Biomedical Applications of Nanotechnology

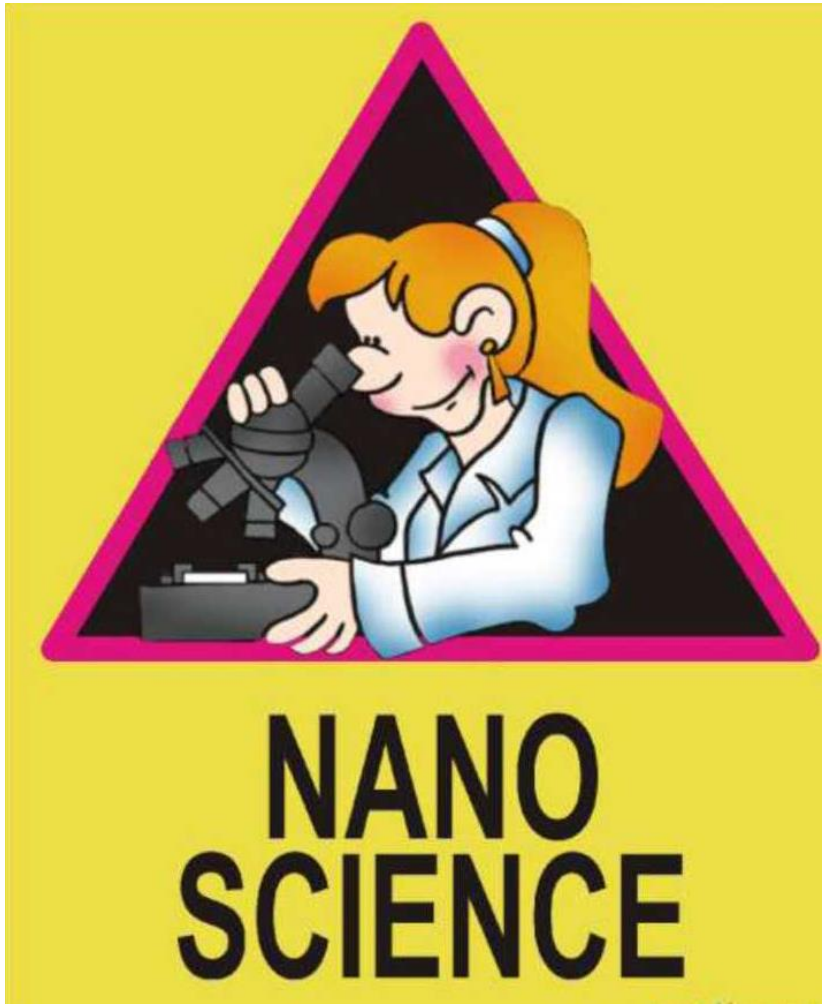
LECTURE

NANOSCIENCE

- **Nanosciene**

  is the Science of

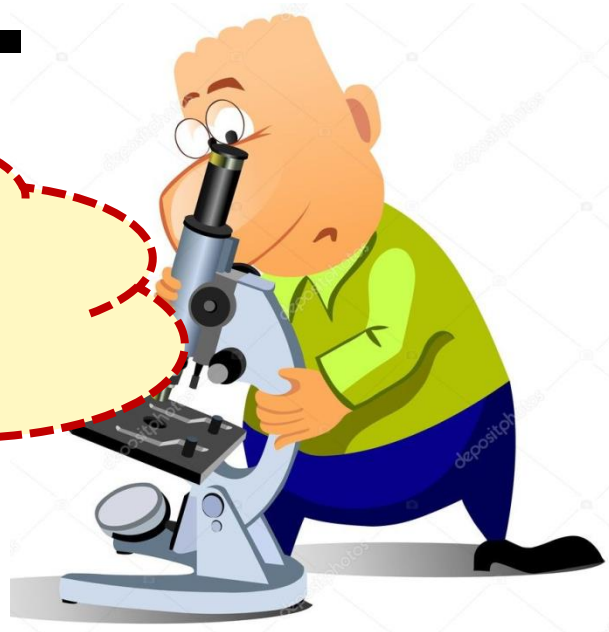
  Tiny Things



Nano:

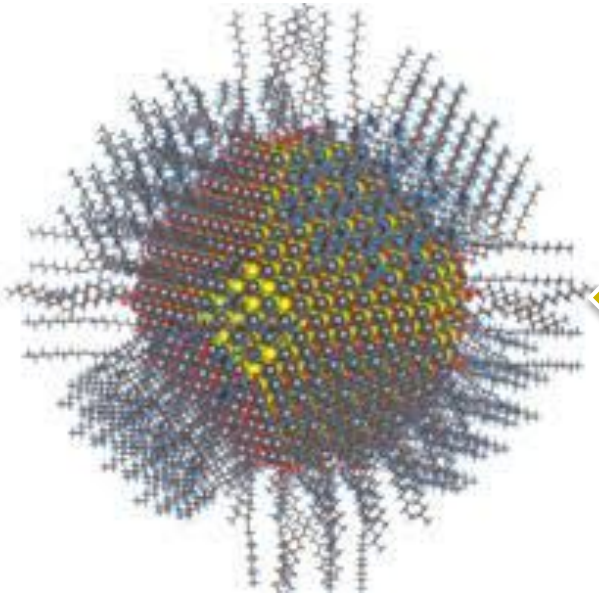
A prefix that means very, very, small.

The word nano is from the Greek word ‘Nanos’ meaning Dwarf. It is a prefix used to describe "one billionth" of something, or 0,000000001.



Nanoscience

A part of science that studies small stuff.



It's not biology, physics or chemistry. It's all sciences that work with the very small.

Best Definition of Nanoscience

- Probably the best definition comes from the NanoSci-ERA©2006 (www.nanoscience-europe.org): the term “Nanoscience” encompasses the common unifying concepts and physical laws that prevail in the nanoscale.
- Research in nanoscience is an interdisciplinary knowledge-generating activity that strives to understand these laws and how they govern the behaviour of nano-scale objects of physical, chemical or biological interest.

Nanoscience

Nanoscience is the study of atoms, molecules, and objects whose size is on the nanometer scale (1-100 nanometres).

Nanotechnology

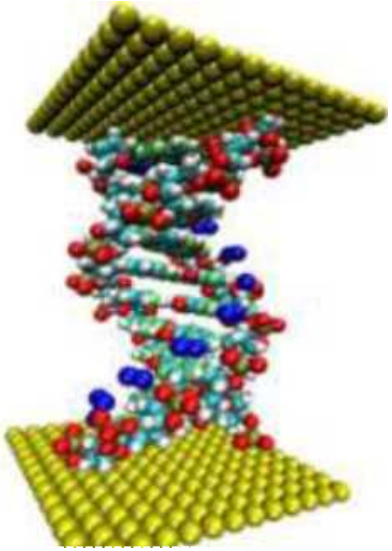
Nanotechnology, shortened to "**nanotech**", is the study of the controlling of matter on an atomic and molecular scale.

Generally nanotechnology deals with structures sized 100 nanometers or smaller in at least one dimension, and involves developing materials or devices within that size.

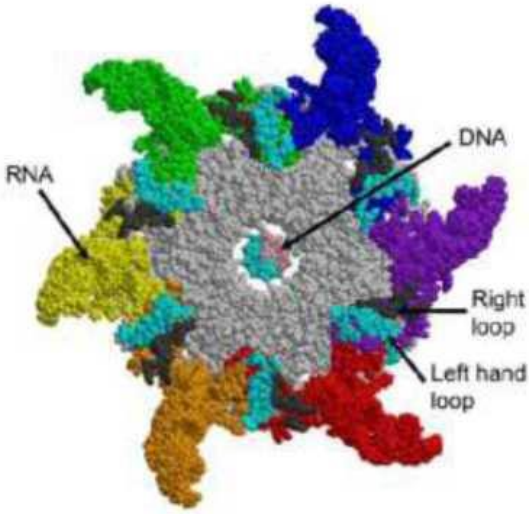
Nanotechnology

- Measure anything smaller than microns
- Anything at nanoscale 0.1 nm – l00 nm
- To study the function and structure of those smallest units in materials or living organisms
- The major research objective of Molecular
- Nanotechnology are the design, modelling, and fabrication of molecular machines and molecular devices.
- Capable to build systems and materials with exact specifications and characteristics.

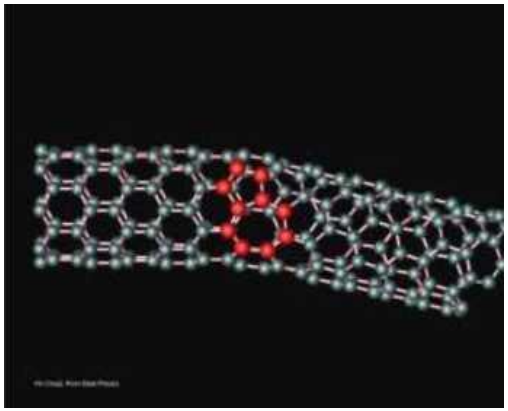
What is Nanotechnology



An engineered DNA strand



Protein coding RNA



Semiconducting metal junction formed by two carbon nanotubes.

Nanotechnology is the creation of functional materials, devices and systems, through the understanding and control of matter at dimensions in the nanometer scale length (1-100 nm), where new functionalities and properties of matter are observed and harnessed for a broad range of applications.

What is Nanoscale

1.27 x 107 m

0.22 m

Fullerenes C_{60}

0.7 x 10-9

10 millions times smaller

10 billion time smaller

What is nanotechnology ?

A Brief History of Nanotechnology

On **December 29, 1959, physicist Richard Feynman** suggested that it should be possible to **make machines at a nano-scale that "arrange the atoms the way we want", and do chemical synthesis by mechanical manipulation**.

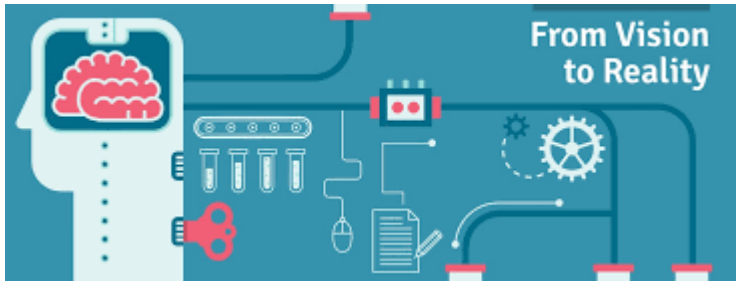
Hibbs's Idea on Nanotechnology in Medicine

Albert R. Hibbs – a noted mathematician was fascinated by self-actuated machines. **According to Feynman, Hibbs originally suggested to him** (1959) **the idea of a *medical* use for Feynman's theoretical micromachines.**

What Feynman and Hibbs considered a possibility today is becoming a reality.

- Private and public research efforts worldwide are developing nanoproducts aimed at improving health care and advancing medical research.

Some of these products have entered the marketplace on the verge of doing so.

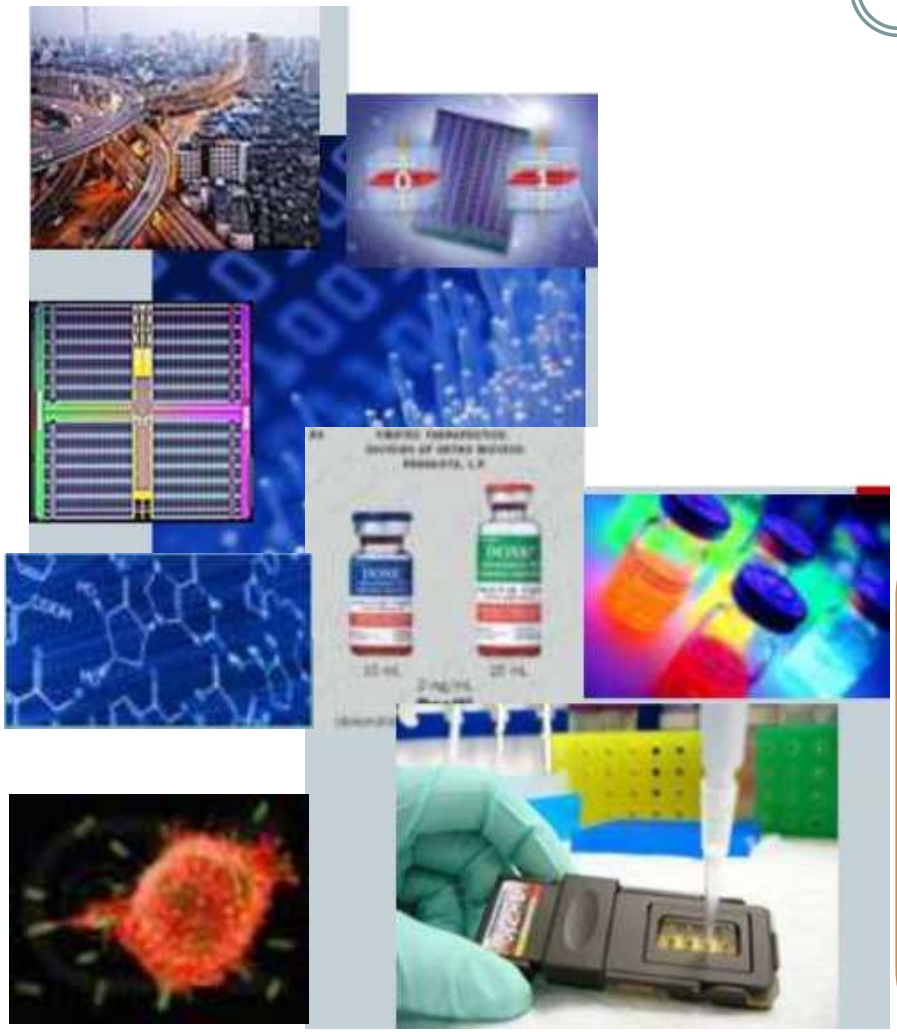


Other products remain more a vision that a reality.

The potential for these innovations is enormous

But! What about their longterm safety and the risk–benefit characteristics of their usage?

Nanotechnology Applications



Information Technology

Smaller, faster, more energy efficient and powerful computing and other IT-based systems.

Medicine

Cancer treatment
Bone treatment
Drug delivery
Drug development
Appetite control
Medical tools
Diagnostic tests
Imaging.

Nanotechnology Applications

Energy

More efficient and cost effective technologies for energy production

- Solar cells
- Fuel cells
- Batteries
- Bio fuels

Consumer Goods

Foods and beverages

Advanced packaging materials, sensors, and lab-on-chips for food quality testing.

Appliances and textiles.

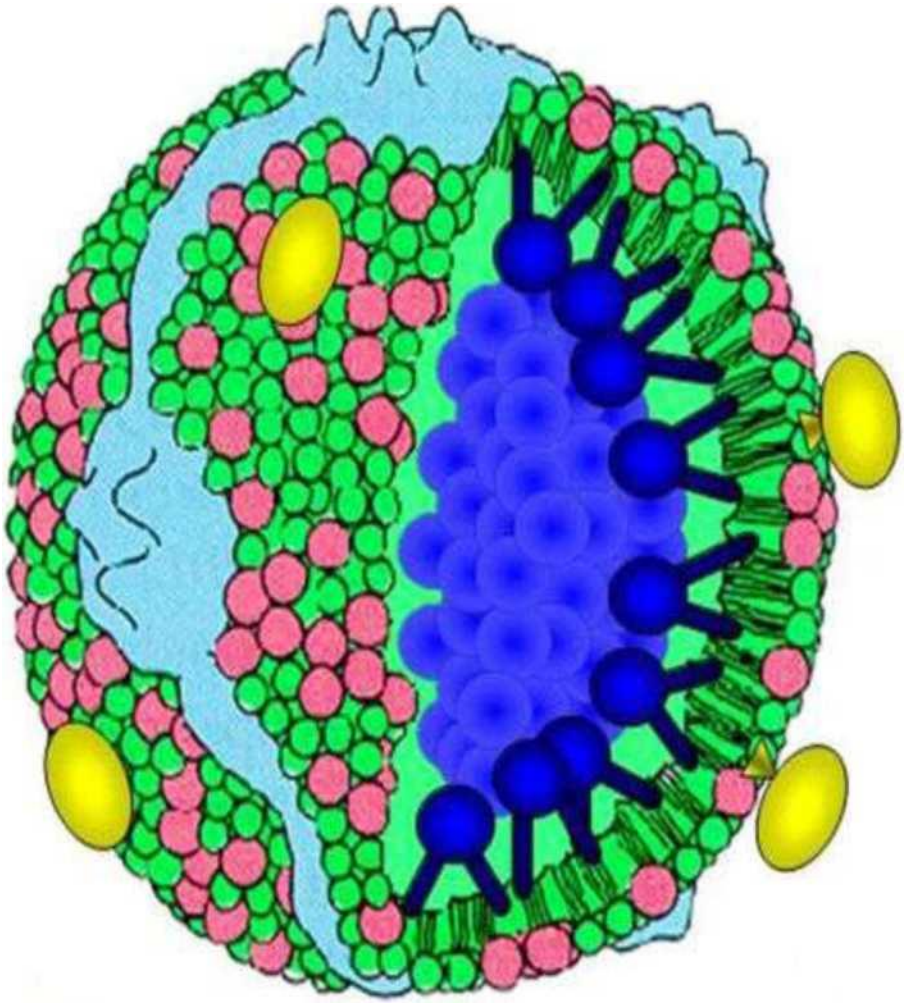
Stain proof, water proof and wrinkle free textiles.

Household and cosmetics.

Self-cleaning and scratch free products, paints, and better cosmetics.

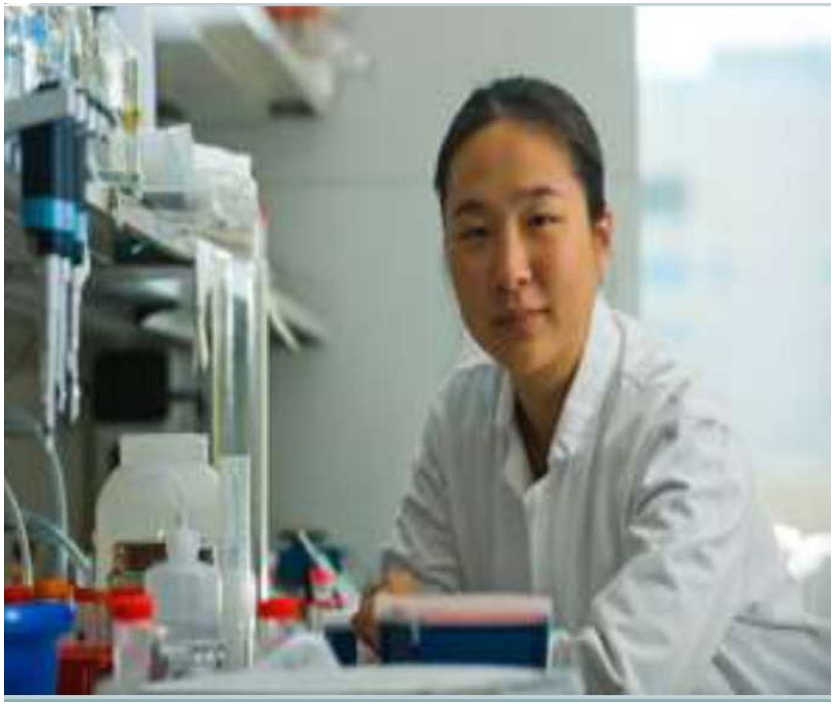
Medical Nanotechnology or Nanomedicine

Nanomedicine is the application of nanotechnology in medicine, including to cure diseases and repair damaged tissues such as bone, muscle, and nerve.



New Technologies Needed in Medicine

- Translating breakthroughs in understanding of disease into preventive medicine.
- How to design affordable healthcare for the bottom-of-the-pyramid.
- How to reap the benefits of healthcare while reducing the inefficiencies.
- Creating technologies for a country's economic growth.



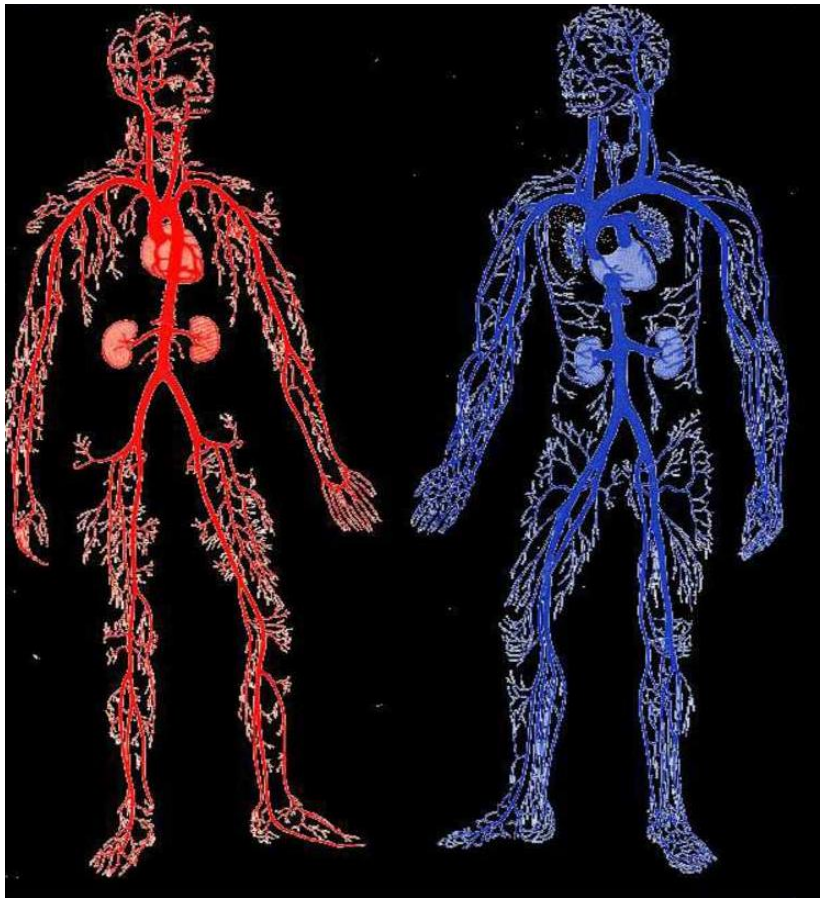
Uses of Nanotechnology in Medicine

Biological imaging for medical diagnostics.

Advanced drug delivery systems.

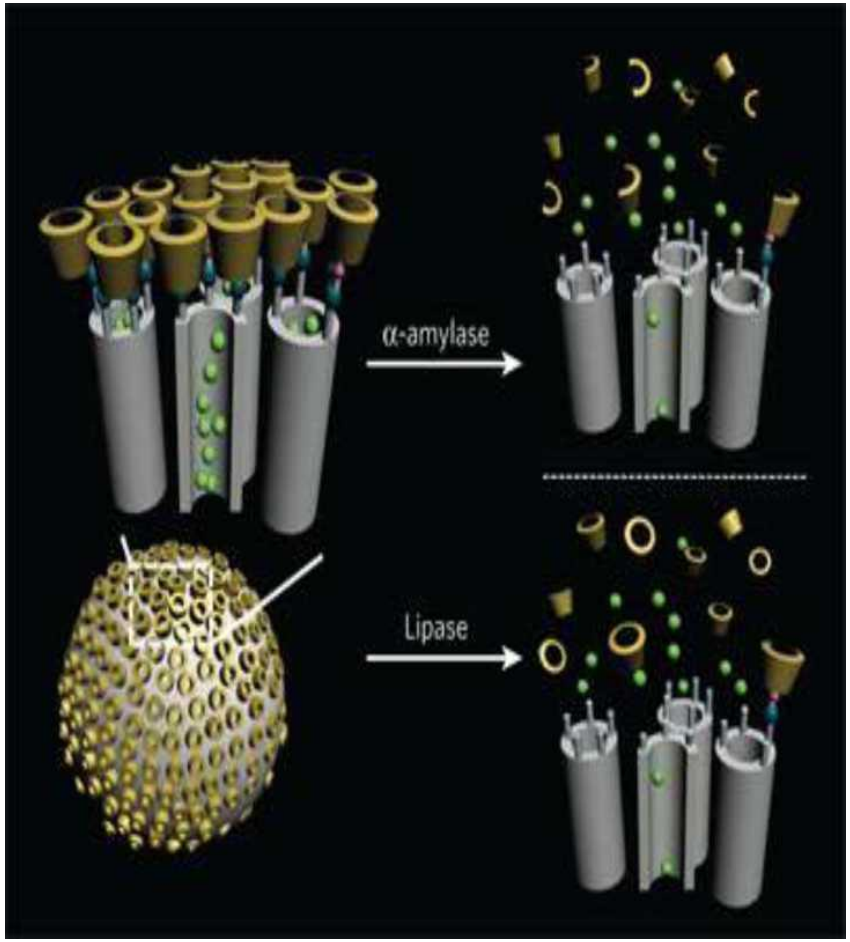
Biosensors for airborne chemicals or other toxins.

Regenerative medicine: More durable, rejection-resistant artificial tissues and organs.

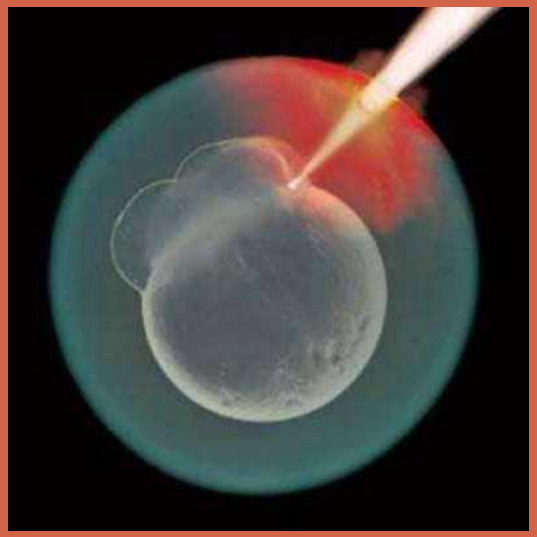


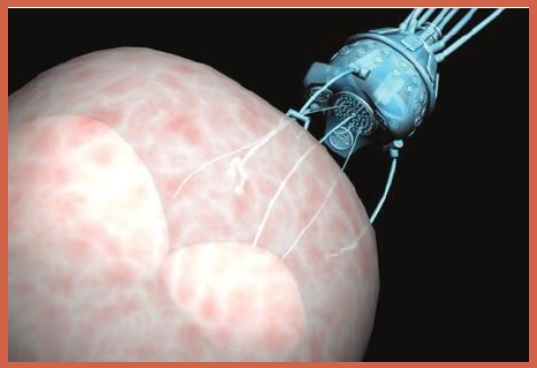
Nanosciences Influences Microbiology

- Nanoscience does have an impact on several areas of microbiology. It allows for the study and visualization at the molecular-assembly levels of a process.
- It facilitates identification of molecular recognition and self-assembly motifs as well as the assessment of these processes.



Applications in Surgery





- **With nanotechnology**, minute surgical instruments and robots can be made which can be used to perform microsurgeries on any part of the body.
- Instead of damaging a large amount of the body, these instruments would be **precise and accurate**, targeting only the area where surgery should be done.
- **Visualization** of surgery can also be improved. Instead of a surgeon holding the instrument, computers can be used to control the nano-sized surgical instruments. "Nanocameras" can provide close up visualization of the surgery
- **Less chance of any mistakes or faults**
- **Surgery** could also be done **on tissue, genetic and cellular levels**.

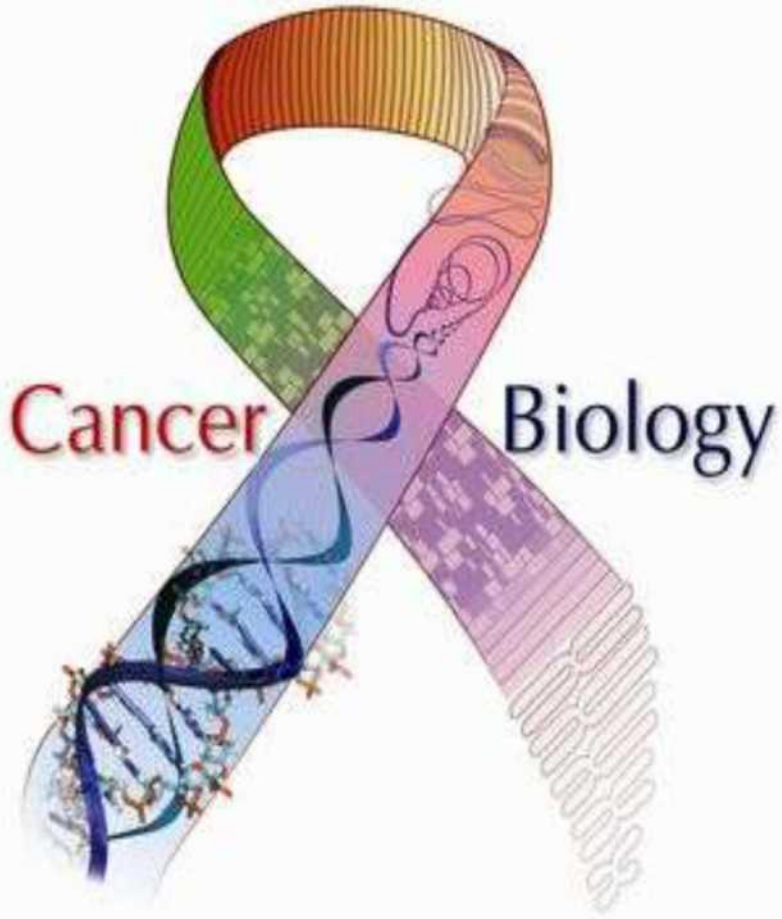
Nano Diagnostics: Early and Accurate Diagnosis

- Biosensors and miniaturized devices targeted imaging agents to highlight of disease.

Targeted Drug Delivery: on the spot bring the drug to the target site and monitor its impact.

- Regenerative Medicine: stimulated repair help the body to (re)build organs or systems.
- Meeting “Ethical, Legal and Social Aspects” (ELSA) challenges.
- For the main diseases in the world: cancer, cardiovascular disease, musculo-skeletal, mental and infectious disease, and diabetes.

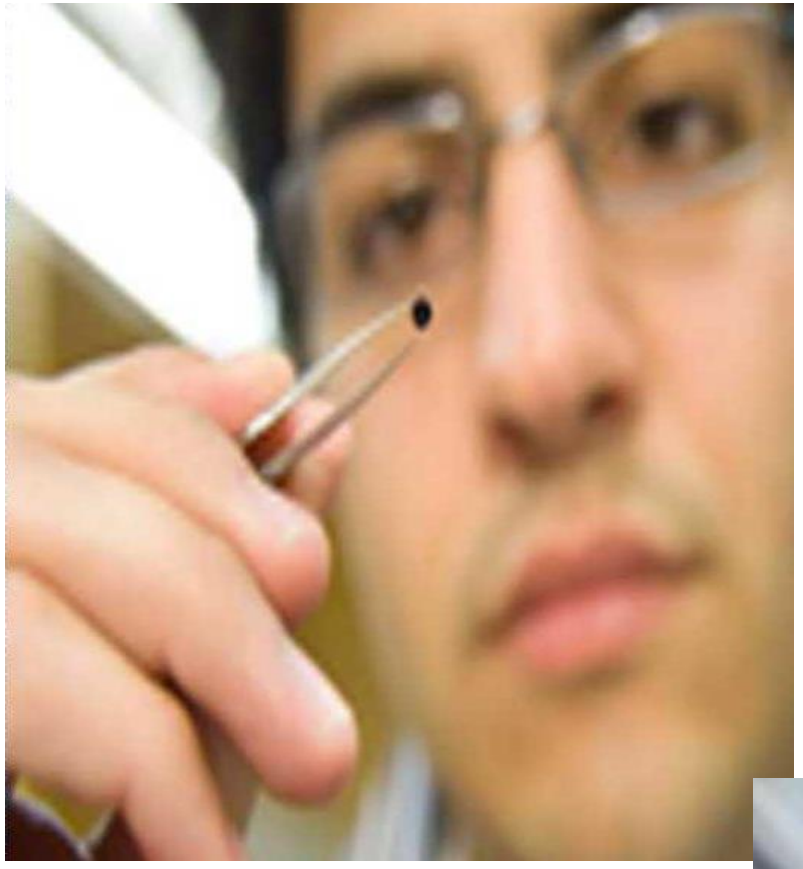
Nano Technology in Cancer



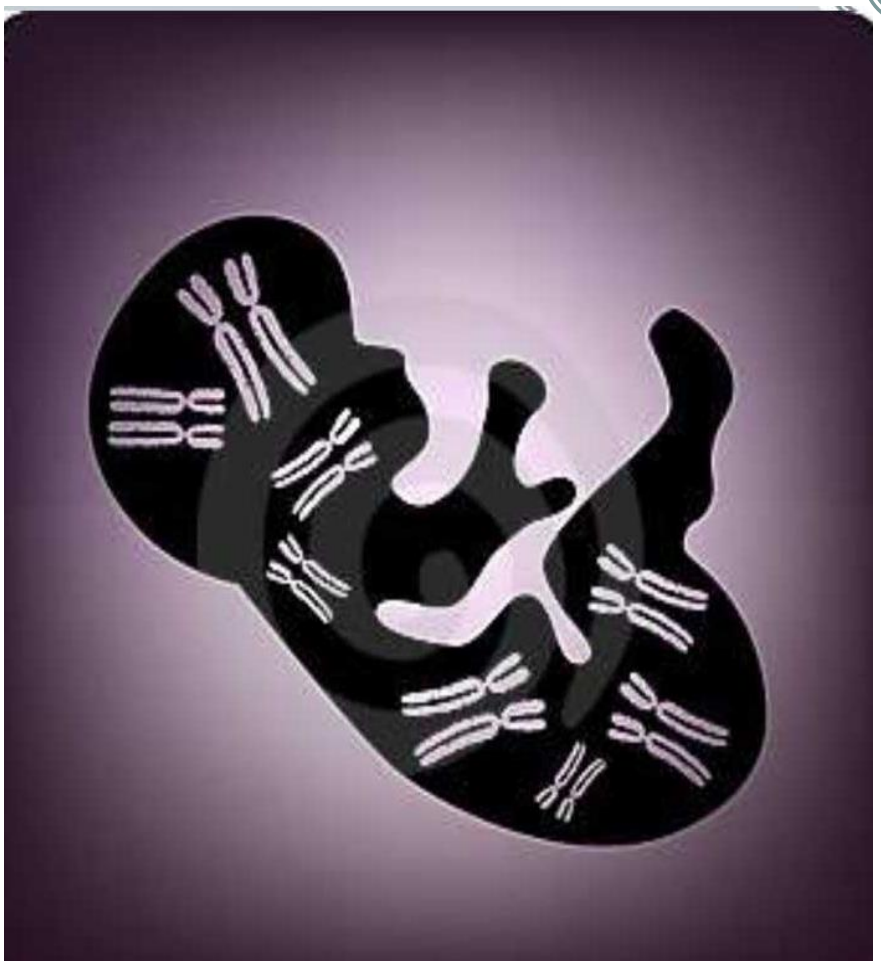
- To develop cure for traditionally incurable diseases (e.g. cancer) through the utilization of nanotechnology.
- To provide more effective cure with fewer side effects by means of targeted drug delivery systems.

Nano Diagnostics Opportunities

- Screening of personal risk factors.
- Identification of population at risk.
- Prediction of risk factors.
- Earlier, more sensitive, faster diagnostic.
- Diagnosis of asymptomatic patients.



Nanomedicine Helps in Early Diagnosis

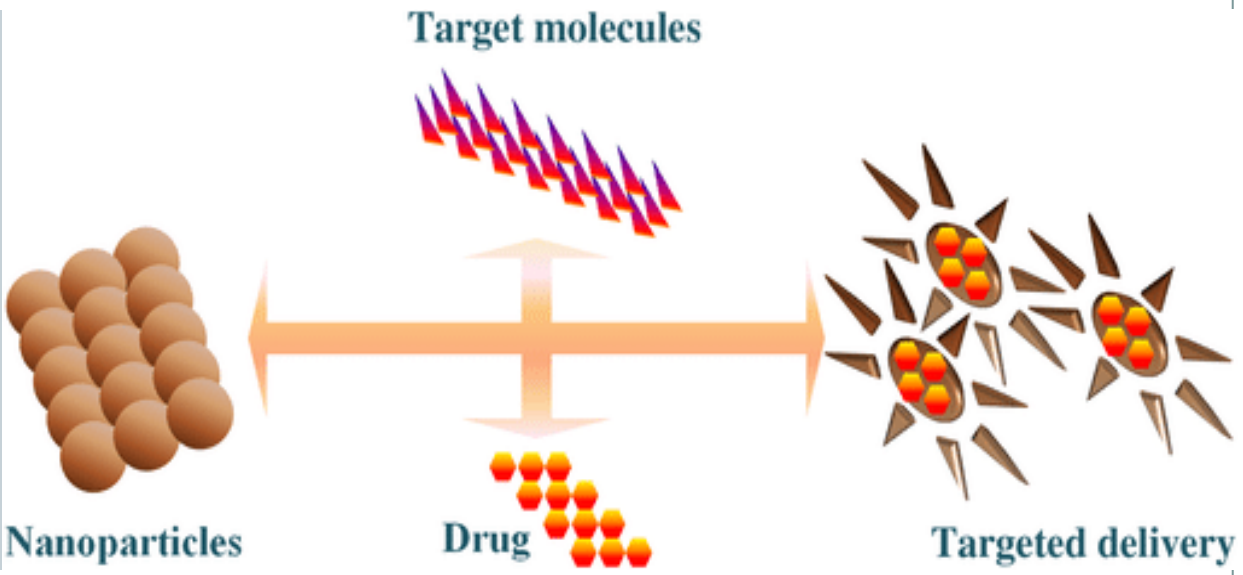


- Higher sensitivity: detection of early biomarkers.
- Non-invasive and painless diagnostic techniques.
- From Central Lab to physician’s office and the home.
- Genetic testing for individual therapy selection.

Helps Targeted Drug Delivery

Protected Drug delivery to target sites:

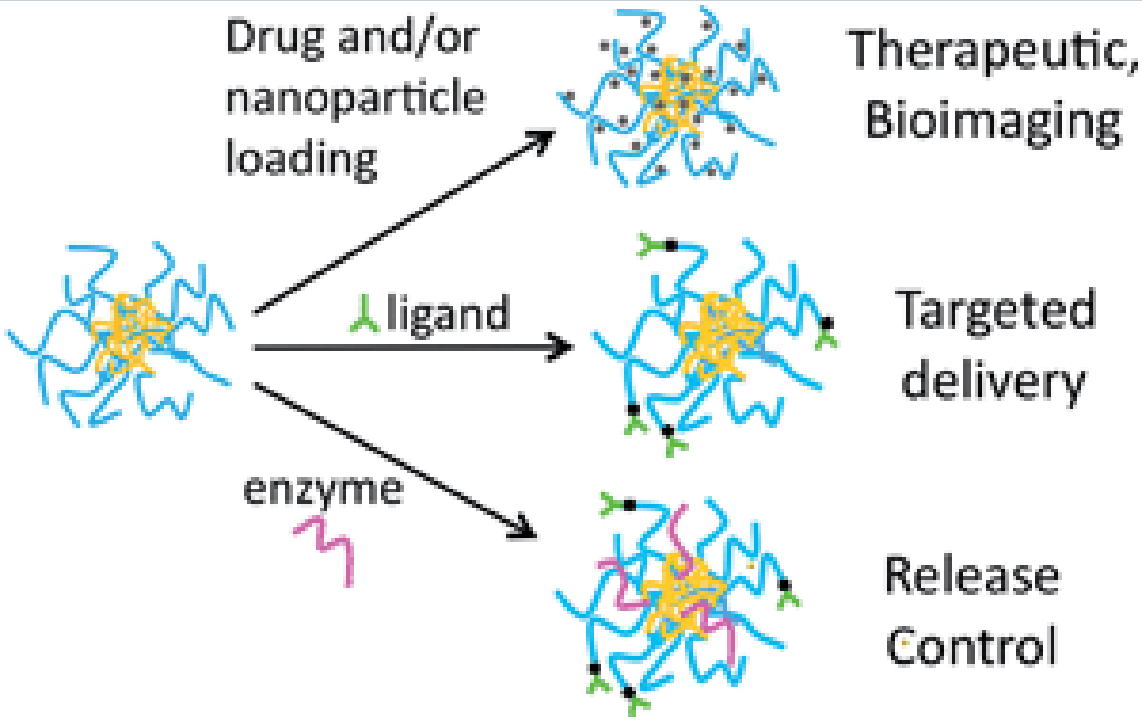
- Nanoparticles
- Miniature devices
- Higher doses
- Healthy tissue not affected
- Theranostics



Theranostics is a new field of medicine which combines specific targeted therapy based on specific targeted diagnostic tests. It is a combination of diagnostics and therapy.

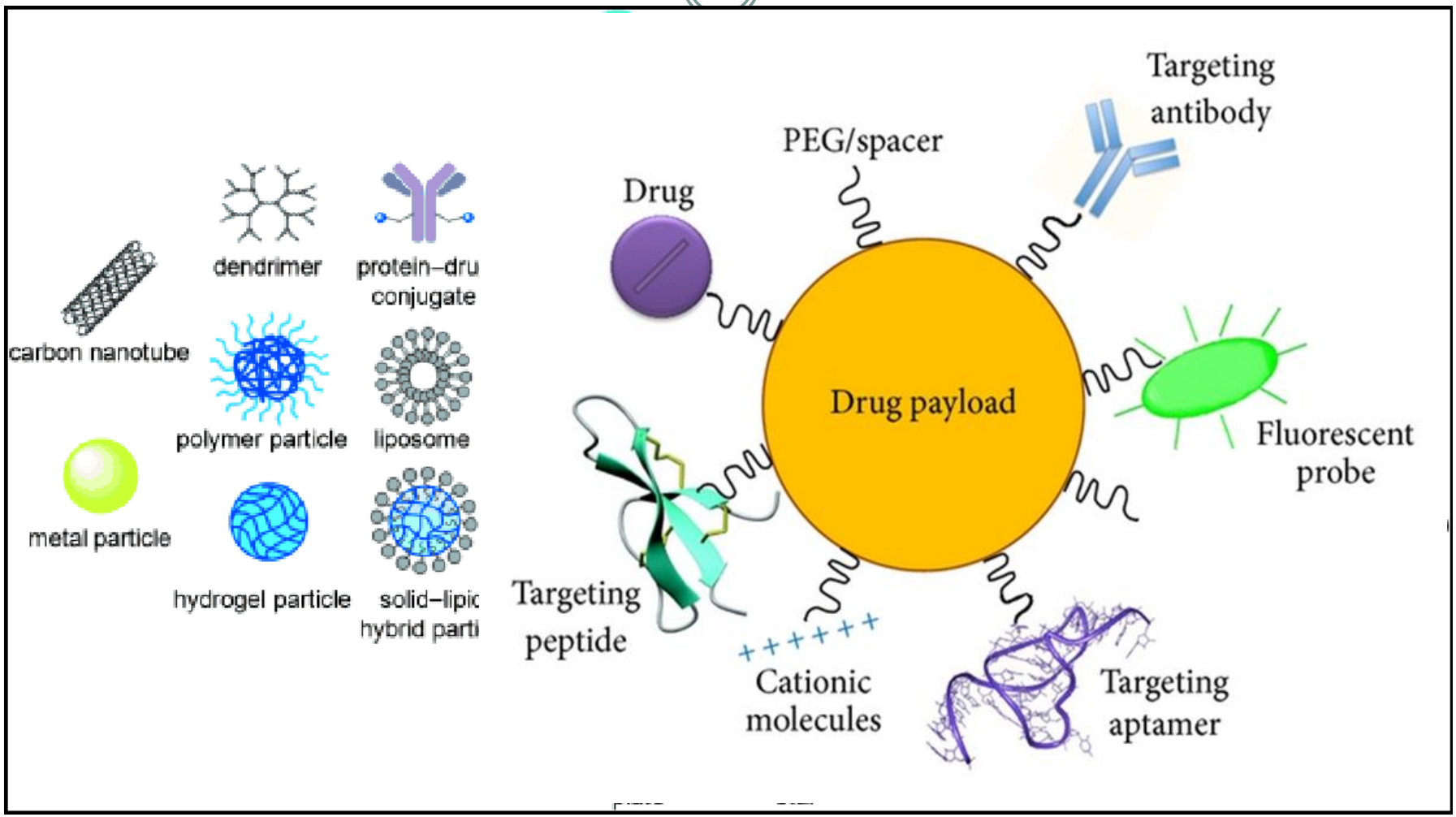
Targeted Drug Delivery

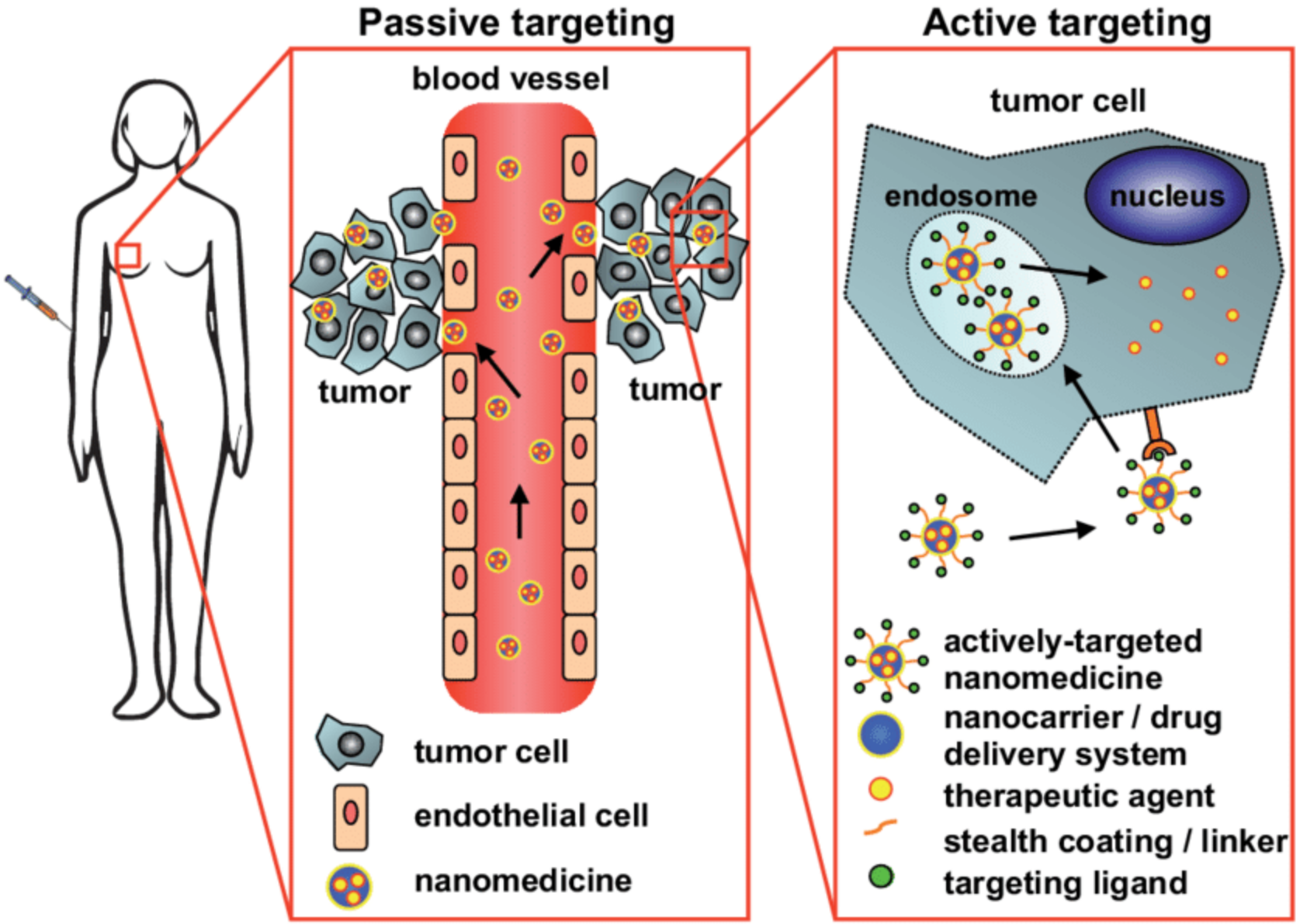
- Nanoparticles containing drugs are coated with targeting agents (e.g. conjugated antibodies).
- The nanoparticles circulate through the blood vessels and reach the target cells.
- Drugs are released directly into the targeted cells.



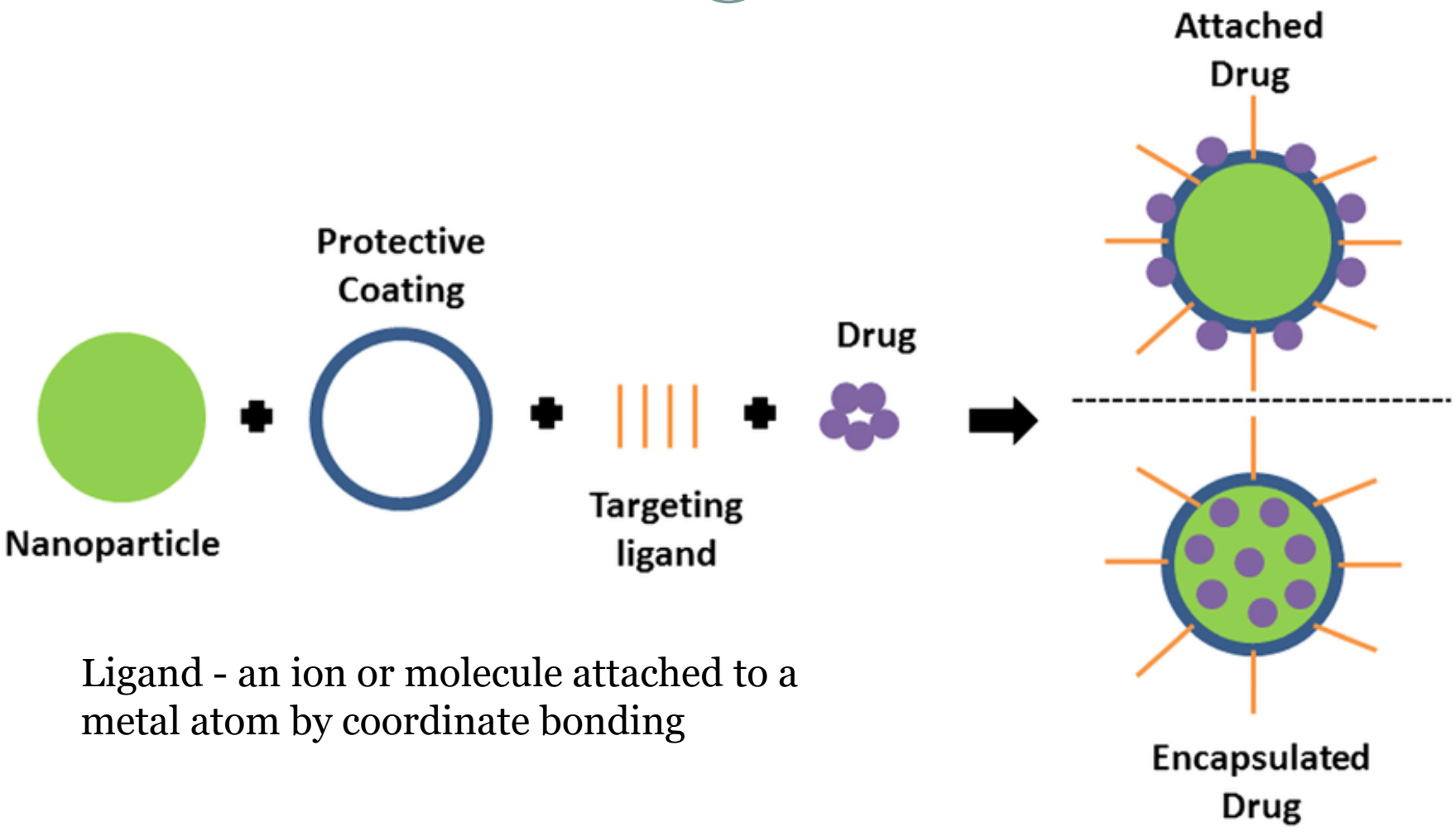
Nanoparticles

Nanoparticles

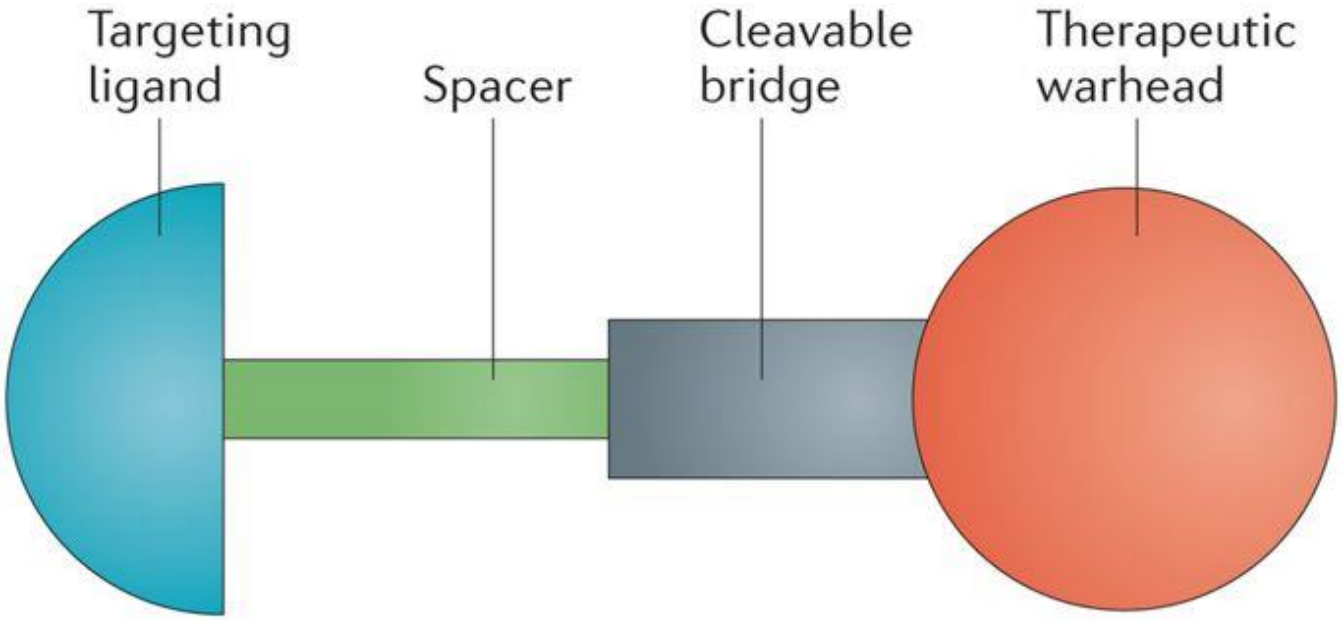


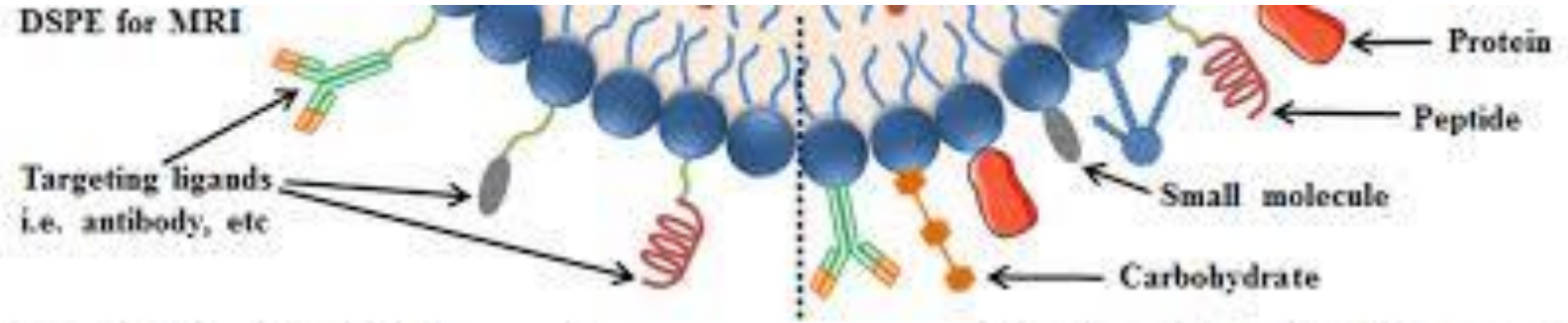

Passive targeting
blood vessel
tumor
tumor
tumor cell
endothelial cell
nanomedicine
Active targeting
tumor cell
endosome
nucleus
actively-targeted nanomedicine
nanocarrier / drug delivery system
therapeutic agent
stealth coating / linker
targeting ligand

Targeted Drug Delivery



Ligand - an ion or molecule attached to a metal atom by coordinate bonding





(D) Multifunctional liposome i.e. theranostic liposome

(C) Ligand targeted liposome

Regenerative Medicine

- Targeted Cell implantation.
- Biomimicking cell membranes.
- Polymers with programmable conformation.
- Control of implant rejections.

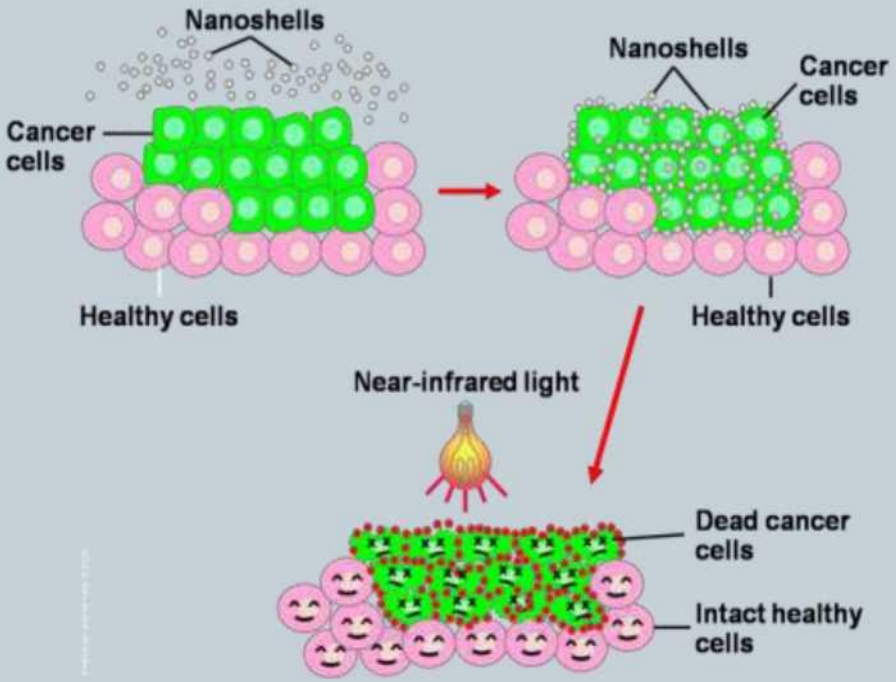
ELSA Compliance

- Nanomedicine touches familiar **Ethical, Legal and Social Aspects (ELSA) known from biomedical ethics such as** gap between diagnostics and therapy sensitivity of genetic information.

Nanotechnology in Health Care

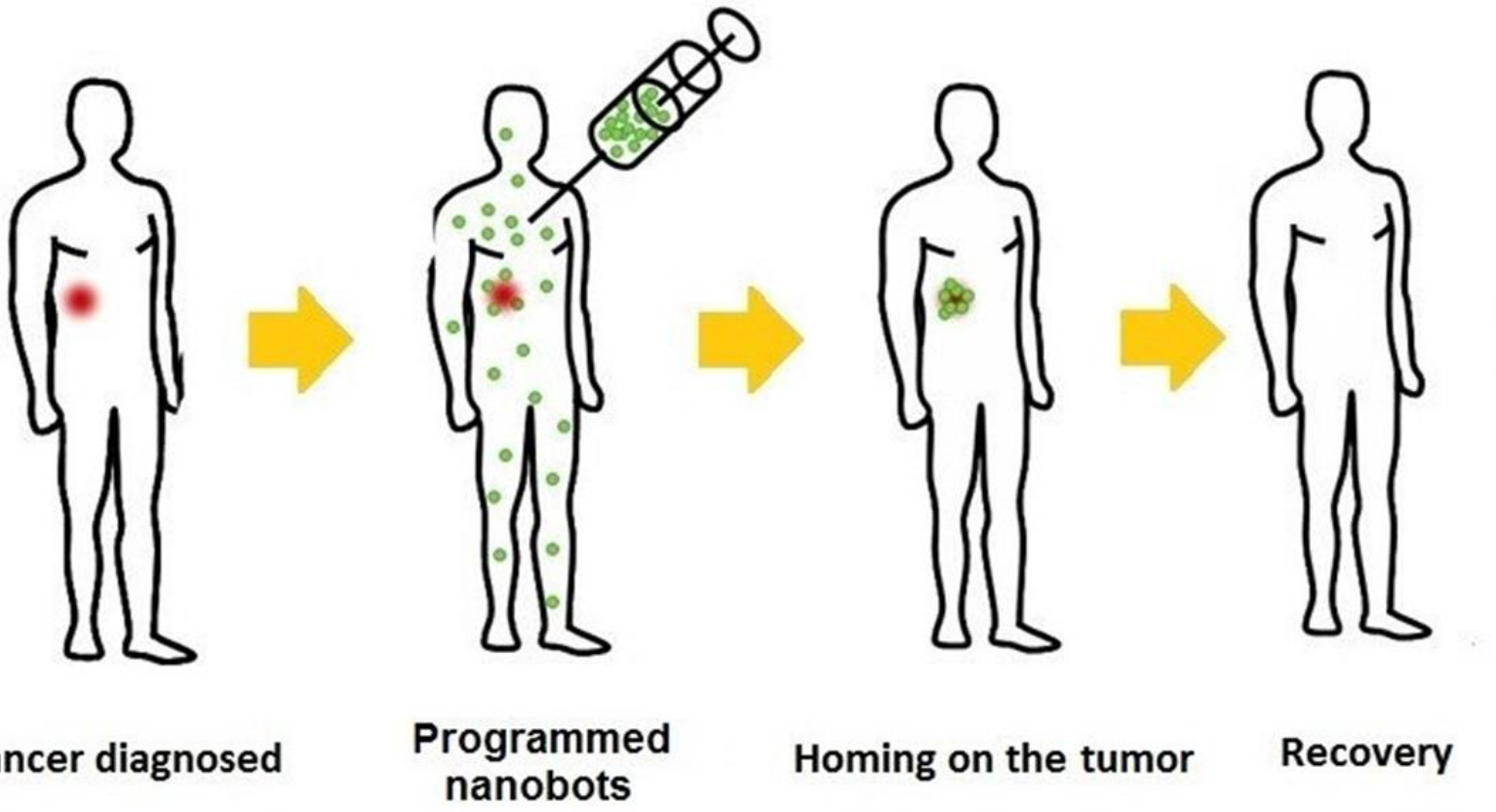
Thermal ablation of cancer cells

- Nanoshells have metallic outer layer and silica core
- Selectively attracted to cancer shells either through a phenomena called enhanced permeation retention or due to some molecules coated on the shells.
- The nanoshells are heated with an external energy source killing the cancer cells.

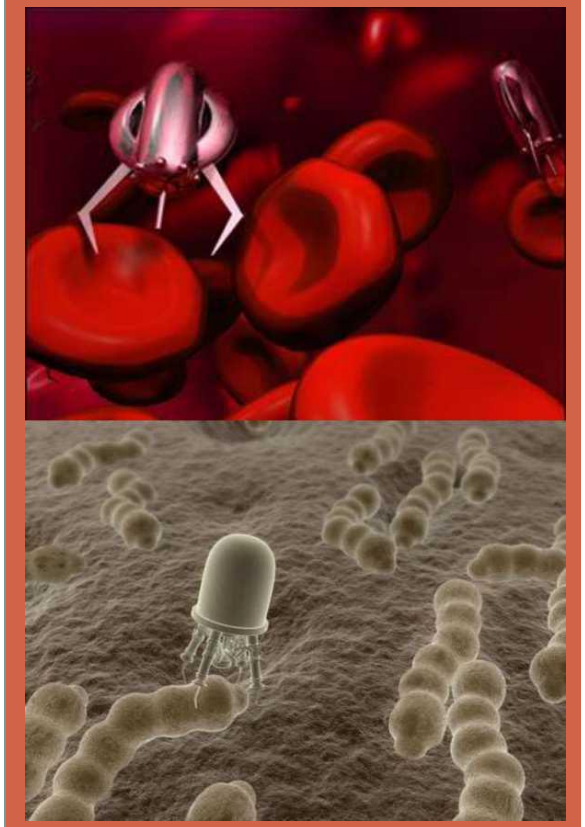


Thermal ablation of cancer cells assisted by nanoshells coated with metallic layer and an external energy source

Use of Nanobots in Treatment of Cancer Deseases

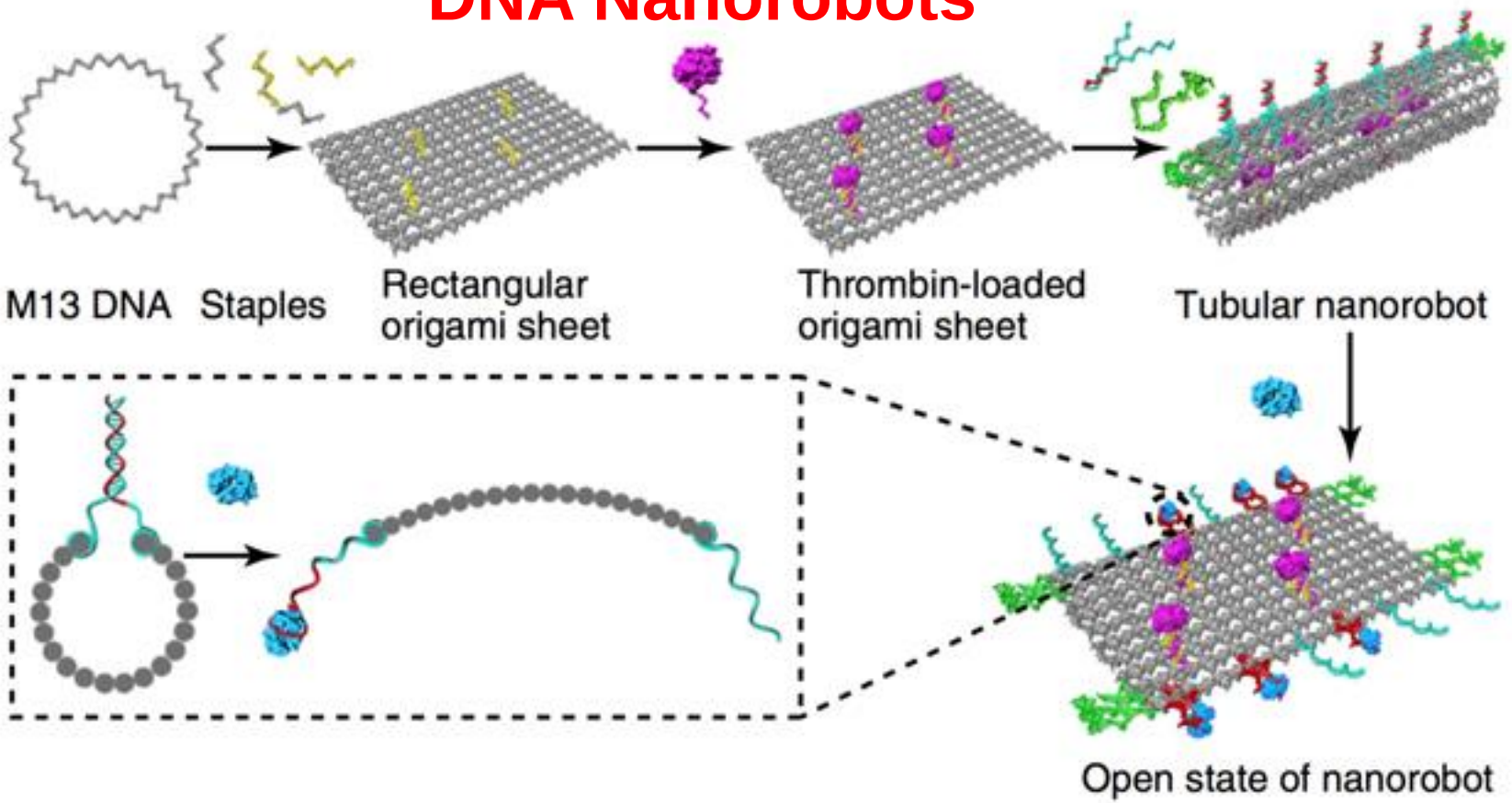


Nano-robotics



- Nano-robotics, although having many applications in other areas, have the most useful and variety of uses in medical fields.
- Potential applications include early **diagnosis** and **targeted drug delivery** for cancer, **biomedical instrumentation**, **surgery**, **pharmacokinetics**, **monitoring** of diabetes, and health care.
- Future medical nanotechnology expected to employ nanorobots injected into the patient to perform treatment on a cellular level.

DNA Nanorobots



- Using experimental mice with malignant tumors, we show how intravenously administered DNA nanorobots deliver thrombin specifically to blood-related tumor-associated vessels and cause intravascular thrombosis, resulting in tumor necrosis and inhibition of its growth (DNA nanorobots, Nature Biotechnology, 2018).

Miscellaneous Applications of Nanotechnology in Health Care

- Snapshots of the human body for better understanding of how it works.
- The workings of cells, bacteria, viruses etc can be better explored. The causes of relatively new diseases can be found and prevented.
- Restore vision. Genome sequencing can be made much easier. Biological causes of mental diseases can be monitored and identified. Simple curiosity can be answered.
- Tissue engineering" could also be done using nano-materials. Tissue engineering makes use of artificially stimulated cell proliferation by using suitable nanomaterial-based scaffolds and growth factors.
- Advances in nanotechnology-based tissue engineering could also lead to life extension in humans and other animals.

Nanotechnology is Potential Science

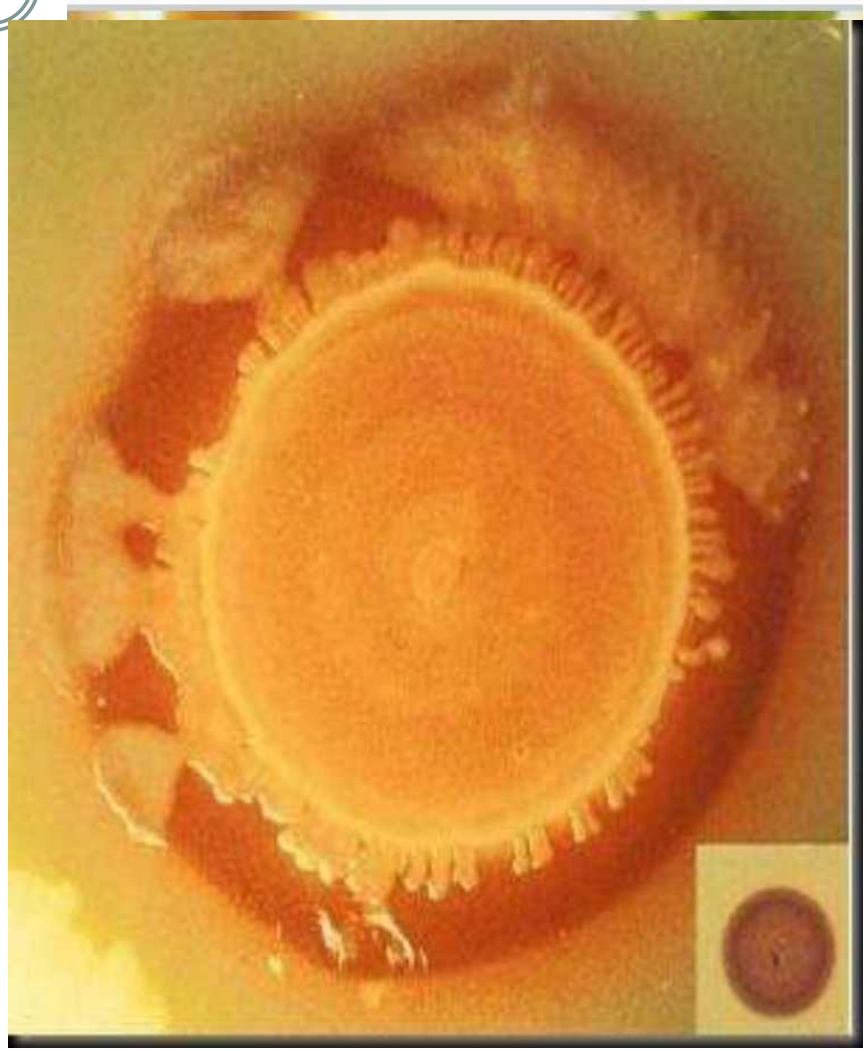
Nanotechnology has the potential to create many new materials and devices with a vast range of applications, such as in medicine, electronics, biomaterials and energy production.

Nanotechnology in Food Industry

- A microscopic biological sensor that detects Salmonella bacteria in lab tests.

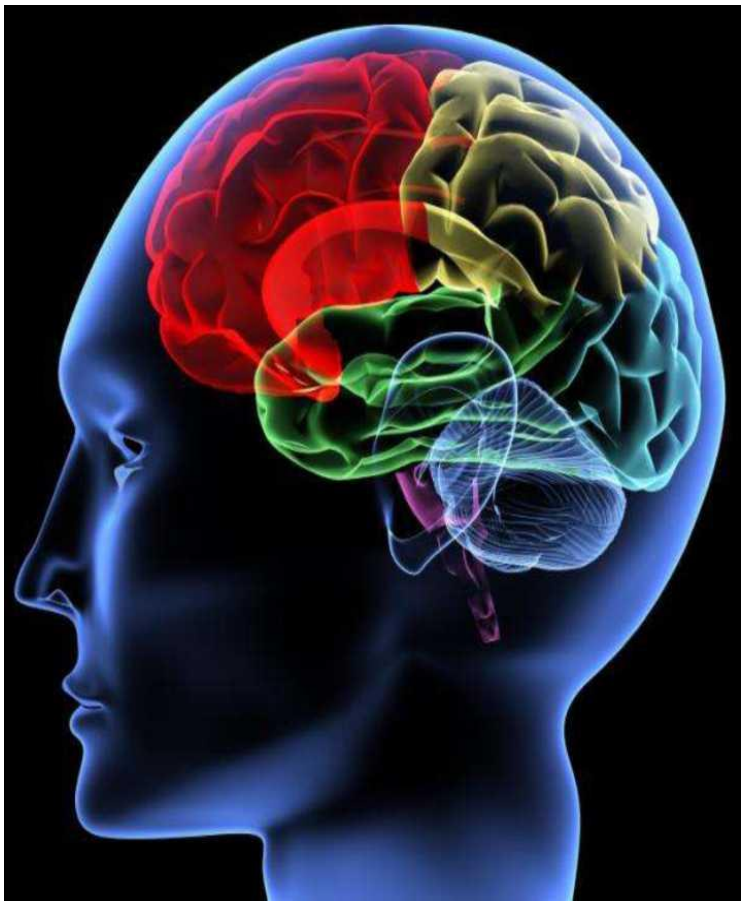
It has been developed by an Agricultural Research Service (ARS) scientist and university colleagues.

The sensor could be adapted to detect other food borne pathogens as well.

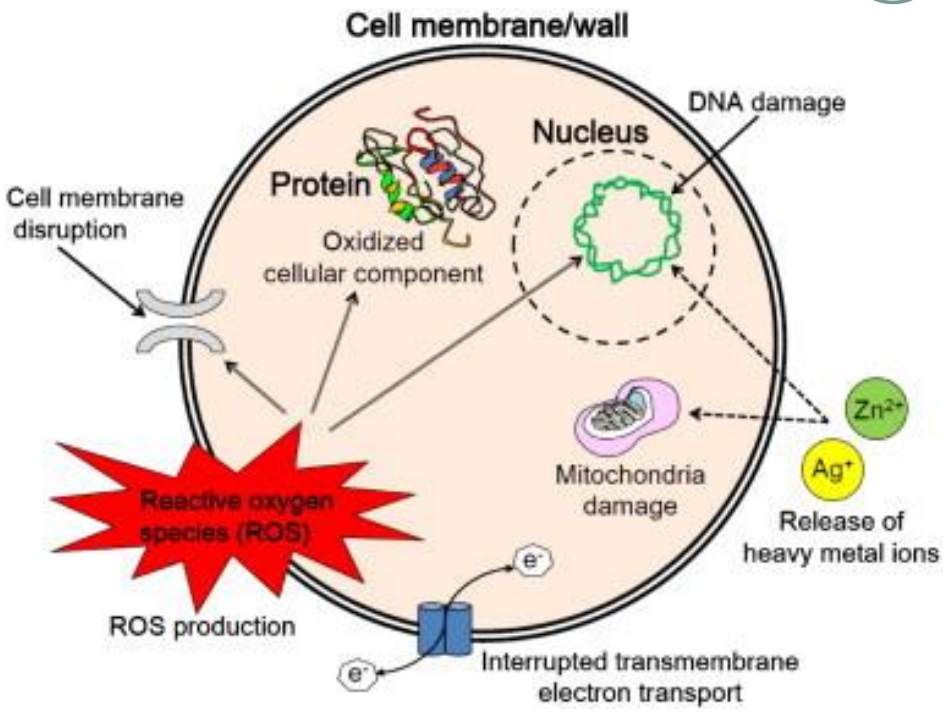


Nano Technology Helps Particles Pass Through Blood Brain Barrier

- IBN's (the Institute of Bioengineering and Nanotechnology) peptide nanoparticles, on the other hand, contain a membrane-penetrating component that enables them to pass through the blood brain barrier to the infected areas of the brain that require treatment.



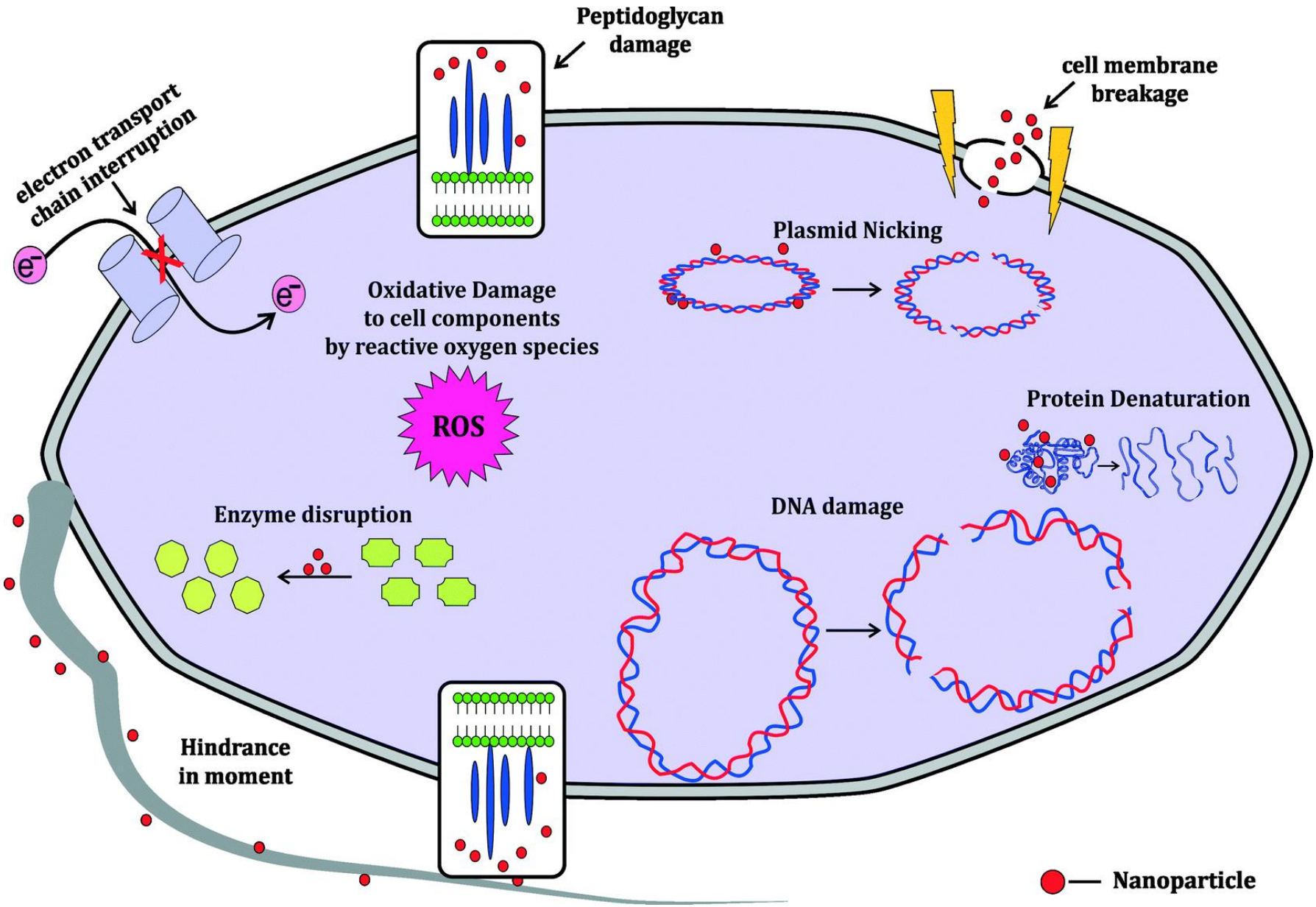
Nanoantibiotics Can Penetrate Blood Brain Barrier



Reactive oxygen species (**ROS**) are formed as a natural byproduct of the normal metabolism of oxigen and have important roles in cell signalization and homestasis.

The ability of IBN's peptide nanoparticles to traverse the blood brain barrier offers a superior alternative to existing treatments for brain infections.

The brain membrane is impenetrable to most conventional antibiotics because the molecular structure of most drugs is too big to enter the membrane.


Peptidoglycan damage
cell membrane breakage
electron transport chain interruption
e-
e-
Plasmid Nicking
Oxidative Damage to cell components by reactive oxygen species
ROS
Protein Denaturation
Enzyme disruption
DNA damage
Hindrance in moment
Nanoparticle

Nanoparticles Overcome Drug Resistance

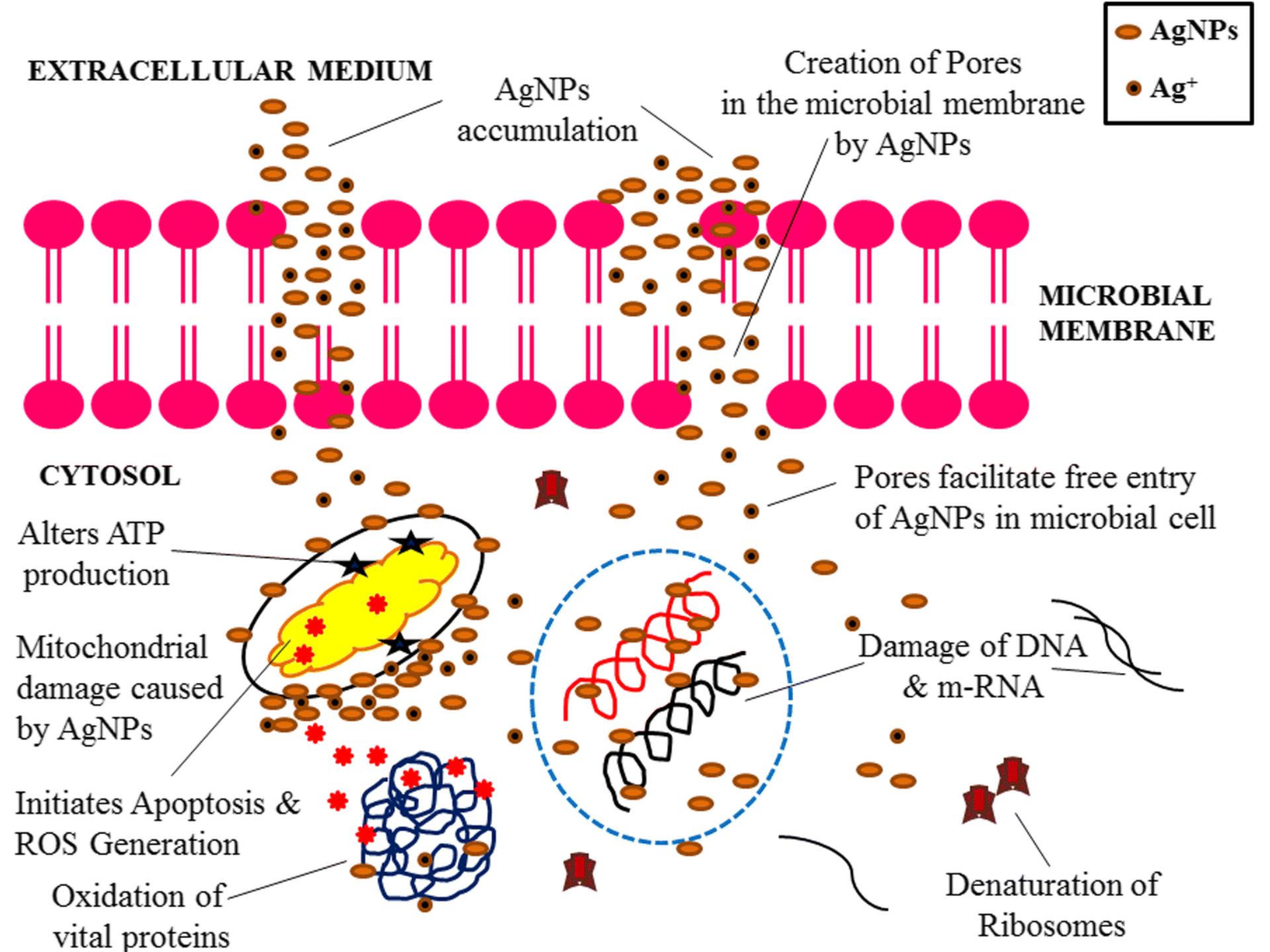
The treatment of multi drug-resistant bacterial infections is a great challenge for medicine. IBN's peptide nanoparticles provide doctors with a novel means of treating infections that do not respond to conventional antibiotic.

The Most Serious Infections & Oligodynamic Silver

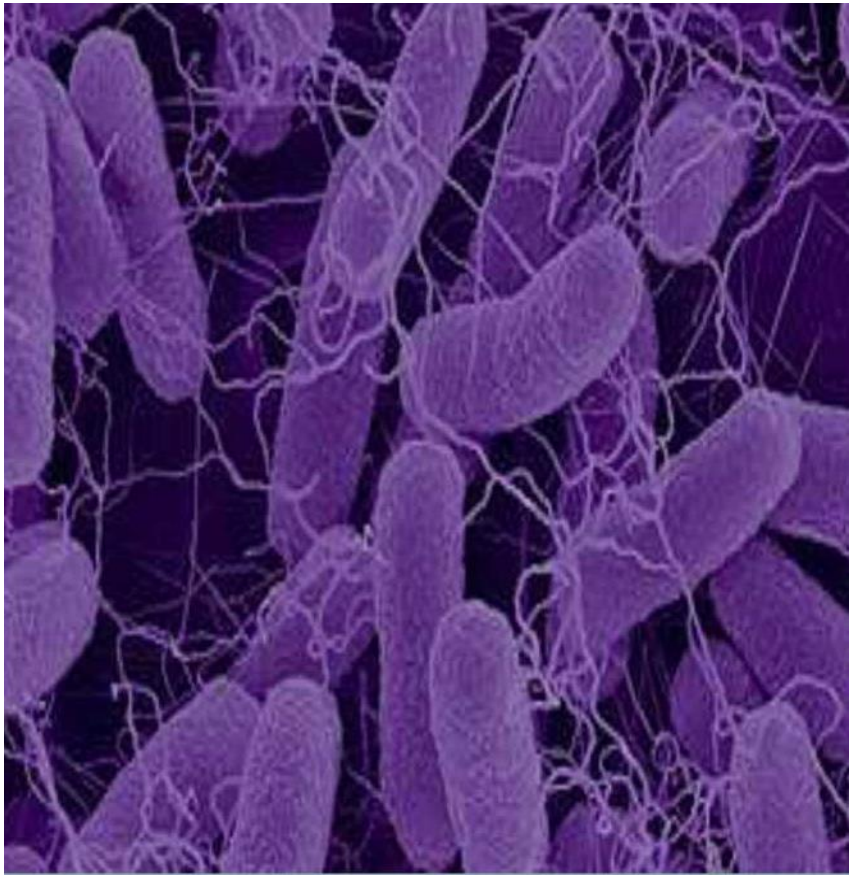
Silver ions can easily reach into the nucleus of the germ, where its vital gene pool is located. Once silver ions combine with these genes, the genes become paralyzed, and the germ cannot replicate itself.

Most recently, another researcher found that silver, when tied to oxygen, can actually electrocute the germ which has turned out to be a powerful way to destroy viruses such as HIV!

It is very difficult to imagine that germs can develop resistance to the onslaught made possible with UPOSH (Uniform Picoscalar Oligodynamic Silver Hydrosol) when it is properly delivered to the locations of the infection.


AgNPs
Ag+
EXTRACELLULAR MEDIUM
AgNPs accumulation
Creation of Pores in the microbial membrane by AgNPs
MICROBIAL MEMBRANE
CYTOSOL
Pores facilitate free entry of AgNPs in microbial cell
Alters ATP production
Mitochondrial damage caused by AgNPs
Damage of DNA & m-RNA
Initiates Apoptosis & ROS Generation
Oxidation of vital proteins
Denaturation of Ribosomes

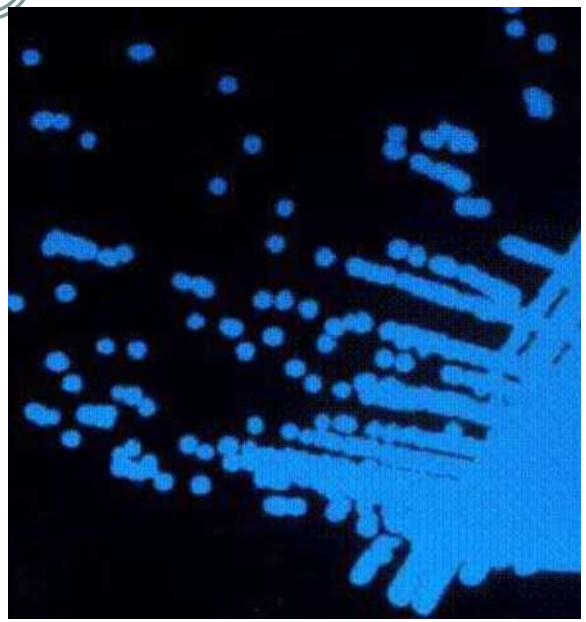
Stopping Bacterial Infections Without Antibiotics



- Nanoengineering could prevent bacterial infections using tiny biochemical machines nanofactories – that can confuse bacteria and stop them from spreading, without the use of antibiotics.

Nanomethods can alter Quorum Sensing

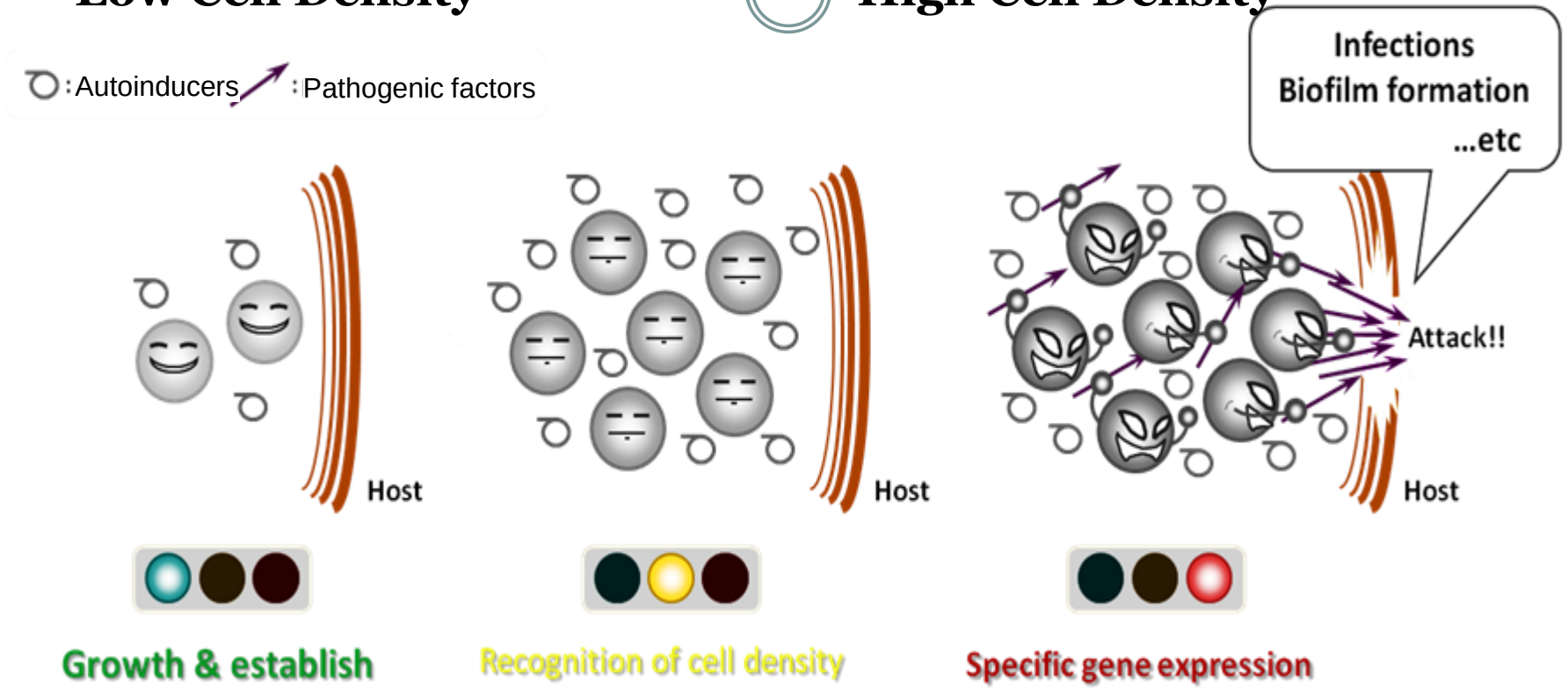
- The nanofactories could trick the bacteria into sensing a quorum too early. Doing so would trigger the bacteria to try to form an infection before there are enough bacterial cells to do harm. This would prompt a natural immune system response capable of stopping them without the use of drugs.



Autoinducers are signaling molecules that are produced in response to changes in cell-population density. As the density of quorum sensing bacterial cells increases so does the concentration of the autoinducer.

Quorum Sensing

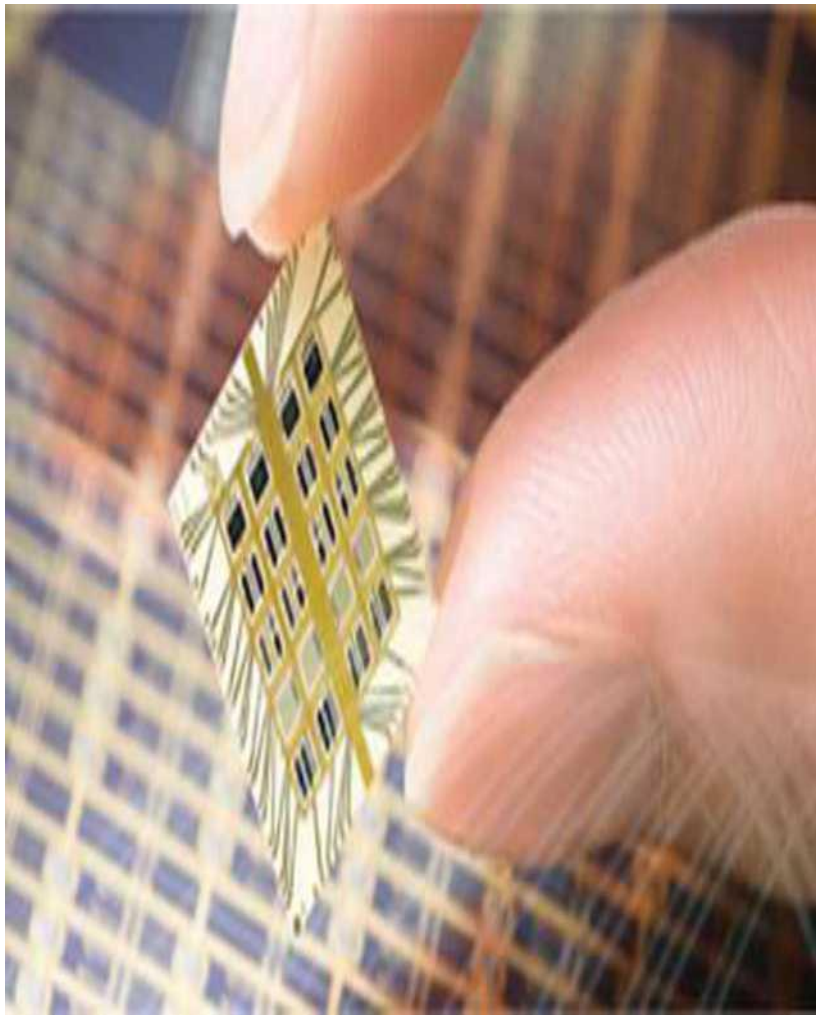
Low Cell Density — **High Cell Density**



Cell density dependent gene expression in quorum sensing
(e.g. virulence expression)

Nanotechnology in Health Care

Nanotechnology offers tools and techniques for more effective detection, diagnosis and treatment of diseases.



Detection and Diagnosis

Lab on chips help detection and diagnosis of diseases more efficiently

Nanowire and cantilever lab on chips help in early detection of cancer biomarkers.

Nano-medicine in Cancer Study

- To study cancer ***at molecular level***
- To understand the relationship between gene mutation and the cause of cancers.
- To identify tumor markers for early diagnosis of different cancers.
- Collect clinical information in order to find out which treatment has best result for patients representing different ***gene expression pattern for the same cancer.***
- To provide Oncologists with personal gene information in order to select most suitable ***personalized medicine and treatment for each individual patient.***

PRIORITY AREAS on Nanomedicine

- **DNA Vaccines for parasitic, bacterial and viral diseases**
- **Oral and pulmonary routes for systemic delivery of proteins and peptides**
- **Nanotechnology in Tissue Engineering**

Impacts of Human Genome Research to Medicine

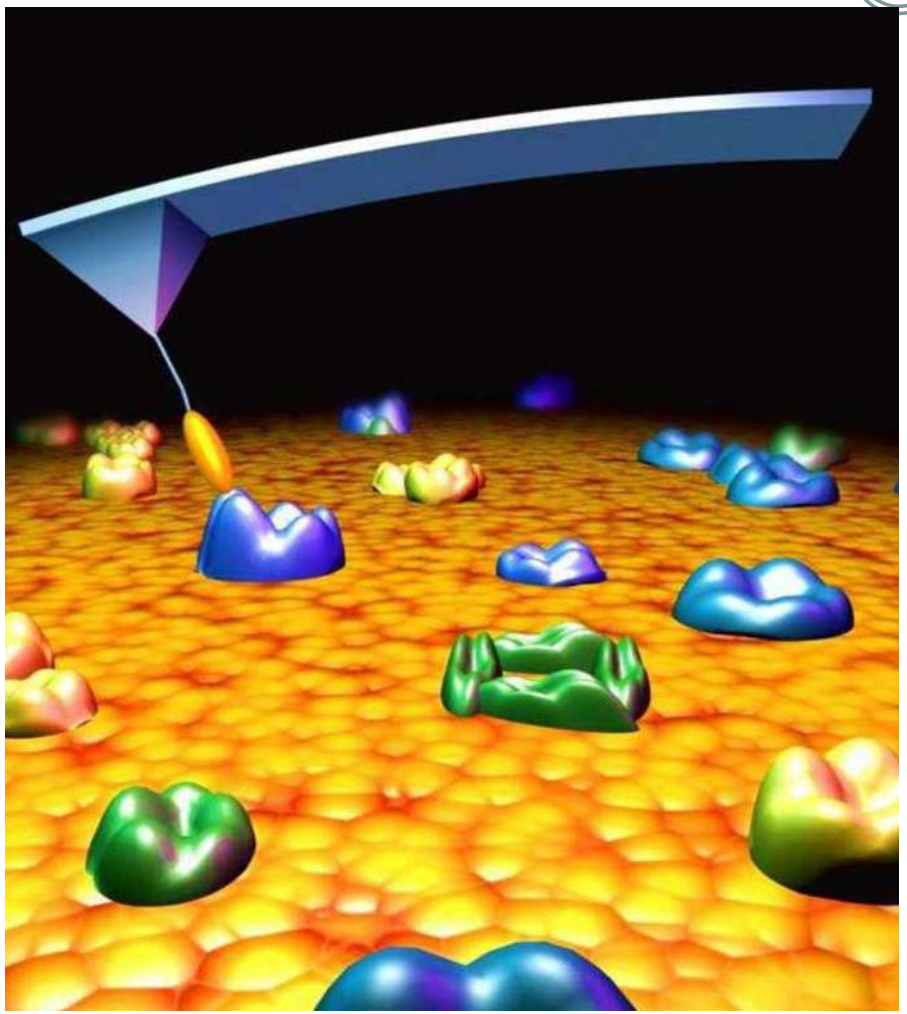
Enter the era of personalized medicine.

- Genetic profiling for cancer risk - to identify the molecular changes of genes that underlie the high risk of cancer.
- Precise diagnosis of the special types of cancer
- Pro-active cancer management - life-style modification and monitoring.
- Pharmaco-genomic profiling for drug responses - to identify the genetic predisposition for drug responses to assist drug selection, optimize efficacy and minimize toxicity.
- Gene therapy development.

Nanotechnology and Water Microbiology

Nanotechnology offers the potential of novel nanomaterials for the treatment of surface water, groundwater and wastewater contaminated by toxic metal ions, organic and inorganic solutes and microorganisms. At the present time many nanomaterials are under active research and development.

Nanomicrobiology and Atomic Force Microscopy

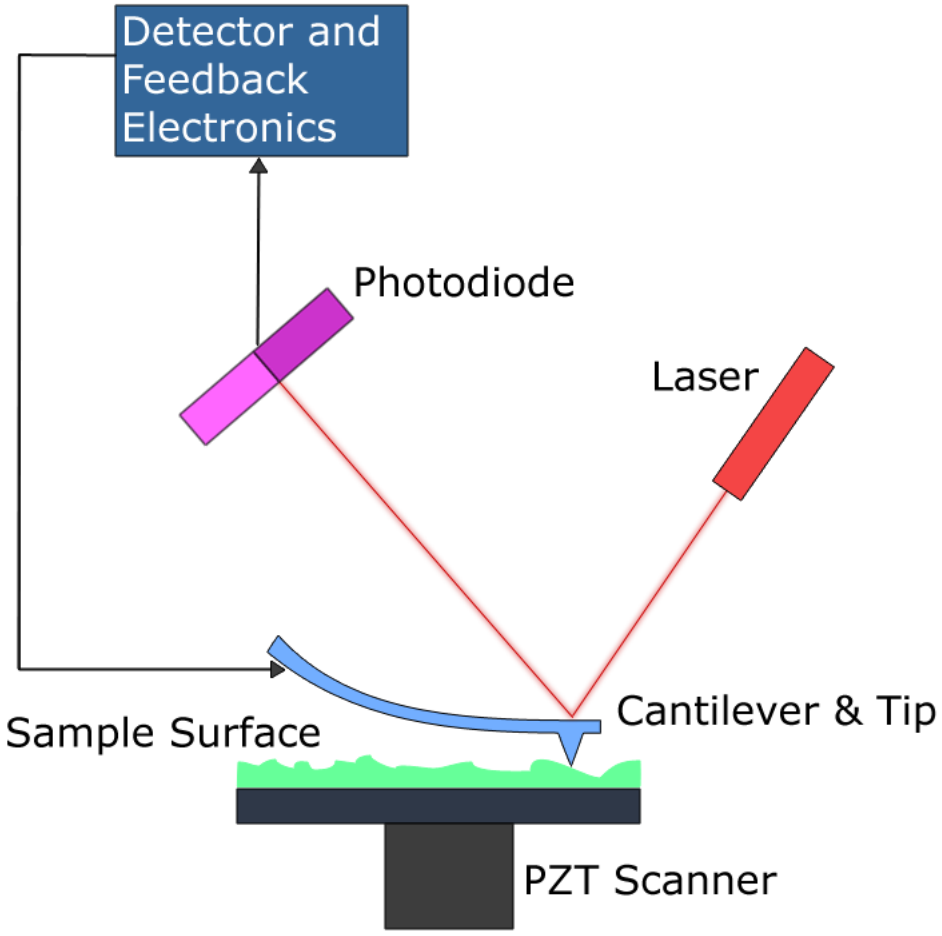


Nanoscience and microbiology, the nanoscale analysis of microbial cells using atomic force microscopy (AFM) is an exciting, rapidly evolving research field.

Over the past decade, there has been tremendous progress in use of AFM to observe membrane proteins and live cells at high resolution.

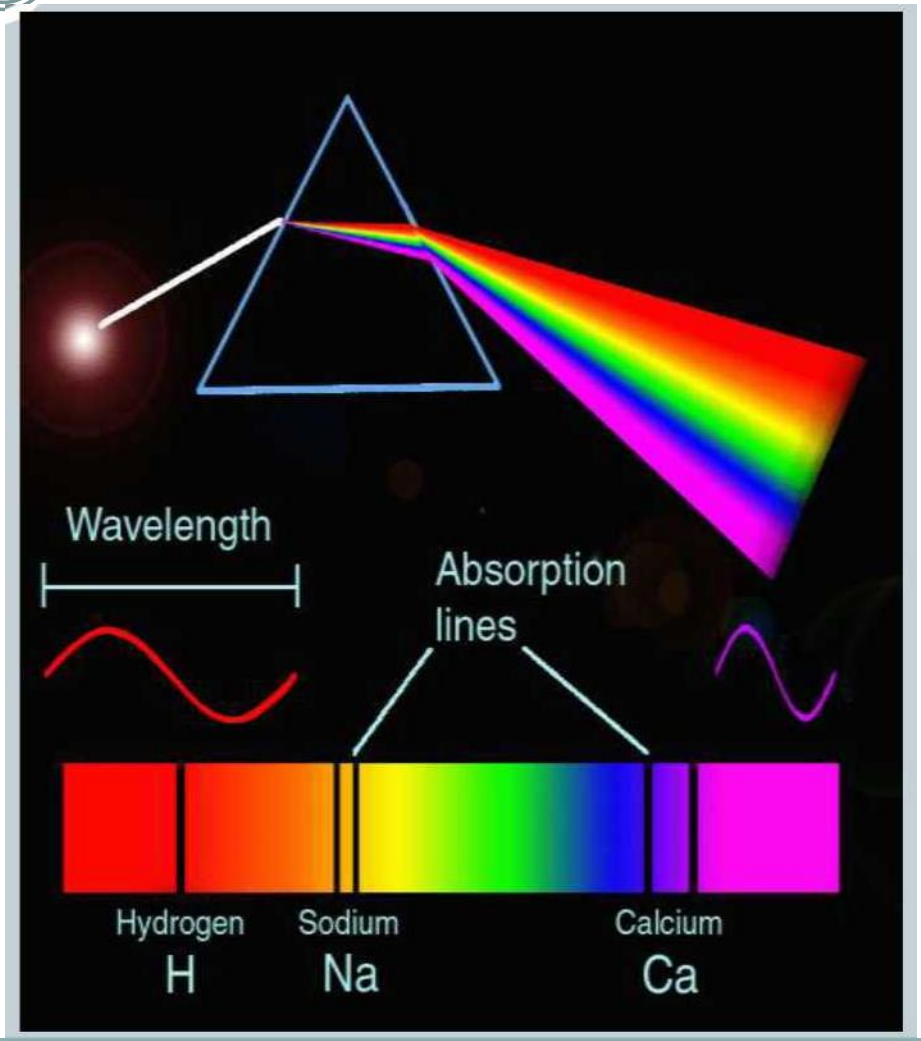
Atomic Force Microscopy

Atomic force microscopy (**AFM**) or scanning **force microscopy** (SFM) is a very-high-resolution type of scanning **probe microscopy** (SPM), with demonstrated resolution on the order of fractions of a nanometer, more than 1000 times better than the optical diffraction limit.

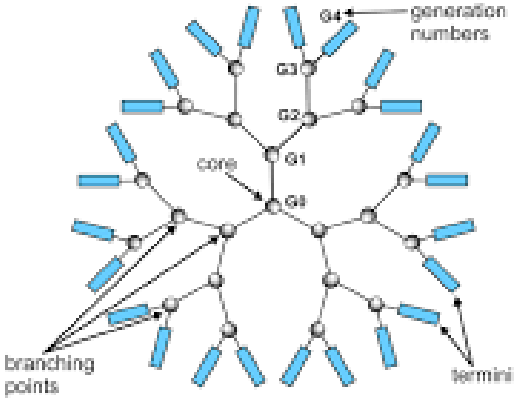


Spectroscopy and Nanotechnology

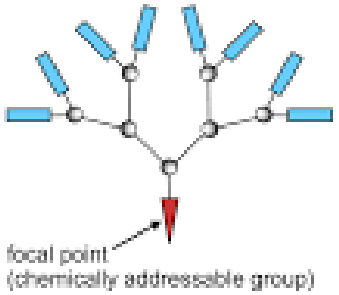
- Advances have also been made in applying force spectroscopy to manipulate single membrane proteins, to map surface properties and receptor sites on cells and to measure cellular interactions at the single-cell and single molecule levels.



Dendrimers and Nanotechnology



DENDRIMER



DENDRON

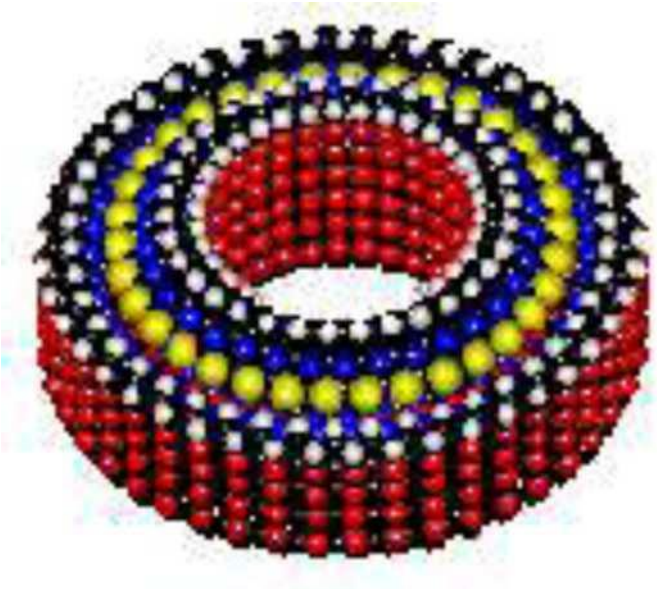
Dendrimers are another interesting and powerful use of nanotechnology in medicine.

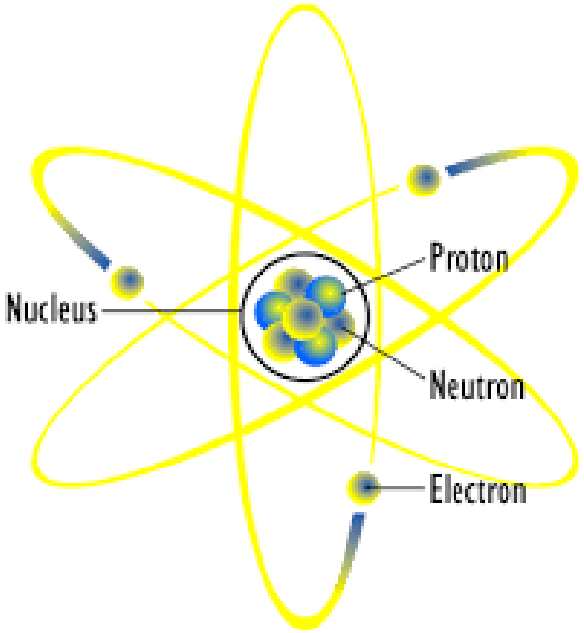
Dendrimers are nanostructured synthetic molecules with a regular branching structure projecting from a central core.

Dendrimers may act as effective agents for delivering DNA into cells during gene therapy.

While viral vectors typically trigger an immune response, in principle, Dendrimers should not.

Medicine May Become Atomic Medicine





Ultimate Nanotechnology would be to build at the level of one atom at a time and to be able to do so with perfection.

Possible Concerns on Nanoparticles ?

Experts report smaller particles are more bioactive and toxic.

Their ability to interact with other living systems increases because they can easily cross the skin, lung, and in some cases the blood/brain barriers.

Once inside the body, there may be further biochemical reactions like the creation of free radicals that damage cells.

Nanoparticles Can Be Industrial Hazard?

Highest at risk are workers employed by manufacturers producing products that contain nanoparticles.
The National Institute for Occupational Safety and Health (NIOSH) reports over 2 million Americans are exposed to high levels of nanoparticles and they believe this figure will rise to 4 million in the near future.

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Social Issues of Nanotechnology in Medicine

- How many nanotechnology implementations in the human body (to protect against diseases and to offer "enhanced immunization") would it take for a human to no longer remain human?
- Fear of decrease the gap between humans and robots/computers
- Who will have control over nanomedicinal technology?
- Will this possesion/control render a bias for treatment and use on basis of ethnicity, color and race, not to mention political standings and viewpoints?

Economical Issues of Nanotechnology in Medicine

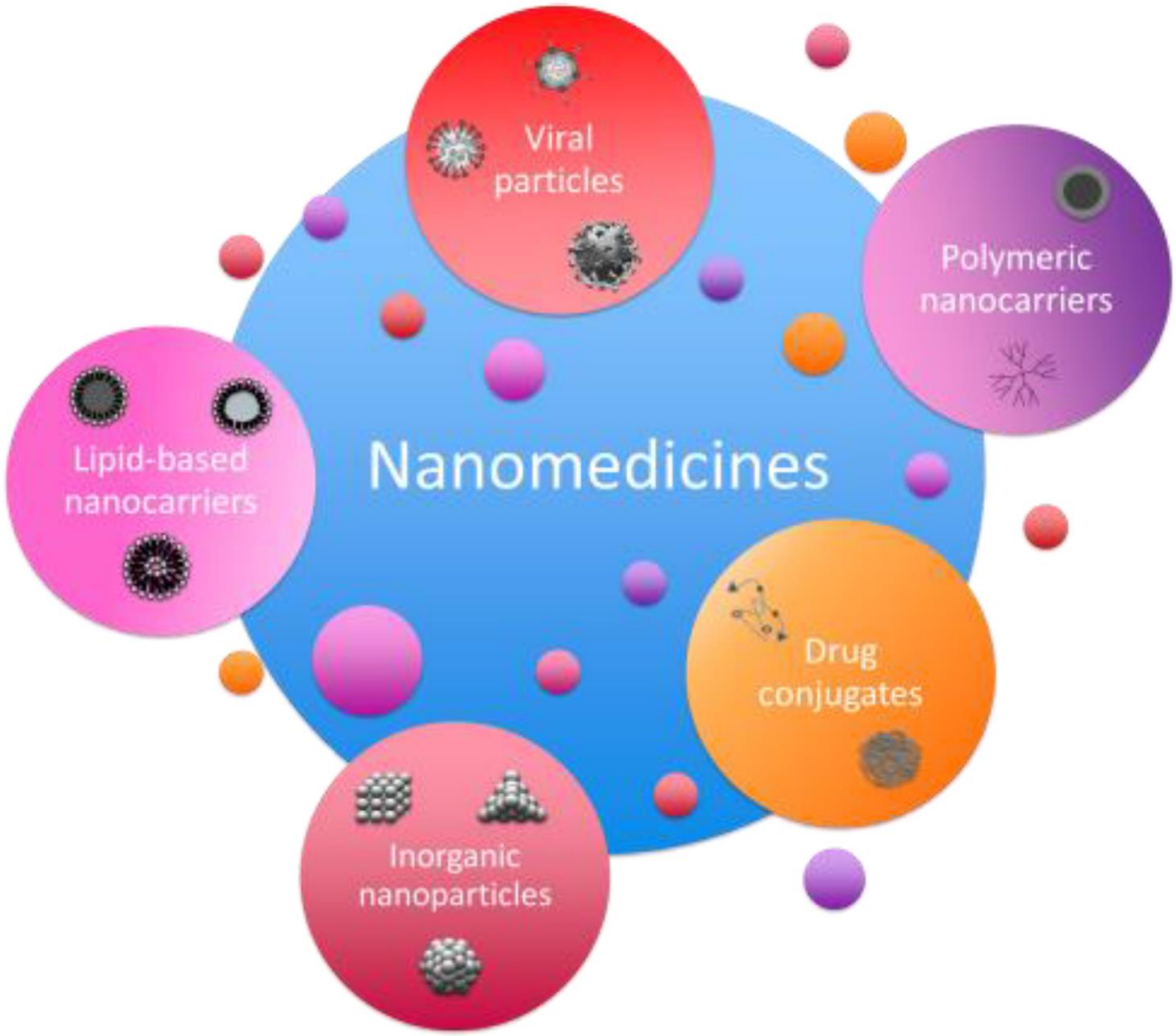
- Will "nanomedicine" widen the gap between the rich and the poor in its initial stages like many disruptive technologies of the past?
- Is there a certain patent for nanomedicine? How much will the ideas of nanomedicine sell for?
- Does nanomedicine favor the rich or the poor? Will the poor get equal access to nanomedicine and other nano-medicinal technologies?

Ethical Issues of Nanotechnology in Medicine

- Bioethical researchers believe that nanomedicine could be manipulated to harm the human body rather than healing it.
- How would the use of a technology that can't be seen be regulated? What if, they say, the guiding system on the medicine malfunctions and takes the medicine to the wrong part of the body, such as the brain?
- What if the nanomedicine technology is used for terrorism purposes? Particles that can't be seen or easily controlled would enter the body and deliver harmful substances such as toxins.
- Will the materials used for the nano-medicinal technologies be non-toxic and eco-friendly?

Conclusion

- There certainly are more questions than adequate answers.
- Every technology made till date has been made in hopes of improving or benefiting human life. However, it is only misuse of technology that impacts humankind in a negative way.
- Scientists are currently researching better electronics and safe materials for nanomedicine alongside nanomedicine itself. The technology is being regulated by the government with the primary concern being safety of the people.
- We can certainly say that nanomedical technology, if used carefully and meticulously, will guarantee great benefits.



Thank for your attention