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Use of Nanotechnology in Cancer Diagnosis and Treatment

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Abstract*— Nano scale objects with dimensions smaller than 100 nanometers can be useful by themselves or as part of larger devices containing multiple nano scale objects. Nanotechnology is being applied to almost every field including biosciences, electronics, magnetics, optics, information technology, and materials development, all of which have an impact on biomedicine. The use of nanotechnology in cancer treatment offers some exciting possibilities, including the possibility of destroying cancer tumors with minimal damage to healthy tissue and organs, as well as the detection and elimination of cancer cells before they form malignant tumors. We have discussed the various medical applications of nanotechnology in cancer diagnosis and treatment. Most efforts to improve cancer treatment through nanotechnology are at the research and development stage.

***Index Terms*— nanotechnology, malignant, tumors, diagnosis, metastatic.**

I. INTRODUCTION

Human body is a wonder created by god. Human cells grow and divide to form new cells as per the requirement of the body. When cells grow old or become damaged, they die, and new cells replace them. However, this orderly process breaks down and gives rise to the cancer. If old and damaged cell survives and new cells form when they are not needed, they can divide without stopping and lead to growths called tumors. Cancer occurs when cells begin to multiply more rapidly than usual and tumors or malignant growths of tissue are formed. Cancerous tumors are malignant, which means they can spread into, or invade, nearby tissues. In addition, as these tumors grow, some cancer cells can break off and travel to distant places in the body through the blood or the lymph system and form new tumors far from the original tumor.

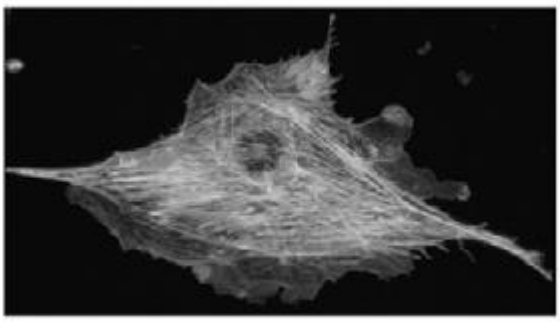

Fig. 1 Cancer cell

Unlike malignant tumors, benign tumors do not spread into, or invade, nearby tissues. However, benign tumors can sometimes be quite large. When removed, they usually don't grow back, whereas malignant tumors sometimes do. Unlike most benign tumors elsewhere in the body, benign brain tumors can be life threatening.[1]

II. HOW CANCER ARISES

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 for growth. A molecule causes neighboring blood vessel to grow towards the cell to supply the oxygen and valuable nutrients. Cancer is curable by the rectification of the damaging mechanism of the genes or by stopping the blood supply to the cells. [2].Genetic changes that cause cancer can be inherited from our parents. They can also arise during a person's lifetime as a result of errors that occur as cells divide or because of damage to DNA caused by certain environmental exposures. Cancer-causing environmental exposures include substances, such as the chemicals in tobacco smoke, and radiation, such as ultraviolet rays from the sun. In general, cancer cells have more genetic changes, such as mutations in DNA, than normal cells as shown in fig. 2.

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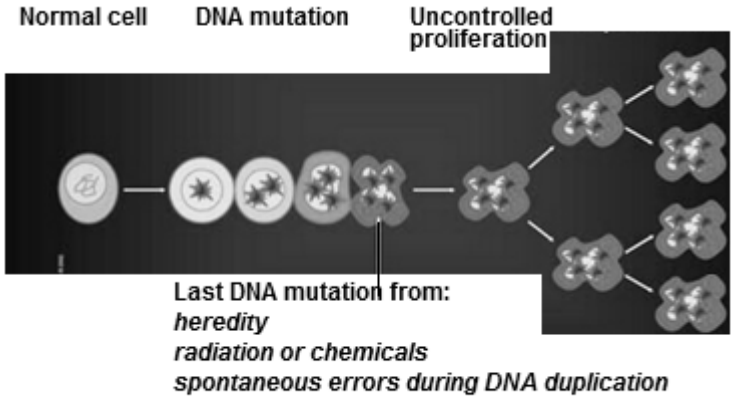

Fig. 2 Formation of cancer by DNA mutations in cells

Spread of Cancer

A cancer that has spread from the place where it first started to another place in the body is called metastatic cancer. The process by which cancer cells spread to other parts of the body is called metastasis.[2] Metastatic cancer has the same name and the same type of cancer cells as the original, or primary, cancer. For example, breast cancer that spreads to and forms a metastatic tumor in the lung is metastatic breast cancer, not lung cancer. Metastasis can occur in three ways:

1. They can grow directly into the tissue surrounding the tumor;
2. Cells can travel through the bloodstream to distant locations; or
3. Cells can travel through the lymph system to nearby or distant lymph nodes.

Under a microscope, metastatic cancer cells generally look the same as cells of the original cancer. Moreover, metastatic cancer cells and cells of the original cancer usually have some molecular features in common, such as the presence of specific chromosome changes.

Scientists reported in *Nature Communications* (October 2012 issue) that they have discovered an important clue for the cancer cells spread. It has something to do with their adhesion (stickiness) properties. Certain molecular interactions between cells and the scaffolding that holds them in place (extracellular matrix) cause them to become unstuck at the original tumor site, they become dislodged, move on and then reattach themselves at a new site. "As cancer cells become more metastatic, there can be a loss of adhesion to normal tissue structures. Then, as they become more aggressive, they gain the ability to stick to, and grow on, molecules that are not normally found in healthy tissues but are found in sites of tumor metastases."The scaffolding that helps cells form a three-dimensional structure in tissue is the extracellular matrix. The matrix also plays an important role in controlling what cells do. Proteins called integrins sit on the surface of cells and behave like anchors, they keep the cells tethered to the matrix.[3]

III. TREATMENT OF CANCER

- One of the treatment options 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 are not uniform and the burnt part may become dead and nonfunctional.
- A next option can be chemotherapy; 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. If the cancer is in advanced stage, these are not very sensitive and the detection is possible only after substantial growth of the cancerous cells.[2]

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- Fig 3 shows four various important tools used for the detection of cancer cells, out of which two are discussed above and remaining two will be discussed later.

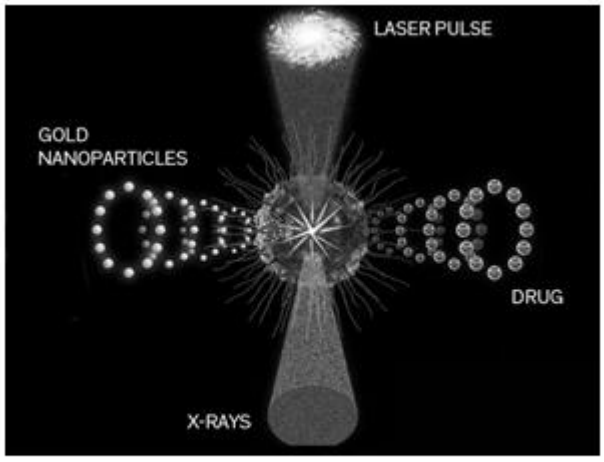

Fig. 3 Use of four tools in detection of the cancer cells: gold nanoparticles, laser pulses, X rays and chemotherapy drugs

IV. APPLICATION OF NANOTECHNOLOGY IN CANCER TREATMENT

Nanoscale devices are one hundred to ten thousand times smaller than human cells. They are similar in size to large biological molecules ("biomolecules") such as enzymes and receptors. As an example, hemoglobin, the molecule that carries oxygen in red blood cells, is approximately 5 nanometers in diameter. Nanoscale devices smaller than 50 nanometers can easily enter most cells, while those smaller than 20 nanometers can move out of blood vessels as they circulate through the body. Because of their small size, nanoscale devices can readily interact with biomolecules on both the surface and inside cells. By gaining access to so many areas of the body, they have the potential to detect disease and deliver treatment in ways unimagined before now.[4]

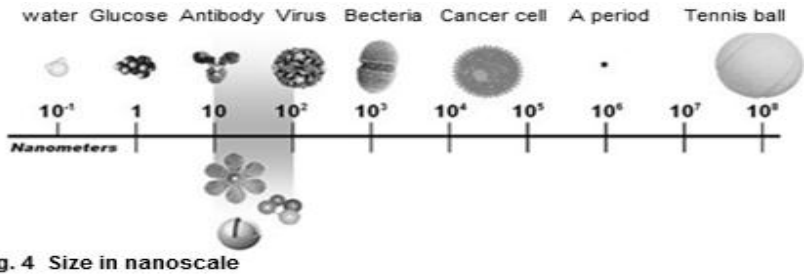

Fig. 4 Size in nanoscale

- **Targeted drug therapies:** If scientists can load their cancer-detecting gold nanoparticles with anticancer drugs, they could attack the cancer exactly where it lives. Such a treatment means fewer side effects and less medication used. Nanoparticles also carry the potential for targeted *and* time-release drugs. A potent dose of drugs could be delivered to a specific area but engineered to release over a planned period to ensure maximum effectiveness and the patient's safety.

- These treatments aim to take advantage of the power of nanotechnology and the voracious tendencies of cancer cells, which feast on everything in sight, including drug-laden nanoparticles. The dye in blue jeans or ballpoint pen has also been paired with gold nanoparticles to fight cancer. This dye, known as **phthalocyanine**, reacts with light. The nanoparticles take the dye directly to cancer cells while normal cells reject the dye. Once the particles are inside, scientists "activate" them with light to destroy the cancer. Similar therapies have existed to treat skin cancers with light-activated dye, but scientists are now working to use nanoparticles and dye to treat tumors deep in the body.[5] A nanoparticle designed for photodynamic cancer therapy consists of a core of europium-doped strontium aluminate

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(SAO) surrounded by layers of solid silica (blue) and mesoporous silica (dark gray). The SAO absorbs X-rays and then emits visible light (green), which activates merocyanine dye (tan spheres) inside the silica pores. The dye then triggers the production of reactive oxygen species that can kill cancer cells.

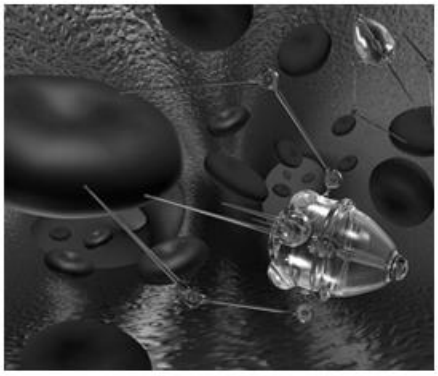

Fig. 5 Use of gold nano particle to carry anticancer drug straight to tha cancer

A multifunctional nanoparticle could make it possible to use a cancer treatment called photodynamic therapy (PDT) to destroy tumors deep inside the body. PDT offers a way to target treatments to diseased cells. Doctors first inject a photosensitizer molecule into a patient's bloodstream or apply it to the skin. Then, shining light of a particular wavelength onto tumors activates the molecules, which transfer their energy to nearby oxygen molecules to generate reactive oxygen species that kill nearby cells as shown in figure 6. But existing PDT photosensitizers, work with near-infrared or visible light, which can travel only a few millimeters through tissue before it's absorbed or scattered. So PDT has only worked for tumors on the skin or near the surface of the body.[6]

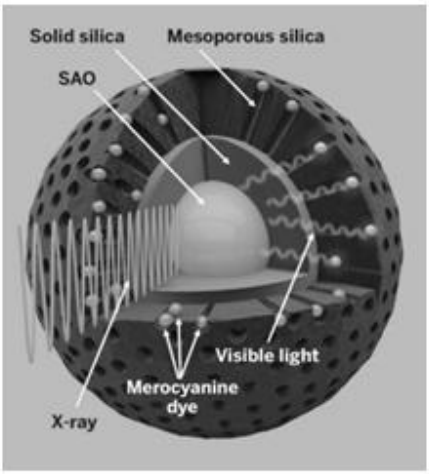

Fig 6 Cancer killer nanoparticle designed for photodynamic cancer therapy

- **Nanowires and Cantilevers:** As shown in figure 7, nano sized sensing wires are laid down across a micro fluidic channel. These nanowires by nature have incredible properties of selectivity and specificity. As particles flow through the micro fluidic channel, the nanowire sensors pick up the molecular signatures of these particles and can immediately relay this information through a connection of electrodes to the outside world.

These nanodevices are man-made constructs made with carbon, silicon and other materials that have the capability to monitor the complexity of biological phenomenon and relay the information, as it is monitored, to the medical care provider. They can detect the presence of altered genes associated with cancer and may help researchers pinpoint the exact location of those changes.[7]

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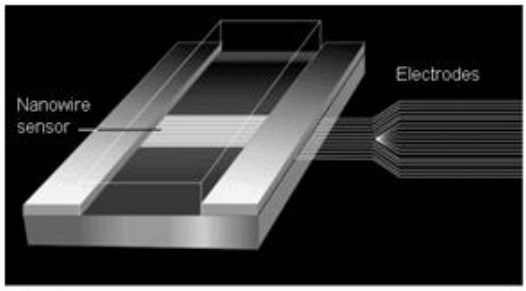

Fig. 7 Nanowire sensor

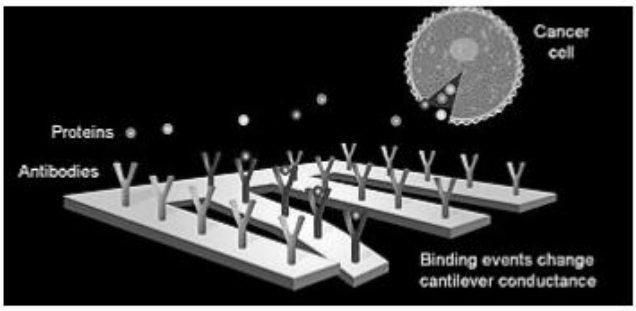

Fig. 8 Nanoscale cantilevers

Nanoscale cantilevers - microscopic, flexible beams resembling a row of diving boards - are built using semiconductor lithographic techniques. These can be coated with molecules capable of binding specific substrates-DNA complementary to a specific gene sequence, for example. Such micron-sized devices, comprising many nanometer-sized cantilevers, can detect single molecules of DNA or protein.

As a cancer cell secretes its molecular products, the antibodies coated on the cantilever fingers selectively bind to these secreted proteins. These antibodies have been designed to pick up one or more different, specific molecular expressions from a cancer cell. The physical properties of the cantilevers change as a result of the binding event. Researchers can read this change in real time and provide not only information about the presence and the absence but also the concentration of different molecular expressions. Nanoscale cantilevers, constructed as part of a larger diagnostic device, can provide rapid and sensitive detection of cancer-related molecules.[8]

- **Nanoshells:** Nanoshells have a core of silica and a metallic outer layer and can be injected safely. Because of their size, these nanoshells preferentially concentrate in cancer lesion sites as shown in figure 9. This physical selectivity occurs through a phenomenon called enhanced permeation retention (EPR). Scientists can further decorate the nanoshells to carry molecular conjugates to the antigens that are expressed on the cancer cells themselves or in the tumor microenvironment. This second degree of specificity preferentially links the nanoshells to the tumor and not to neighboring healthy cells.

Energy can then be externally supplied to these cells. The specific properties associated with nanoshells allow for the absorption of this directed energy, creating an intense heat that selectively kills the tumor cells.[9]

- **Quantum dots:** A quantum dot is a semiconductor nanocrystal with a diameter of a few nanometers. Because of its small size it behaves like a potential well that confines electrons in three dimensions to a region on the order of the electrons' de Broglie wavelength in size [10]. Quantum dots are photo luminescent with a wide absorption spectrum and a narrow emission peak.

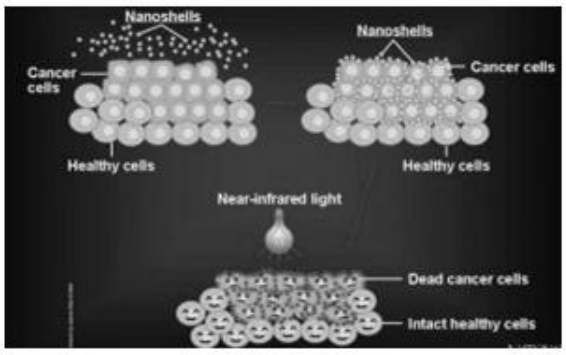

Fig. 9 Nanoshells as cancer therapy

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- **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.[10]

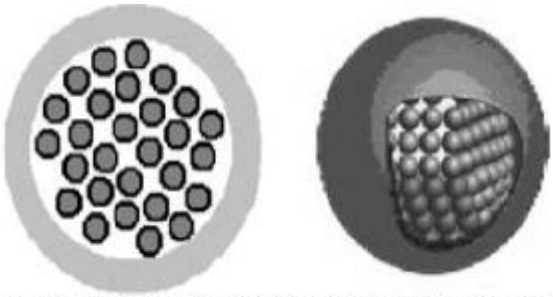

Fig 10 Semiconductor nanosize crystaline quantum dots

V. NATIONAL LEVEL DIAGNOSIS

Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS) of Lucknow would be able to diagnose whether tumor is benign or malignant with almost 80% accuracy, by the help of elastography technology that is being integrated into the institute for medical imaging and diagnosis. Elastography maps the elastic properties of soft tissue. This technique helps to know whether tissue is hard or soft thus provides diagnostic information about the presence or status of disease.

The finding is assessed in the light of the fact that a benign tumor is soft while diseased tumors will often be harder than the surrounding tissue. The technology adds precision to diagnosis of cancers in thyroid and breast besides aiding specific management of liver related ailments.

This will reduce the number of patients undergoing surgery for removal of tumors only on the basis of doubt. Hence reducing the risks and side effects of surgery.[11]

VI. INTERNATIONAL LEVEL DIAGNOSIS

Sugar trail may lead to early cancer detection

In continuation for cancer detection and treatment, it has been identified that a glucose delivery mechanism helps cancer cells to survive and grow. This discovery can help in early detection of not only pancreatic and prostate cancer but many others like cancer of the breast and colon. Announcing the findings, scientists from the University of California, Los Angeles (UCLA) also suggested the use of certain anti-diabetic drugs to reduce the growth of tumors. According to experts and doctors, the findings can give a new protocol worldwide for cancer detection and treatment. Cancer cells require large amounts of glucose to survive and grow. So far, passive glucose transporters — membrane proteins known as GLUTS — were known to be the primary method used by the body to deliver glucose to tumors. However, through a n extensive three-year study, UCLA scientists published an article in leading American science journal, PNAS according to which a new mechanism was identified to import glucose into pancreatic and prostate cancer cells, namely active glucose transport mediated by sodium-dependent glucose tran8s8porters (SGLTs). The researchers suggest probing the new pathway through specific radioactive imaging probe along with positron-emission tomography (PET) that can enable early detection of these cancers cells. Experts say this is the first promising evidence that PET imaging techniques and SGLT2 inhibitors could be used to better diagnose and treat pancreatic and prostate cancers.

The findings also provide strong evidence that certain type-2 diabetic drugs, belonging to a new class known as SGLT2 inhibitors which are already approved by the US Food and Drug Administration and were recently launched in India, could potentially block glucose uptake and reduce tumour growth and increase survival among

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pancreatic and prostate cancer patients. Researchers at UCLA will next begin a clinical study to further investigate the importance of sodium-dependent glucose transporters in glucose delivery. They hope that these findings will lead to the potential use of the existing anti-diabetic medicines to reduce the viability of pancreatic and prostate cancer cells and improve the survival rate in patients.[12]

'Glowing' new nanotechnology guides cancer surgery, also kills remaining malignant cells

Researchers at Oregon State University have developed a new way to selectively insert compounds into cancer cells - a system that will help surgeons identify malignant tissues and then, in combination with phototherapy, kill any remaining cancer cells after a tumor is removed.

The work is based on the use of a compound called naphthalocyanine, which possess some unusual properties when exposed to near-infrared light. It makes a cell glow as to guide a surgeon, heat the cell to kill it and produce reactive oxygen species that can also kill it. By adjusting the intensity of light, the action of the compound can be controlled and optimized to kill just the cancer cells. This research was done for ovarian cancer cells.[13]

VII. CANCER TREATMENT UNDER DEVELOPMENT

- One treatment involves targeted chemotherapy that delivers a tumor-killing agent called tumor 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. The company developing this targeted chemotherapy method to deliver TNF and other chemotherapy drugs to cancer tumors is called **CytImmune**.[14]
- Another technique works on destroying cancer tumors by applying heat. Nanoparticles called AuroShells absorb infrared light from a laser, turning the light into heat. This technique is currently being used in **clincal trials**.
- Researchers at MIT are developing nanoparticles that carry **precise ratios** of three different drugs. They are testing the effectiveness of this approach on ovarian cancer cells.
- Researchers are connecting different DNA strands together into a structure they call a "**nanotrain**". They have demonstrated in lab studies that these nanotrains are effective in delivering chemothreapy drugs to cancer cells, and that by using different DNA strands they can customize which type of cancer cells the nanotrains target.

VIII. CONCLUSION

Biological processes, including ones necessary for life and those that lead to cancer, occur at the nanoscale. Thus, in fact, we are composed of a multitude of biological nano-machines. Nanotechnology has already revolutionized cancer therapy in many aspects and is radically changing the treatment pattern. It has made a great impact on selective recognizing of the cancerous cells, targeted drug delivery, and overcoming limitations of the conventional chemotherapies. Nanotechnology is providing a critical bridge between the physical sciences and engineering and modern molecular biology. Nanotechnology provides researchers with the opportunity to study and manipulate macromolecules in real time and during the earliest stages of cancer progression.

The application of nanotechnology to medicine includes the use of precisely engineered materials to develop novel therapies and devices that may reduce toxicity as well as enhance the efficacy and delivery of treatments. As a result, the application of nanotechnology to cancer can lead to many advances in the prevention, detection, and treatment of cancer. The first nanotechnology-based cancer drugs have passed regulatory scrutiny and are already on the market including Doxil® and Abraxane® [15]. As cancer is one of the most serious lethal diseases, the contribution of nanotechnology in precise treatment avoiding the life threatening side effects can potentially contribute to a positive movement in clinical practice for life saving approach.

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