY NEW?

Nanoscale and nanotechnology are not new. Chemists have been making polymers for decades. A polymer is a large macromolecule made up of nanoscale subunits. Take a simple example of silk that consists of two proteins, one very large and one much smaller. They combine to form nanoscale morphology of domains composed of ordered (crystalline) and disordered (amorphous) polymers. The ordered domains can be attributed to oriented beta-sheet crystals with strong amide-amide hydrogen bonding, while the disordered domains assume a wide range of structures with varying degrees of hydrogen bonding. The structural simplicity but functional complexity of the nanoscale interactions gives silk its desirable and highly tuneable properties. Michael Faraday created gold nanoparticles way back in 1857. We all have been using computers. Nanotechnology has been used to create tiny features in computer chips for the past two decades.

III. WHY NANOTECHNOLGY IS DIFFERENT?

You have heard about miniature Ganesha carved out on a grain of rice, or miniature Geeta written on a leaf. This is miniaturization, not nanotechnology. Miniatures are very small, but are still governed by the conventional laws of physics and chemistry. The laws that apply to large-scale (macro) particles do not necessarily apply to nano-sized particles. This is primarily because of large surface area to volume ratio of nanoparticles [4]. Due to the significant role of surface atoms, the laws of physics, chemistry, metallurgy and biology and related phenomena undergo modifications, some more dramatically than others. Some properties that undergo changes are Surface Energy, Adsorption, Desorption, Diffusion, Physical Density, Crystal Structure, Elasticity, Electrostatic charge and discharge effects due to modification of the Coulomb law and polarization effects for finite size charged matter, ferromagnetism and superconductivity. Also, novel science associated with nanometer has resulted in the discovery of many new phenomena of considerable scientific and technological interest, some of which are Giant Magneto resistance, Super hardness, Super elasticity and Quantum Confinement etc.

IV. NANOTECHNOLOGY IN MEDICINE

The size of the nanoparticles has a lot to do with successful employment in nanomedicine. If they are too small, they will be rapidly cleared by the reticuloendothelial system (the scavenger system) of the body. However, if they are too large, they may accumulate in vital organs of the body and cause toxicity.

Of course, use of nanotechnology in medicine has several advantages:

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- No physical alteration of cells/tissues that are used for diagnosis. They can be preserved in their active state and can be re-used for further tests.
- One nanoparticle can serve multiple functions by placing different tools together on the same small device. This is possible because of large surface area to volume ratio of nanoparticles.
- Targeted Drug Delivery. Over 65 billion dollars is wasted every year because of poor bioavailability in US alone. Bioavailability refers to the presence of drug molecules where they are needed in the body and where they will do the most good. Targeted drug delivery results in maximizing bioavailability to cancerous tissues in the body as well as prolonged over a period of time. Most patients are afraid to agree to chemotherapy [5] because they have heard about serious toxicities (alopecia or hair loss, protracted vomiting, diarrhoea, neutropenia leading to fevers, infection and even death).

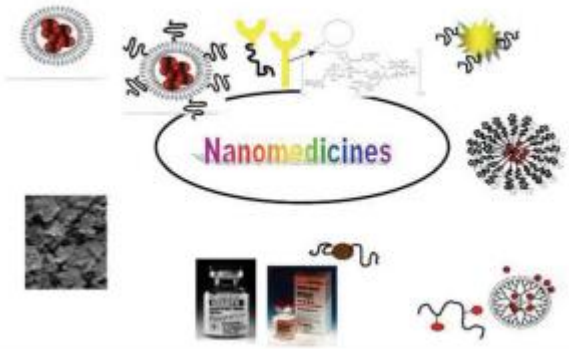

Figure 1 Many Nano medicines are already in routine clinical use

V. APPLICATIONS IN NANOMEDICINE

A. Diagnosis

Nanomedicine could play a major role in diagnosis. For instance, Prof V. Ramagopal Rao of Electrical Engineering, IIT-Mumbai has developed nano-cantilevers that can identify myoglobin – a protein found in cases of myocardial infarction or heart attack. This has a reduced cost – in the range of Rs 500-600 as against Rs 25,000 for the prevalent method of detection of heart attacks.

Similarly, currently detection and diagnosis of cancer usually depend on changes in cells and tissues that are detected by a doctor's physical touch or imaging modalities. If it were possible to detect the earliest molecular changes, long before a physical examination or imaging technology can pick them up, cancers could be prevented before they advanced to a fatal stage. For this, tools need to be extremely sensitive to be able to detect a change even in a small number of cells. Tapan Jain and colleagues from Cleveland, USA have used (multifunctional) magnetic nanoparticles made up of iron oxide coated with oleic acid. These magnetic nanoparticles extravagate (leak out of blood vessels) into tumour tissues and can be used for better imaging (MRI) of tumours. A quick and sensitive procedure for detection of bacterial infections has also been developed. A biosensor [6] using gold nanodevice, with a linker arm attached to specific Escherichia coli antibodies can detect E. coli at cellular level.

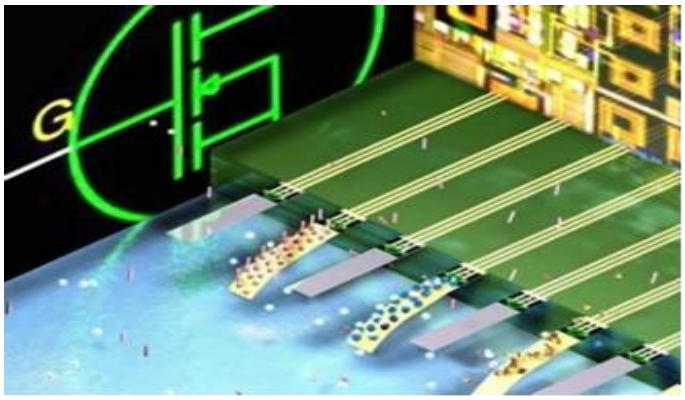

Figure 2 Nano Cantilevers

B. Treatment

Current "chemo" is a blunderbuss therapy, as it kills not only cancer cells but also other rapidly dividing cells (for example, blood WBCs, skin and hair cells, and bone marrow cells) causing significant toxicity to patients. If somehow

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we could deliver "chemo" exclusively and directly to cancer cells, or even in the vicinity of a tumour, the side effects could be minimized.

This delivery can be done by two approaches:

Passive Targeting: Most tumours have leaky blood vessels and dysfunctional lymphatic drainage, which has been exploited for accumulation of nanocarriers in tumour tissue and for releasing of "chemo" in the neighbourhood of cancer cells.

Active Targeting: Cancer cells have over-expressed antigens or receptors. If we can take a nanocarrier having "chemo" and conjugate it with molecules that bind to antigens or receptors on cancer cell surface, it is called 'Active Targeting'. Paclitaxel (a taxane or antimicrotubule agent; a promising "chemo" drug for several types of cancers) has been loaded onto gelatin nanoparticles for intra-vesicle (into urinary bladder) delivery.

It was found to increase the penetration of Paclitaxel into bladder (cancer) tissue. Another interesting approach is thermal therapy of cancers by nanocarriers. Magnetic liposomes generate heat in an alternating magnetic field. The tumour temperature can increase to 45ºC, whereas the body temperature remains around 38ºC. Significant tumour regression is observed in hyperthermia group. For injectable drugs, nanotechnology is already generating new dosage forms that are easier to administer, more pleasant for the patient to receive and confer a competitive advantage in the marketplace.

Researchers at the University of Texas at Austin have described a means of using nanospheres for oral drug delivery. These nanosphere carriers are derived from hydrogels [7], which are highly stable organic compounds that swell when their environment becomes more acidic. They have been successfully formulated into controlled-release tablets and capsules, which release active compounds when the hydrogel body swells.

Nanoparticles of a platinum derivative 'Carboplatin' [8] have been used in India to treat retinoblastoma, a highly malignant tumour of the eye by collaboration between Prof Jayesh Bellare from IITBombay's Chemical Engineering Department and doctors from Tata Memorial Hospital, Mumbai and Apollo Hospital in Hyderabad. Dr Debraj Shome reported in February 2010 that he was planning multi-center clinical trials on nanoparticles loaded with carboplatin in treatment of retinoblastoma. Yet another method to attack cancers is photodynamic therapy in which a particle is placed within the body and is illuminated with light from the outside. The light gets absorbed by the particle and if the particle is a metal, energy from the light heats the particle and surrounding tissue. Light may also be used to produce high-energy oxygen molecules that chemically react with and destroy most organic molecules that are next to them (like tumours). This therapy is appealing for many reasons. It does not leave a toxic trail of reactive molecules throughout the body (chemotherapy) because it is directed only where the light is shone and the particles exist. Photodynamic therapy has potential for non-invasive procedure for treating cancers as well as some other diseases.

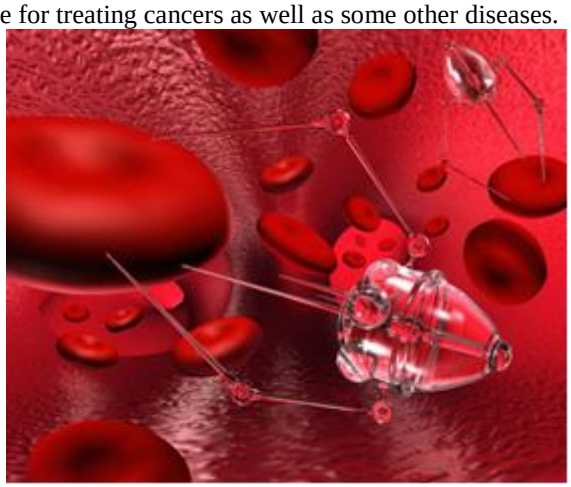

Figure 3 Nano-scale robot killing cancer cells

C. Nano devices

Nanodevices that have already been proven are:

1) Cantilevers: These are tiny levers anchored at one end. They can be designed such that they bind to molecules that represent a deviation from normality, such as altered DNA sequences or proteins present in infected cell. When these molecules bind to the cantilevers [9], surface tension changes cause the cantilever to bend. By monitoring this bending, scientists can identify the type of molecule that has caused the bending. This may help in identifying infected cells even if they are present in very low concentrations.

2) Nanopores: These are tiny holes that allow the DNA molecule to pass through one strand at a time. By monitoring the shape and electrical properties of each base or letter on the strand of DNA, scientists can decipher the encoded information on DNA. This is possible because shape and electrical properties are unique for each of the four bases that make up the genetic code. Errors in the genetic code associated with a particular disease can also be located.

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3) Nanotubes: Carbon rods [10], about half the diameter of a molecule of DNA, can detect the presence of altered genes and also pinpoint the exact location of those changes (mutations).

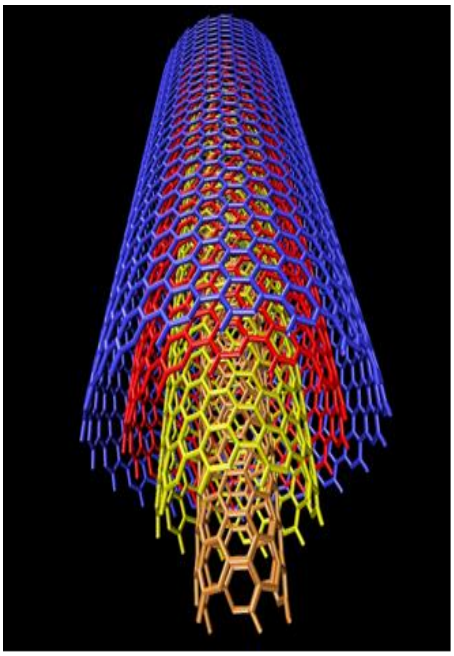

Figure 4 Multi-walled Nanotube

4) Quantum Dots: Nanoparticles of cadmium selenide (quantum dots) glow when exposed to ultraviolet light. The wavelength or the colour of the light depends on the size of the dot. When injected, they seep into cancer tumours. The surgeon can see the glowing tumour, and use it as a guide for more precise cutting of tumours.

Quantum dots [11] demonstrate the nanoscale property that colour is size dependent. By combining different sized quantum dots within a single bead, scientists can create probes that release distinct colours and intensities of light. When the crystals are hit by UV light, each latex bead emits light that serves as a sort of spectral bar code, identifying a particular region of DNA, which is associated with a particular type of cancer. We know that most cancers arise from multiple mutations within DNA. Thus several quantum dots can be designed to show several cancer-associated regions of DNA simultaneously. This can potentially eliminate the need for surgical biopsy (removal of tissue for histopathological examination under microscope).

Figure 5 Nanosys Quantum dot remote

5) Nano Shells: These are miniscule beads coated with gold that absorb specific wavelengths of light. These shells then get heated up and kill the surrounding cell. By engineering the nanoshells to selectively link with the antibodies associated with a diseased cell, we can ensure that the nanoshells [12] seep only into the tumour and destroy it, leaving the neighbouring normal cells intact. This has already been done using near-infrared light on animal cancer cell line cultures.

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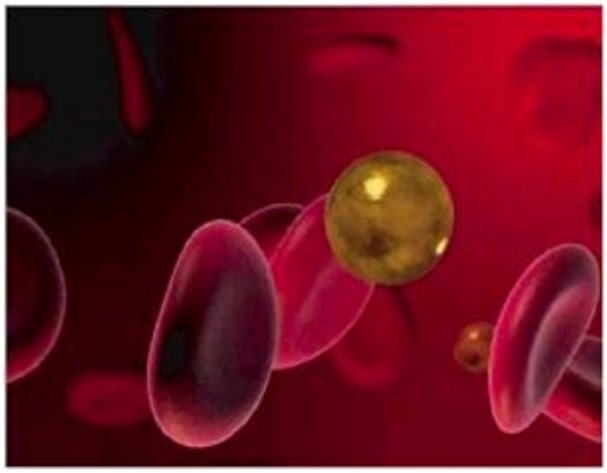

Figure 6 Nanoshell

6) Dendrimers: This molecule has over a hundred hooks on it that provide a large surface area and hence allow it to attach to cells in the body for a variety of purposes like identification, diagnosis or therapy. For example, scientists have attached folic acid to a few of the hooks (folic-acid being a vitamin is received by cells in the body). Cancer cells have more vitamin receptors than normal cells, so these vitamin-laden dendrimers [13] were absorbed by the cancer cell. To the rest of the hooks on the dendrimer, anti-cancer drugs were placed and these were absorbed with the dendrimer into the cancer cell, thereby delivering the cancer drug to the cancer cell and nowhere else.

7) BioMEMS: Biological Micro-Electro-Mechanical Systems are tiny working machines that usually consist of several microsensors coupled with a microprocessor, the processing unit of the device. BioMEMS [14] can be used in the detection of DNA, viruses, proteins and other biologically derived molecules. Nanomedicine has already crossed the threshold of laboratory animals and entered the portals of clinical practice. The coming decade will establish the existing nanotechnology devices and discover new ones, which may take us from blunderbuss treatment to target-specific and efficient therapy of incurable cancers and life-threatening multi drug-resistant bacterial infections.

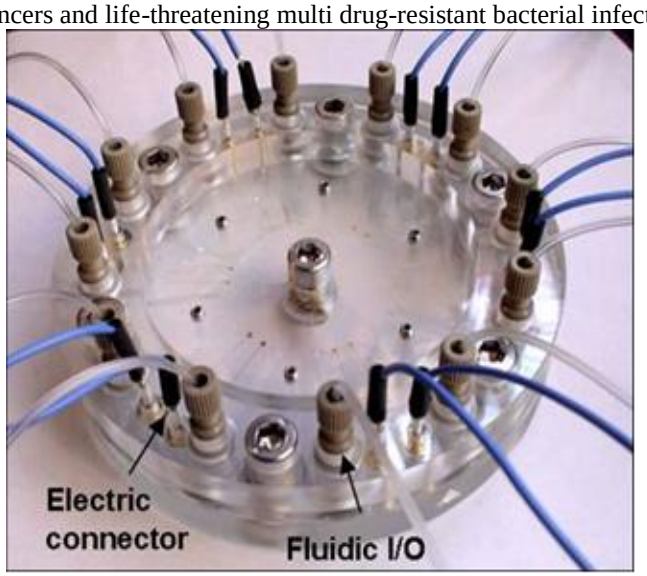

Figure 7 BioMEMS Chip

VI. CONCLUSIONS

Nanoscience has already helped Cancer Researchers to find new ways of fighting the cancer and it has contributed much more in other fields as well. Hence, the main purpose of this paper is to encourage young researchers of Nanomedicine to fight cancer and other deadly diseases using this tiny yet big world of nanotechnology.

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AUTHORS BIBLIOGRAPHY

Raj Kumar Maloth received his B.Tech degree in Computer Science from SVIT, Secunderabad in 2010 and M.Tech in Computer Science from SLCIET, Hayathnagar in 2012. His areas of interest are Distributed computing and Robotics.

L. Kiran Kumar Reddy received his M.Tech degree from BIHER, Chennai in 2005. He has a teaching experience of more than 7 years and has published papers in international journals as well as conferences. He is pursuing PhD and currently working as Associate Professor of Department of Computer Science and Engineering in SLCIET, Hyderabad.

Mohammad Zainuddin received his B.Tech degree in Computer Science from SVIT, Secunderabad in 2010 and M.Tech degree in Computer Science from CMRIT, Kandlakoya in2012. He has published more than 5 papers in International Journals. His areas of Interests are Nanotechnology and Artificial Intelligence.

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