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A Review on Nanotechnology in Cancer Treatment

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Abstract

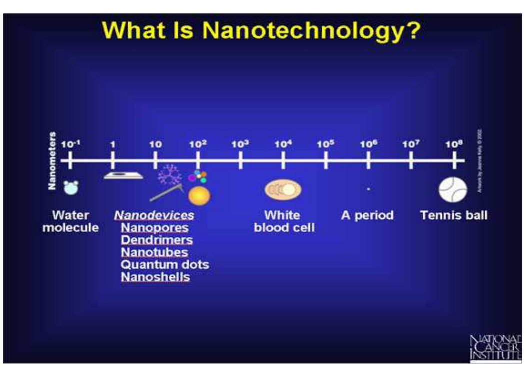
Nanotechnology is the science that refers to the interactions of cellular and molecular components and engineered materials typically clusters of atoms, molecules, and molecular fragments at the most elemental level of biology. Nanoscale devices have the potential to radically change cancer therapy for the better and to dramatically increase the number of highly effective therapeutic agents. Cancer is leading cause of death in world. Nanoparticulate technology can prove to be very useful in cancer therapy allowing for effective and targeted drug delivery by overcoming the, many biological, biophysical and biomedical barriers. Different types of Cancer cells have unique properties that can be exploited by nanoparticles to target the Cancer cells. Nanoparticles can be used to monitor (by utilizing or adding optic, magnetic, and fluorescent properties) and to treat Cancer (by Heat ablation, chemotherapy, gene therapy). Nanotechnology is a multidisciplinary field convergence of basic sciences and applied disciplines. It's definitely a medical boon for diagnosis, treatment and prevention for cancer diseases. Gold nanoparticles (AuNP's) have also been exploited for their potential application in treatment of cancer cells. No human trials have been performed yet and human trials are still at least a few years away.

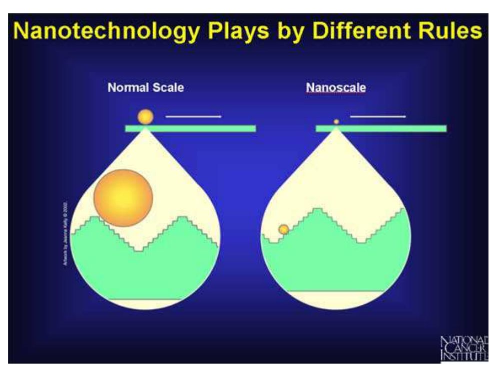
Key Words: Nanotechnology, cancer, nano devices, biomedical barriers.

Introduction

What is Nanotechnology

A nanometer is a billionth of a meter. It's difficult to imagine anything so small, but think of something only 1/80,000 the width of a human hair. Ten hydrogen atoms could be laid side-by-side in a single nanometer. Nanotechnology is the creation of useful materials, devices, and systems through the manipulation of matter on this miniscule scale. The emerging field of nanotechnology involves scientists from many different disciplines, including physicists, chemists, engineers, and biologists. There are many interesting nanodevices being developed that have a potential to improve cancer detection, diagnosis, and treatment.





To help meet the goal of eliminating death and suffering from cancer by 2015, the National Cancer Institute is engaged in efforts to harness the power of nanotechnology to radically change the way we diagnose, image, and treat cancer. Already, NCI programs have supported research. Nanotechnology will change the very foundations of cancer diagnosis, treatment, and prevention on novel nanodevices capable of one or more clinically important functions, including detecting cancer at its earliest stages, pinpointing its location within the body, delivering anticancer drugs specifically to malignant cells, and determining if these drugs are killing malignant cells. As these nanodevices are evaluated in clinical trials, researchers envision that nanotechnology will serve as multifunctional tools that will not only be used with any number of diagnostic and therapeutic agents, but will change the very foundations of cancer diagnosis, treatment, and prevention.

Nanotechnology in Cancer Treatment

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 tumors. Most efforts to improve cancer treatment through nanotechnology are at the research or development stage.

Cancer Treatments under Development

- One treatment involves targeted chemotherapy that delivers a tumor-killing agent called tumor necrosis factor alpha (TNF-α) 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 are called CytImmune.
- One heat therapy to destroy cancer tumors using nanoparticles is called Auroshell. The Auroshell nanoparticles circulate through a patient’s blood stream, exiting where the blood vessels are leaking at the site of cancer tumors. Once the nanoparticles accumulate at the tumor the Auroshell nanoparticles are used to concentrate the heat from infrared light to destroy cancer cells with minimal damage to surrounding healthy cells.
- Targeted heat therapy is being developed to destroy breast cancer tumors. In this method antibodies that are strongly attracted to proteins produced in one type of breast cancer cell are attached to nanotubes, causing the nanotubes to accumulate at the tumor. Infrared light from a laser is absorbed by the nanotubes and produces heat that incinerates the tumor.
- X-ray therapy may be able to destroy cancer tumors using a nanoparticle called nbtxr3. The nbtxr3 nanoparticles, when activated by X-rays, generate electrons that cause the destruction of cancer tumors to which they have attached themselves. Nanobiotix has released preclinical results for this technique.
- An intriguing targeted chemotherapy method uses one nanoparticle to deliver the chemotherapy drug and separate nanoparticle to guide the drug carrier to the tumor. First gold nanorods circulating through the bloodstream exit where the blood vessels are leaking at the site of cancer tumors. Once the nanorods accumulate at the tumor they are used to concentrate the heat from infrared light, heating up the tumor. This heat increases the level of a stress related protein on the surface of the tumor. The drug carrying nanoparticle (a liposome) is attached to amino acids that bind to this protein, so the increased level of protein at the tumor speeds up the accumulation of the chemotherapy drug carrying liposome at the tumor.
- An improved way to shield nanoparticles delivering chemotherapy drugs from the immune system has been developed by forming the nanoparticles from the membranes of red blood cells.
- Delivery of short interfering RNAs (siRNA) is interesting because siRNA simply stops the cancer tumor from growing and there is the potential to tailor synthetic siRNA to the version pf cancer in a individual patient.
- A method to increase the number of cancer fighting immune cells in cancer tumors is interesting. Nanoparticles containing drug molecule called interleukins are attached to immune cells (T-cells). The idea is that when the T-cells reach a tumor the nanoparticles release the drug molecules, which cause the T-cells to reproduce. If enough T-cells are reproduced in the cancer tumor the cancer can be destroyed. This method has been tested on laboratory mice with very good results.
- Magnetic nanoparticles that attach to cancer cells in the blood stream may allow the cancer cells to be removed before they establish new tumors.
- Another method that targets individual cancer cells inserts gold nanoparticles into the cells, and then shines a laser on the nanoparticles. The heat explodes the cancer cells.
- Using gold nanoparticles to deliver platinum to cancer tumors may reduce the side effects of platinum cancer therapy. The key is that the toxicity level of platinum depends upon the molecule it is bonded to

(for the tech types the toxicity depends upon the oxidation state of the platinum). So the researchers chose a platinum containing molecule that has low toxicity to attach to the gold nanoparticles. When the platinum bearing nanoparticle reaches a cancer tumor it encounter an acidic solution which changes the platinum to it's toxic state, in which it can kill cancer cells.

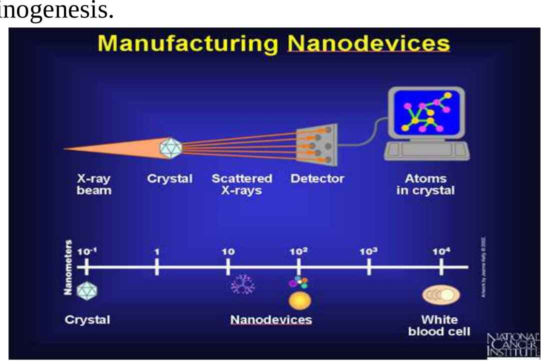
- Using polymer nanoparticles to deliver a molecule called JSI-124 to cancer tumors. This molecule degrades the ability of the cancer cells to suppress the immune system, possibly slowing the growth of cancer tumors.
- Iron oxide nanoparticles can be used to improve MRI images of cancer tumors. The nanoparticle is coated with a peptide that binds to a cancer tumor. Once the naoparticles are attached to the tumor, the magnetic property of the iron oxide enhances the images from the Magnetic Resonance Imaging Scan.
- Sensors based upon nanoparticles or nanowires can detect proteins related to specific types of cancer cells in blood samples. This could allow early detection of cancer. T2 Biosystems uses superparamagnetic nanoparticles that bind to the cancer indicating protein and cluster together. These clusters provide a magnetic resonance signal indicating the presence of the cancer related protein. For another approach researchers at John Hopkins University use quantum dots and molecules that emit a fluorescent glow to detect DNA strands that are early indicators of cancer.

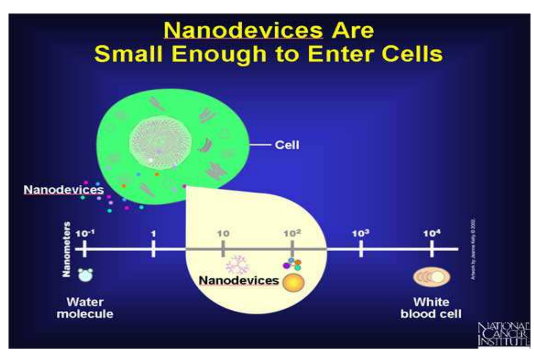
Cancer Treatments using Nanotechnology: Company Directory

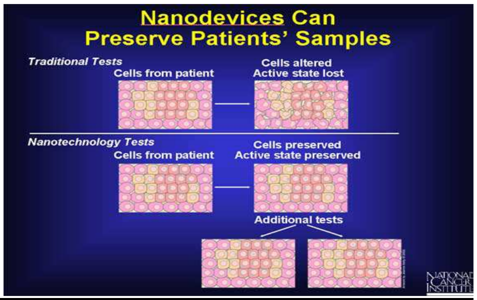
Company	Product
Cytimmune	Gold nanoparticles for targeted delivery of drugs to tumors.
Nano BioMagnetics	Magnetically responsive nanoparticles for targeted drug delivery and other applications.
Abraxis BioScience	Nanoparticles composed of a protein called albumin.
Epeius Biotechnologies	Nanoparticles for targeted delivery of drugs to tumors.
Calando Pharmaceuticals	Nanoparticles for the targeted delivery of siRNA to cancer 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 the cancer tissue.
Nanosphere	Diagnostic testing using gold nanoparticles to detect low levels of proteins indicating particular diseases.
Oxonica	Diagnostic testing using gold nanoparticles (biomarkers)
T2 Biosystems	Diagnostic testing using magnetic nanoparticles
MagArray	Diagnostic testing using magnetic nanoparticles
MagForce	Ironoxide nanoparticles used in heat treatment of solid tumors

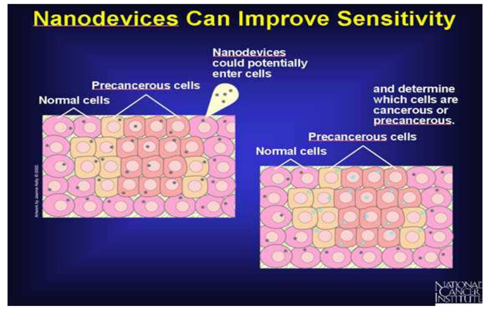
Nanodevices:

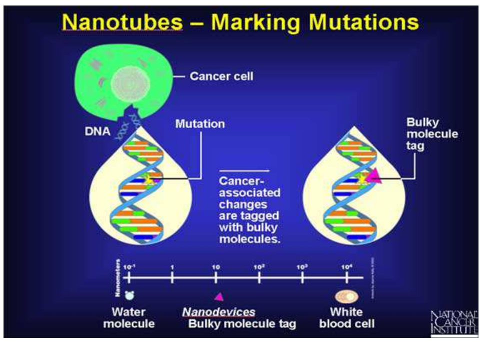
Nanoscale devices and nanoscale components of larger devices are of the same size as biological entities. They are smaller than human cells (10,000 to 20,000 nanometers in diameter) and organelles and similar in size to large biological macromolecules such as enzymes and receptors— hemoglobin, for example, is approximately 5 nm in diameter, while the lipid bilayer surrounding cells is on the order of 6 nm thick. Nanoscale devices smaller than 50 nanometers can easily enter most cells, while those smaller than 20 nanometers can transit out of blood vessels. As a result, nanoscale devices can readily interact with biomolecules on both the cell surface and within the cell, often in ways that do not alter the behavior and biochemical properties of those molecules. From a scientific viewpoint, the actual construction and characterization of nanoscale devices may contribute to understanding carcinogenesis.

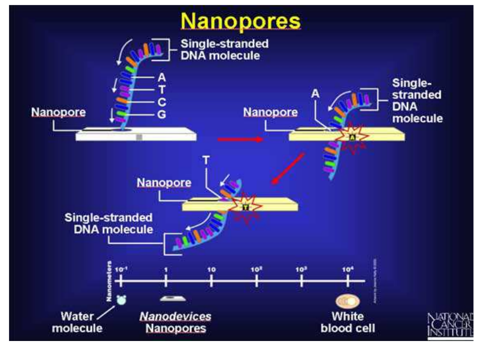


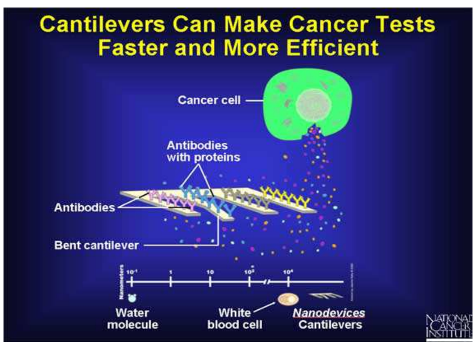


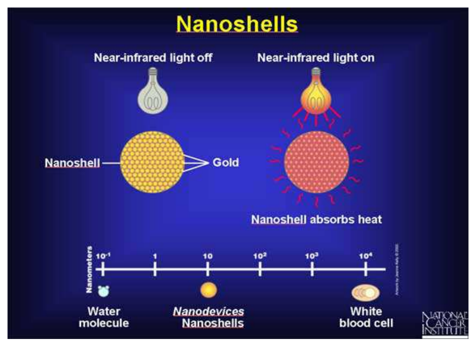

Nanodevices Can
Preserve Patients' Samples
Traditional Tests
Cells from patient
Cells altered
Active state lost
Nanotechnology Tests
Cells from patient
Cells preserved
Active state preserved
Additional tests

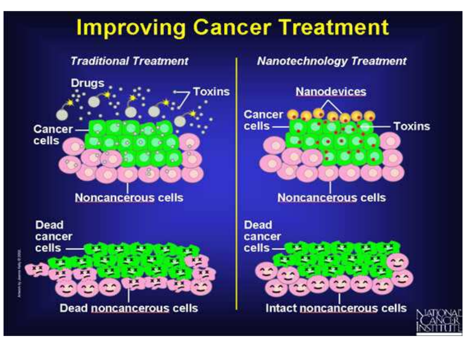

Nanodevices Can Improve Sensitivity
Nanodevices
could potentially
enter cells
Precancerous cells
Normal cells
and determine
which cells are
cancerous or
precancerous.
Precancerous cells
Normal cells

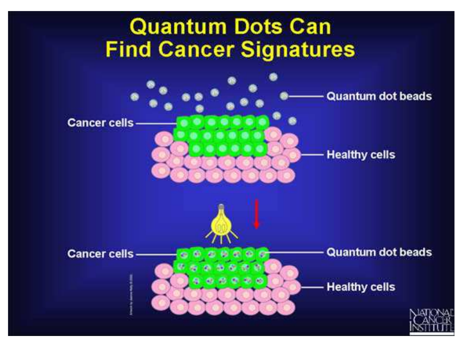

Nanotubes – Marking Mutations
Cancer cell
DNA
Mutation
Bulky
molecule
tag
Cancer-
associated
changes
are tagged
with bulky
molecules.
Water
molecule
Nanodevices
Bulky molecule tag
White
blood cell

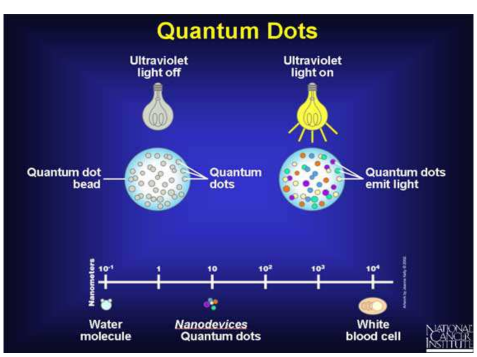

Nanopores
Single-stranded
DNA molecule
A
T
C
G
Nanopore
Nanopore
A
Single-
stranded
DNA
molecule
T
Nanopore
Single-stranded
DNA molecule
Water
molecule
Nanodevices
Nanopores
White
blood cell

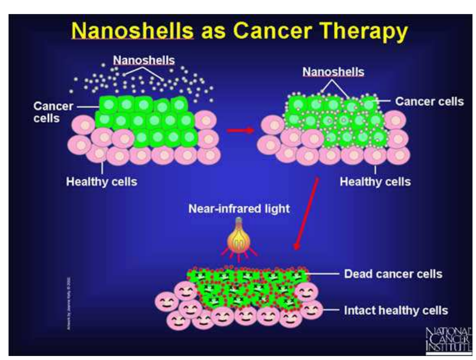

Cantilevers Can Make Cancer Tests
Faster and More Efficient
Cancer cell
Antibodies
with proteins
Antibodies
Bent cantilever
Water
molecule
White
blood cell
Nanodevices
Cantilevers

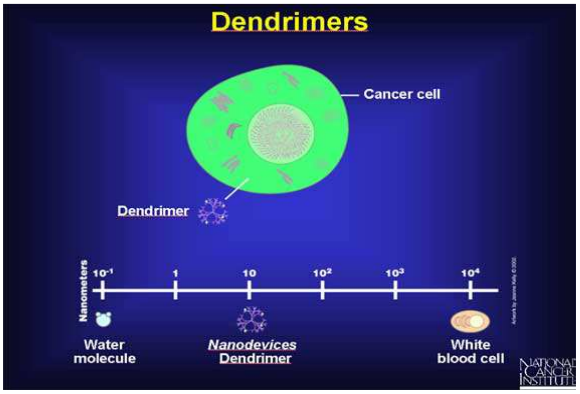

Nanoshells
Near-infrared light off
Near-infrared light on
Nanoshell
Gold
Nanoshell absorbs heat
Water
molecule
Nanodevices
Nanoshells
White
blood cell

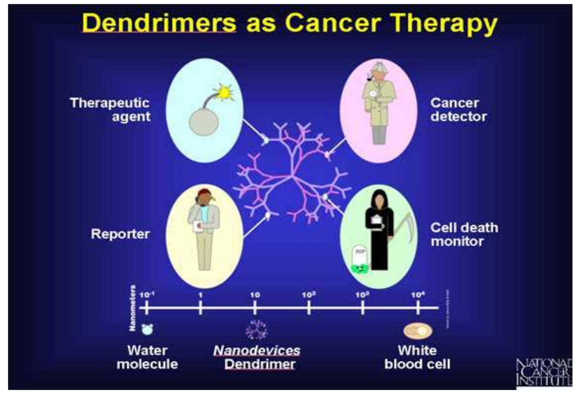

Improving Cancer Treatment
Traditional Treatment
Nanotechnology Treatment
Drugs
Toxins
Cancer
cells
Noncancerous cells
Dead
cancer
cells
Dead noncancerous cells
Nanodevices
Cancer
cells
Toxins
Noncancerous cells
Dead
cancer
cells
Intact noncancerous cells

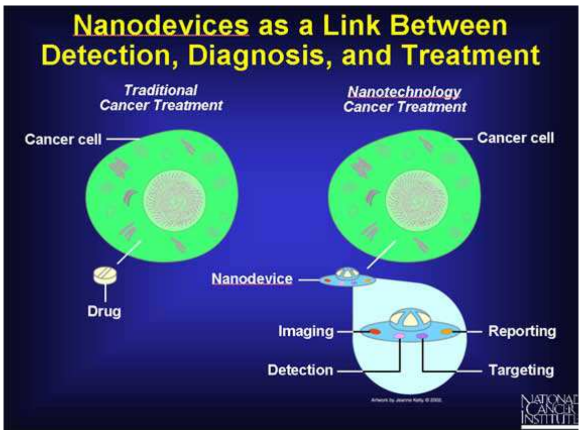

Quantum Dots Can
Find Cancer Signatures
Quantum dot beads
Cancer cells
Healthy cells
Cancer cells
Quantum dot beads
Healthy cells

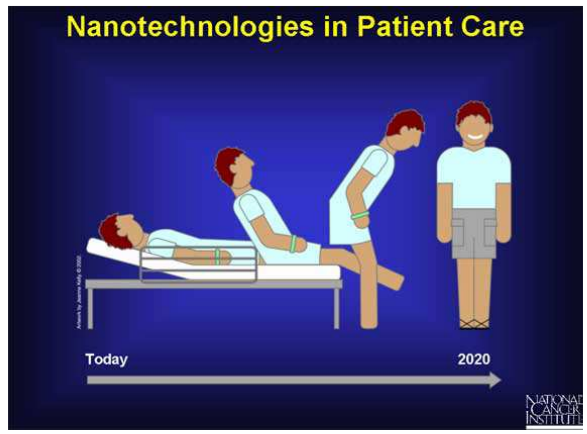

Quantum Dots
Ultraviolet
light off
Ultraviolet
light on
Quantum dot
bead
Quantum
dots
Quantum dots
emit light
Water
molecule
Nanodevices
Quantum dots
White
blood cell


Nanoshells as Cancer Therapy
Nanoshells
Nanoshells
Cancer
cells
Cancer cells
Healthy cells
Healthy cells
Near-infrared light
Dead cancer cells
Intact healthy cells









Developing a Cancer Nanotechnology Plan

NCI's Cancer Nanotechnology Plan will provide critical support for the field though extramural projects, intramural programs, and a new Nanotechnology Standardization Laboratory. This latter facility will develop important standards for nanotechnological constructs and devices that will enable researchers to develop cross-functional platforms that will serve multiple purposes. The laboratory will be a centralized characterization laboratory capable of generating technical data that will assist researchers in choosing which of the many promising nanoscale devices they might want to use for a particular clinical or research application. In addition, this new laboratory will facilitate the development of data to support regulatory sciences for the translation of nanotechnology into clinical applications.

The six major challenge areas of emphasis include:

Prevention and Control of Cancer

1. Developing nanoscale devices that can deliver cancer prevention agents
2. Designing multicomponent anticancer vaccines using nanoscale delivery vehicles

Early Detection and Proteomics

1. Creating implantable, biofouling-indifferent molecular sensors that can detect cancer-associated biomarkers that can be collected for *ex vivo* analysis or analyzed *in situ*, with the results being transmitted via wireless technology to the physician
2. Developing "smart" collection platforms for simultaneous mass spectroscopic analysis of multiple cancer-associated markers

Imaging Diagnostics

1. Designing "smart" injectable, targeted contrast agents that improve the resolution of cancer to the single cell level
2. Engineering nanoscale devices capable of addressing the biological and evolutionary diversity of the multiple cancer cells that make up a tumor within an individual

Multifunctional Therapeutics

1. Developing nanoscale devices that integrate diagnostic and therapeutic functions
2. Creating "smart" therapeutic devices that can control the spatial and temporal release of therapeutic agents while monitoring the effectiveness of these agents

Quality of Life Enhancement in Cancer Care

1. Designing nanoscale devices that can optimally deliver medications for treating conditions that may arise over time with chronic anticancer therapy, including pain, nausea, loss of appetite, depression, and difficulty breathing

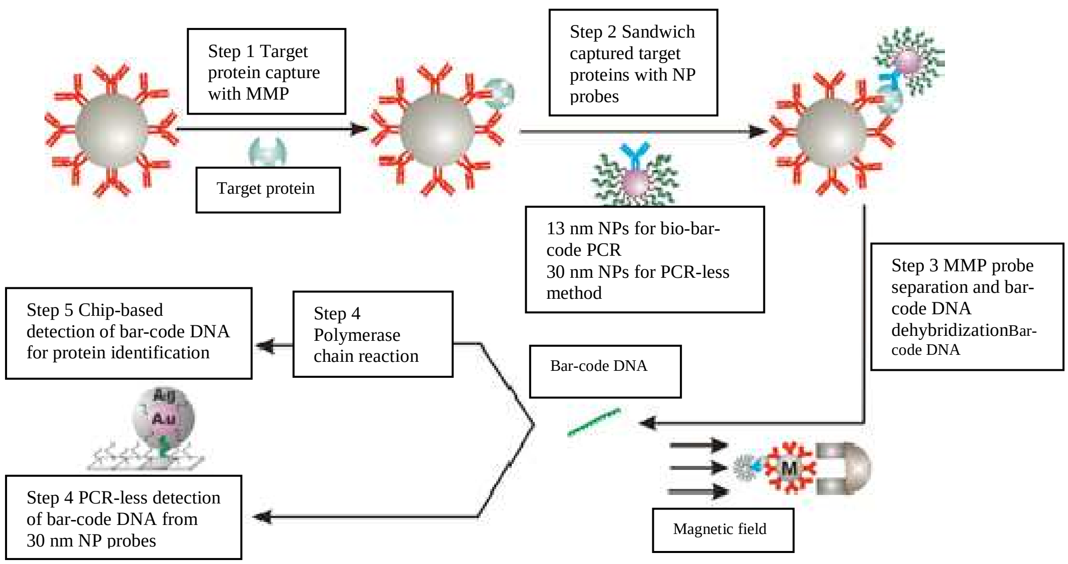
Interdisciplinary Training

Coordinating efforts to provide cross-training in molecular and systems biology to nanotechnology engineers and in nanotechnology to cancer researchers. Creating new interdisciplinary coursework/degree programs to train a new generation of researchers skilled in both cancer biology and nanotechnology.

Nanotechnology and Diagnostics

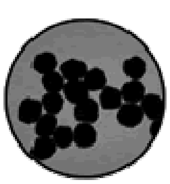
Today, cancer-related nanotechnology research is proceeding on two main fronts: laboratory-based diagnostics and in vivo diagnostics and therapeutics. Nanoscale devices designed for laboratory use rely on many of the methods developed to construct computer chips. For example, 1–2 nanometer-wide wires built on a micron-scale silicon grid can be coated with monoclonal antibodies directed against various tumor markers. With minimal Cancer cell sample preparation,substrate binding to even a small number of antibodies produces a measurable change in the device's conductivity, leading to a 100-fold increase in sensitivity over current diagnostic techniques.

Nanoscale cantilevers, constructed as part of a larger diagnostic device,
can provide rapid and sensitive detection of cancer-related molecules.

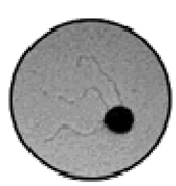


DNA-coated gold nanoparticles (NPs) form the basis of a system that also uses larger magnetic microparticles (MMPs) to detect attomolar (10-18) concentrations of serum proteins. In this case, a monoclonal antibody to prostate specific antigen (PSA) is attached to the MMP, creating a reagent to capture free PSA. A second antibody to PSA, attached to the NPs, is then added, creating a "sandwich" of the captured protein and two particles that is easily separated using a magnetic field.

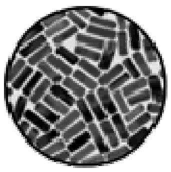
Approved Products



Accurate spherical Gold Nanoparticles
Bare, Conjugated, and Organic in sizes 5-100nm

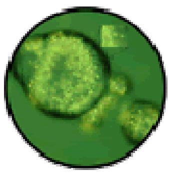


Conjugation Kits and Custom Conjugations
Kits for Customers or Nanopartz conjugation services

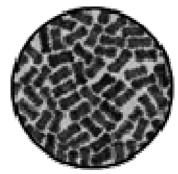


Gold Nanorodz
Bare, Conjugated, and Organic for peak SPRs from 550 to 1400nm including
New! HAR Gold Nanorods

Gold Nanowires
Bare and Conjugated with lengths up to 6.5 microns

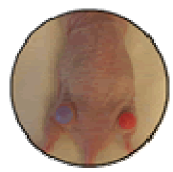


Microgold
Bare and Conjugated micron sized gold particles



Platinum, Palladium and Trimetallic Nanoparticles
Nanoparticles for Catalysis

Gold Nanobeads

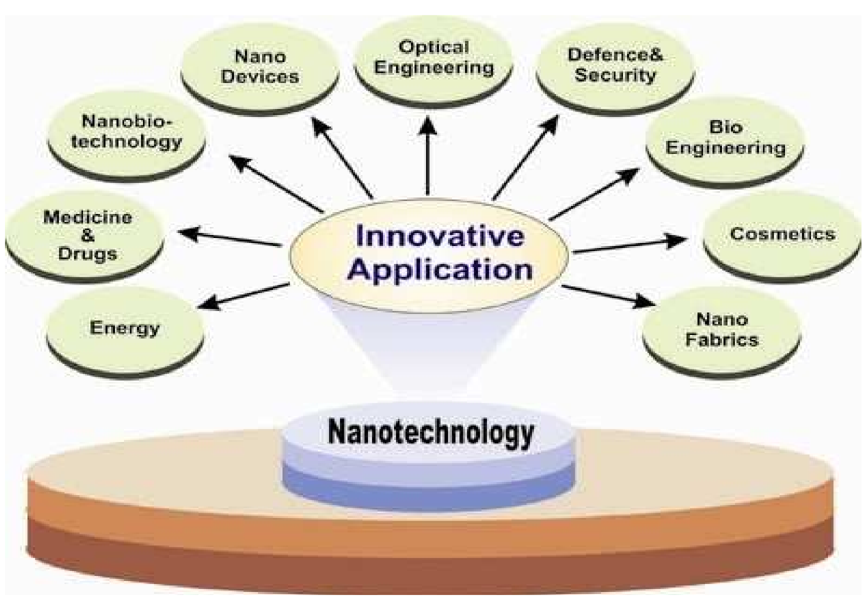


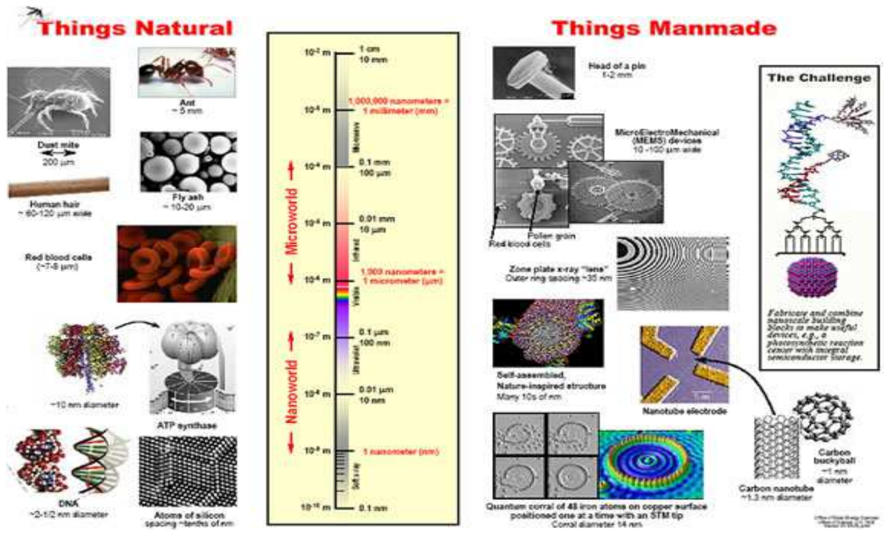
SERS Raman Labels
SERS Labels for excitation from 600 to 800 nm

Preconjugated Products
Spherical and Nanorods Conjugated to anti-EGFR, peptides, and more

Future Herbal Nanoparticles for Cancer:
Aswagandha, Amla, Basil, Rakta vrntaka (Tomato), Neem, Turmeric etc with anticancerous properties. Antioxidants play an important role in mitigating the damaging effects of oxidative stress on cells. Lycopene, a carotenoid, has received considerable scientific interest in recent years.

Applications of Nanotechnology:





Nanotechnology – a powerful research enabler:
Nanotechnology is providing a critical bridge between the physical sciences and engineering, on the one hand, and modern molecular biology on the other.

Conclusion

Nanotechnology will radically change the way we diagnose, treat and prevent cancer to help meet the goal of eliminating, suffering and death from cancer. Although most of the technologies described are promising and fit well with the current methods of treatment, there is still safety concerns associated with the introduction of nanoparticles in the human body. These will require further studies before some of the products can be approved. The most promising methods of drug delivery in cancer will be those that combine diagnostics with treatment. These will enable personalized management of cancer and provide an integrated protocol for diagnosis and follow up that is so important in management of cancer patients. There are still many advances needed to improve nanoparticles for treatment of cancers. Future efforts will focus on identifying the mechanism and location of action for the vector to treat all stages of tumors in preclinical models. Further studies are focused on expanding the selection of drugs to deliver novel nanoparticle vectors. Hopefully, this allows the development of innovative new strategies for cancer cures.

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