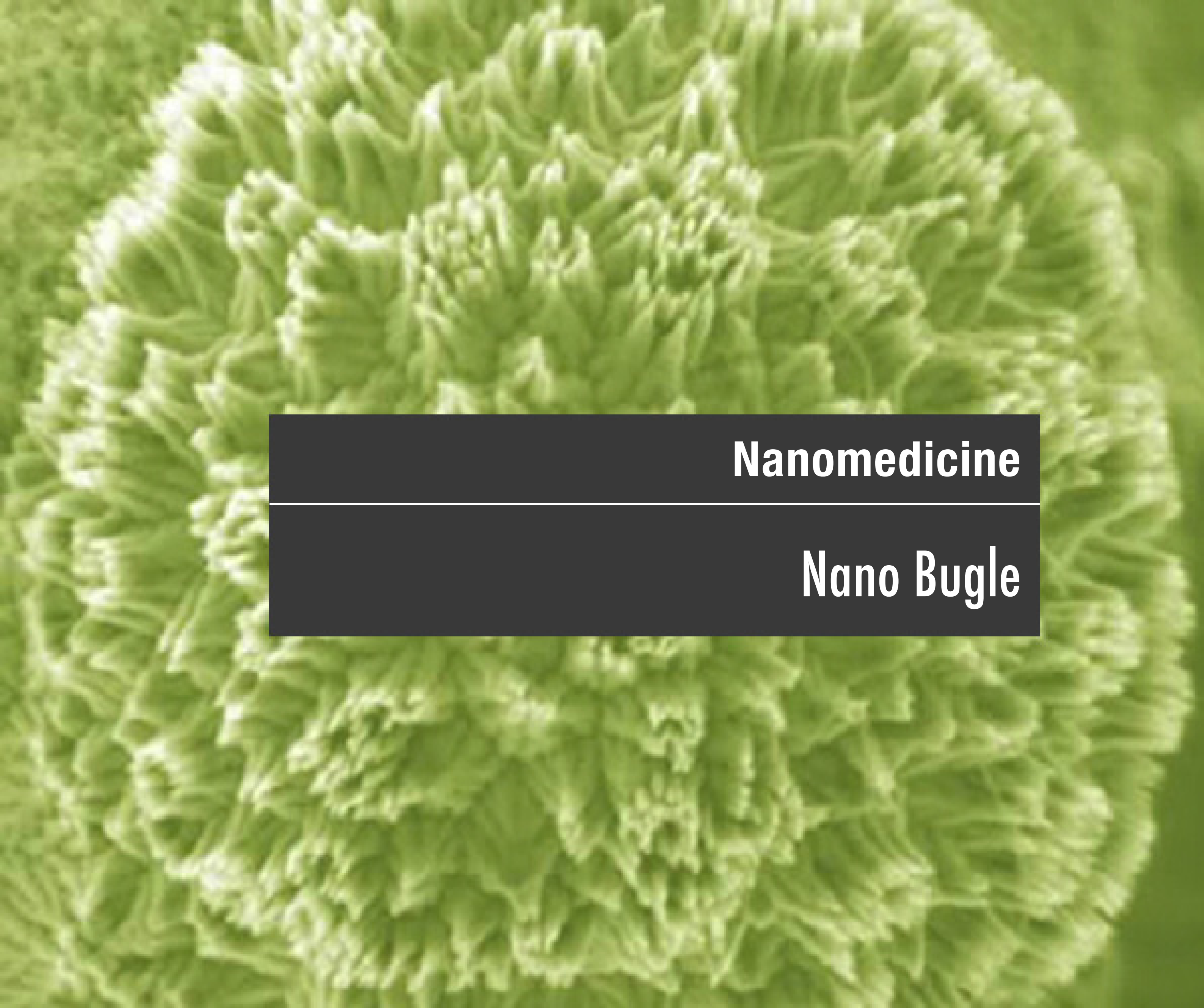


Nanomedicine

Nano Bugle

Nanomedicine

Introduction

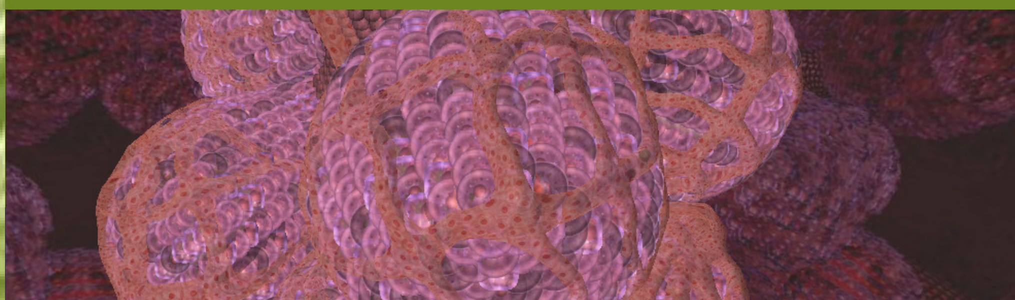
The most advanced machines at the nanoscale are existing cells that regulate and control biological systems and understanding of these cells is one of the major issues in research.

A cell is the unit is the smallest biological unit and the key that is built on the rest. It is a system of molecules and nano-machines.

The full understanding of the molecular nanostructures is vital to understand the cell. Proteins are a typical example of molecular nanostructures. Have many highly specialized functions, and take part in most of the biological activities, such as sensory, metabolic, molecular transport processes and information.
In the biological world there are many biological nanoscale dimensioned structures, devices and machines on which researchers in the field of nanoscience and nanotechnology are concerned, firstly to understand and then to emulate them.

At the present, the synthetic materials used in biomedicine are not a substitute for natural materials; they are just a poor substitute or part thereof.

The use of synthetic materials in biomedicine is more successful when implementing a function that does not exist in nature. For example, the drug delivery and the disruption of the relaxation time of protons in water to improve the contrast in magnetic resonance imaging.



Nanomedicine

What is Nanomedicine?

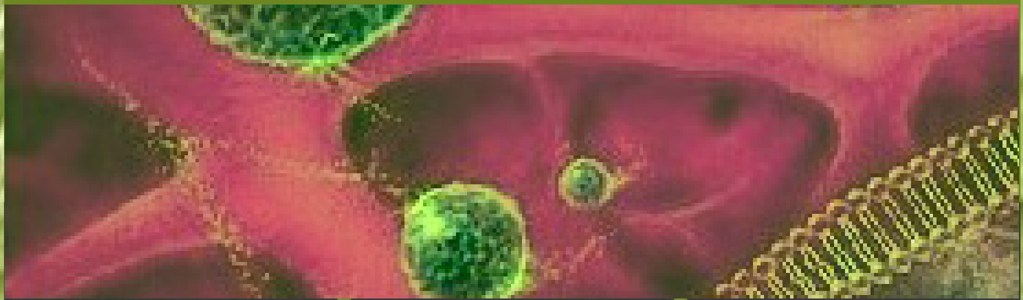
Nanomedicine is at the boundaries between physics, chemistry and biology.

It is originated from the imaginative idea that robots and other machines would be design and build connected to feed into the human body with the intent to repair malignant cells at the molecular level.

Nanomedicine includes those medical practices, including prevention, diagnosis and therapy, which require technology-based interactions between the human body and materials, structures and devices whose properties are defined at the nanoscale.

Advances in medicine caused by the entry of nanotechnology are concentrated mainly on improvements in:

Diagnostic methods
Drug delivery
Regenerative medicine



Nanomedicine

Analytical techniques and diagnostic tools

Currently the diagnosis of certain diseases is possible only when the disease is in a too advanced condition.

The aim of nanotechnology is applied to achieve an early diagnosis, with one or very few molecules or cells.

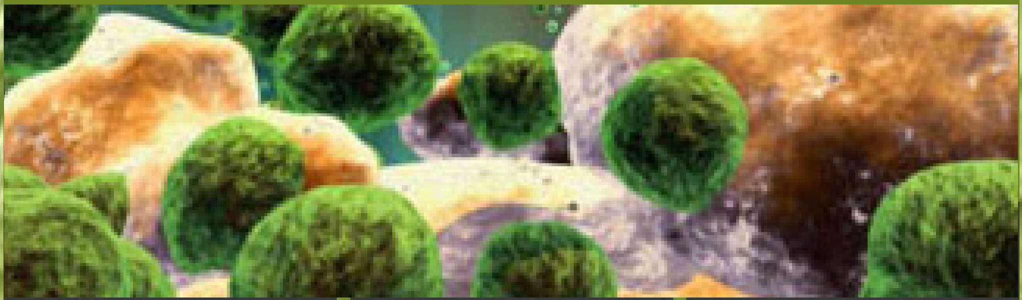
The various analytical techniques and diagnostic tools can be grouped into two major groups:

In vitro diagnostic devices, including:

Biosensors
Gene, proteins, cell
Microarrays
Lab-on-a-chip (LOAC)

Diagnostic imaging:

Optics, spectroscopy and fluorescence
Nuclear imaging techniques
MRI
Proximity Microscopy (STM, AFM)
Electron microscopy (SEM, TEM) and electronic tomography
Ultrasound
Tracer and contrast agents
Quantum dots
Magnetic and Supermagnet Nanoparticles



Nanomedicine

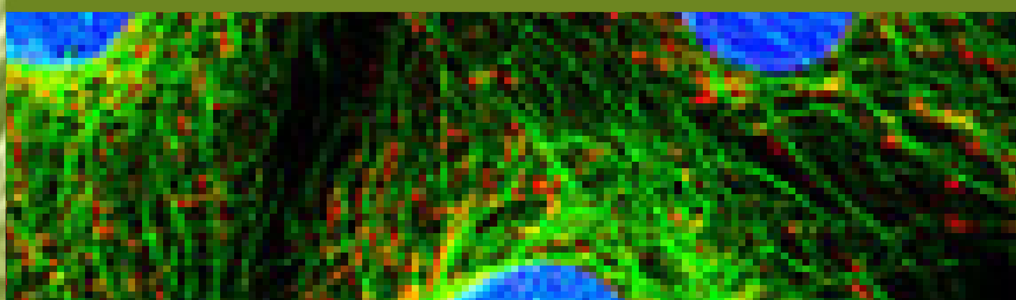
In vitro diagnostic devices

Biosensors

They can recognize the presence, activity or concentration of a biological molecule. The use of nanotechnology allows greater sensitivity, speed and fewer shows in biosensors. By using fewer amount of sample it raises patient sampling methods less traumatic and less invasive. Thanks to the biosensors, healthcare professionals can get profit from simultaneous measures of multi clinical parameter using a simple, effective and accurate test. Biosensors are suitable for high-performance scanning High Throughput Screening (HTS), as the search for disease in several samples or the search of several diseases in a sample.

Biochip or DNA microarray

It is a series of oligonucleotides or DNA fragments anchored to a support with a high spatial density of fragments to allow the simultaneous analysis of thousands of genes. The main applications of DNA microarrays on human health are the monitoring of gene expression, the search for active compounds, personalized medicine and disease prediction.



Nanomedicine

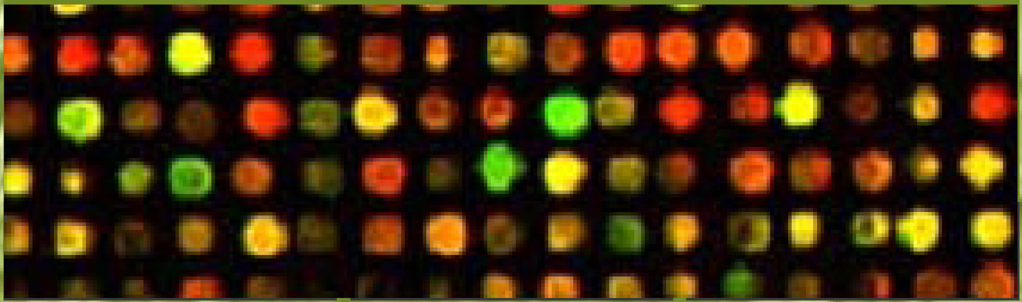
In vitro diagnostic devices

Protein Microarrays

These are anchored in the antibodies libraries support for the binding of specificity, affinity and abundance of proteins in a complex sample search.
It is also possible anchoring functionally active proteins for the observation of biochemical activities of thousands of proteins, such as interactions with other substrates: proteins, DNA and small molecules. Great potential for application in basic research in molecular biology, the search for therapeutic targets and identification of disease markers.

Cell chips

They are the latest development in the technology of microarrays. Its most important applications are the identification of markers of disease, toxicological analysis and the search for pathogens.



Nanomedicine

In vitro diagnostic devices

Lab-on-a-chip devices

They allow the integration of sample preparation, purification, storage, mixing, detection and other functions within a chip. They were developed from advances in microsystems technology and the field of micro fluidic devices, which includes the design of devices that use microscopic sample volumes. They use a phenomena combination: pressure electro osmosis, electrophoresis and other mechanisms to move samples and reagents through microscopic channels and capillaries. The use of these devices provides benefits such as analysis of samples very quickly and in very small volumes, the high degree of automation, cost savings from the low consumption of reagents and samples and they are portable and disposable.

Nanomedicine

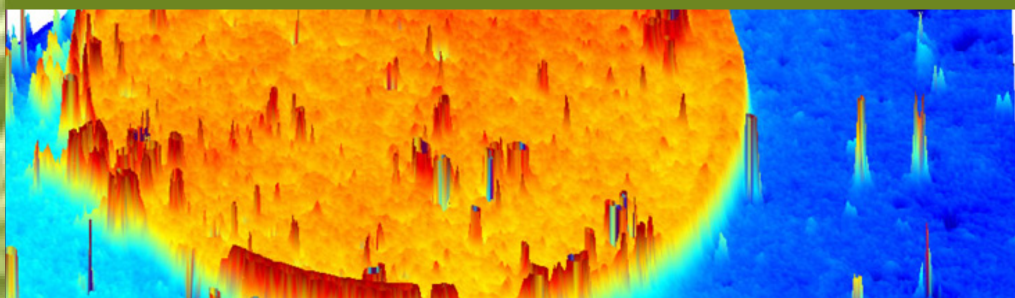
Imaging Diagnostic

It helps to visualize the morphology at molecular-scale structures of the human body.

Nanotechnology has driven a new breakthrough in diagnostic imaging techniques, in some cases, developing new techniques and in others by increasing the resolution and sensitivity of existing techniques.

Molecular diagnostics based on nanotechnology, tries to identify the causes underlying the disease on a molecular scale and not to identify the consequences that will ultimately have the disease.

The main advantages of the convergence of nanotechnology to medical imaging is the early detection of diseases, greatly increasing the chances of cure, the monitoring of various stages of disease, such as the processes of cancer metastasis, the development of personalized medicine and real-time assessment of the effectiveness of methods of surgery and therapy.

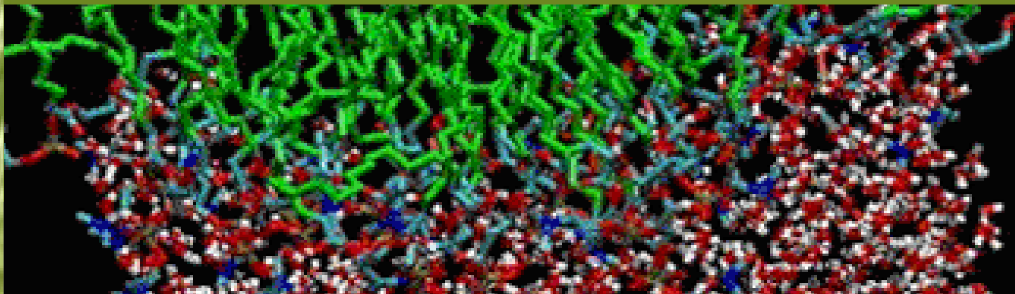


Nanomedicine

Imaging Diagnostic

Parallel to the development of imaging techniques, it has been created a new generation of tracers and contrast agents. The new contrast agents, used to raise awareness and give greater contrast in imaging techniques, will become increasingly complex, consisting of synthetic and biological nanoparticles.

The quantum dots have proven their usefulness in molecular diagnosis of cancer in early stages, due to its ability to identify specific target cells associated with individual types of cancer.



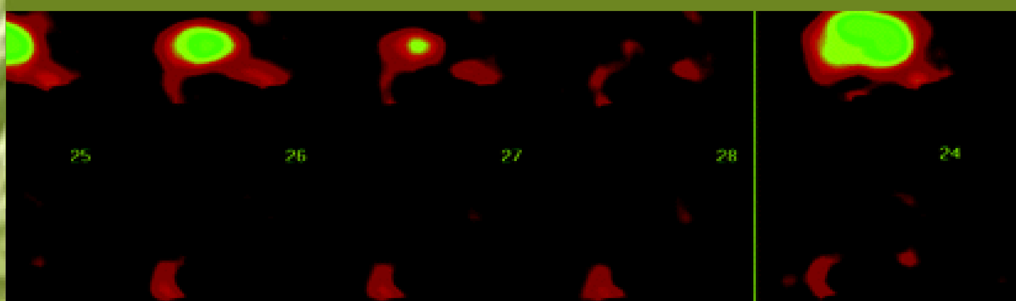
Key imaging techniques used in Nanomedicine

Optics, spectroscopy and fluorescence

It has been described different imaging techniques using absorption, fluorescence and bioluminescence as a source of contrast. Some examples of these techniques are microscopy and confocal microscopy FRET13, FRAP14, TIRF15 and NIRF16. These techniques have proved to be very useful in biomedical research, for example, in monitoring gene expression (mechanism regulatory gene whose malfunction is responsible for certain diseases).

Nuclear imaging techniques

Nuclear imaging techniques are non-invasive diagnostic methods that detect and analyze the distribution taken inside the human body a radioisotope administered (chemical element with an unstable atomic nucleus). The Positron Emission Tomography (PET17) is capable of measuring the metabolic activity of the different tissues of the human body and this allows identifying the tumours in the body. Besides its application in oncology, PET has applications in cardiology and neurology. Other nuclear medicine techniques are SPECT18 tomography and scintigraphy.



Nanomedicine

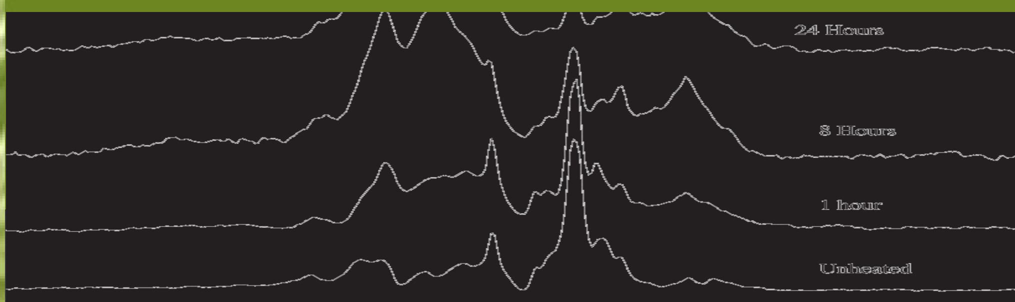
Key imaging techniques used in Nanomedicine

Nuclear magnetic resonance (NMR)

The magnetic resonance images are obtained by exposing the body to a magnetic field generated by a powerful electromagnet. Each tissue produces a different signal and analyzing information obtained three-dimensional structures of the body. Nuclear magnetic resonance can provide information on a cell when using intelligent contrast agents.

Proximity Microscopy (SPM19)

Tunnelling microscopy (STM20) and Atomic Force Microscopy (AFM21) are near microscopic techniques, the principle of which is exploring a surface with a tip while searching some interaction between the tip and surface. These techniques achieve a high spatial resolution that allows visualizing and manipulating atoms.



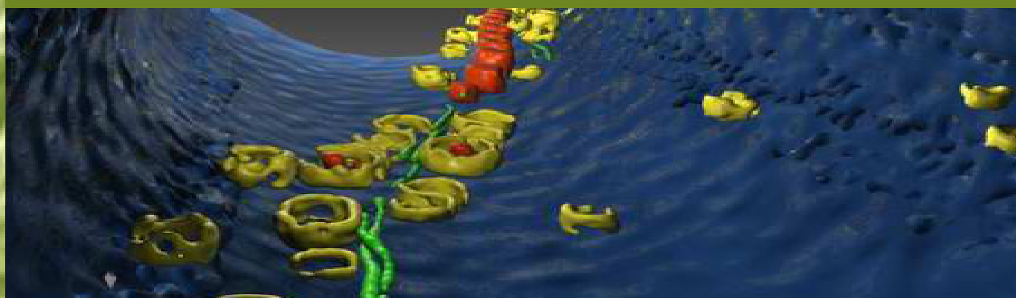
Key imaging techniques used in Nanomedicine

Electronics and electron microscopy tomography

The electron microscope achieves an enlarged picture of the test sample by electrons lighting. There are two basic types of electron microscopes, Transmission Electron Microscopy (TEM22) and Scanning Electron Microscope (SEM23). A special technical interest is the electronic scan, which achieves a three-dimensional reconstruction of a sample from a series of photographs on two dimensions of the sample, which rotates to different angles.

Ultrasound

Ultrasound uses an ultrasonic transmitter. The reflected sound waves to be applied on the issuer tissue are collected and processed in an image.



Nanomedicine

Drug delivery

Its function consists in transport the drug to the place where it should be released in a specific way.

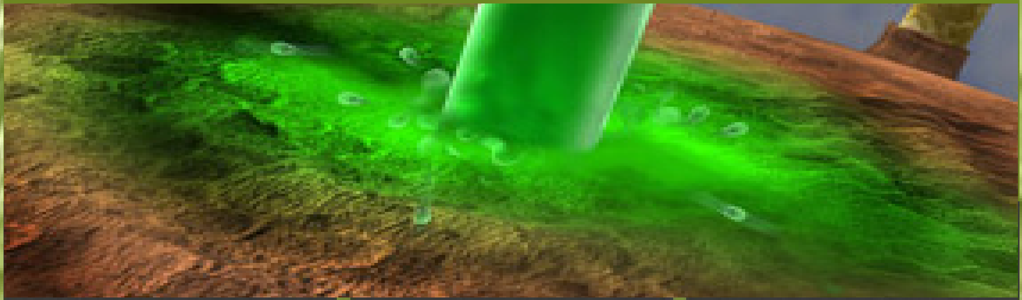
The characteristics that must meet these vehicles are low toxicity, suitable for the transport properties and drug release and long half-life.

Nanotechnology enables that the drug delivery to be minimally invasive because it allows the fabrication of nano-sized devices that can pass through pores and cell membranes.

Another great advantage is that it increases the effectiveness of the drug through the precise control of the dose required and the size, morphology and surface properties of the compound.

Any system of drug delivery has the following objectives:

- Be capable of carrying drugs in a highly specific and controlled way
- Avoid problems associated with the solubility of the drug
- Provide alternatives to traditional routes of administration, much more invasive.



Nanomedicine

Nanosystems for drug delivery

Micelles

molecular aggregates, sphere-shaped, consisting of molecules having a-polar or hydrophilic (water-related) part and a-polar or hydrophobic (water-rejecting) part. In an aqueous environment, the parties will tend to protect a-polar water and form a spherical structure with a hydrophobic core and a hydrophilic exterior. Such structures have a size of approximately 50 nm and are used for transport and release of drugs that are insoluble in water. The drugs are "locked" inside the micelle, protected in the same a-polar nucleus. An interesting feature with these systems is their ability to escape the action of macrophages and thus remain in the body longer than usual for a foreign particles circulating in the bloodstream.

Liposome

vesicles formed by double layered lipid, typical structures of biological membranes, formed by two rows facing the lipid hydrophobic tails. In these membrane-like structures, may include some proteins that act as channels through which the drug is released in a specific manner while remaining protected from the possibility of suffering a premature degradation.

Nanomedicine

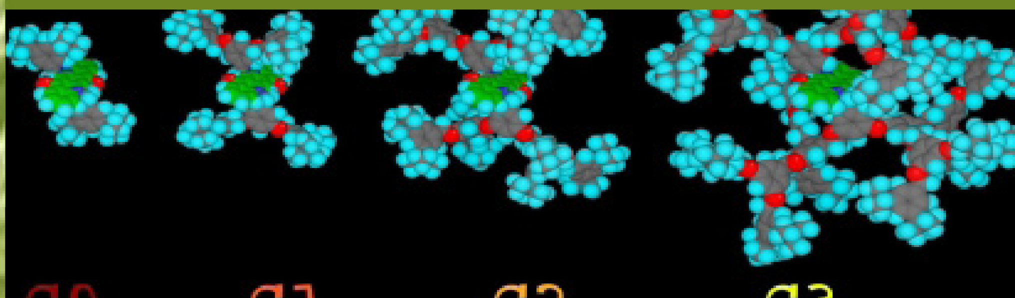
Nanosystems for drug delivery

Dendrimers

dendrimers are macromolecules with the many ramifications, whose shape and size can be controlled very accurately. Dendrimers possess other characteristics such as its high stability and ability to functionalizing surface, which makes them good candidates for transporting drugs28. The investigations are not limited to the field of drug delivery, the Dendrimers are being studied as vectors for gene release, as contrast agents for different imaging techniques such as molecular and nano-supports29. Bioactive agents, which have to be transported, can be encapsulated inside the Dendrimers can join or to its surface by physical or chemical interactions.

Nanoparticles

spherical polymer particles. Within this classification are included the Nanocapsules, which are vesicular systems in which the drug is confined in a cavity surrounded by a unique polymeric membrane systems, and Nanoesferas or matrices in which the drug is dispersed in the particle.



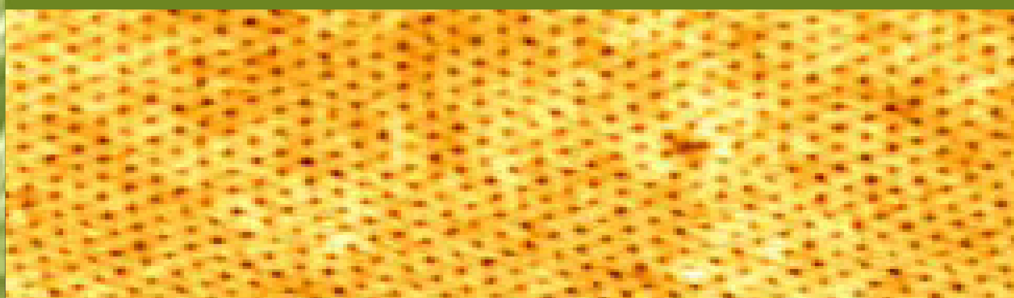
Nanosystems for drug delivery

Carbon nanotubes

cylindrical structures composed of one or more layers of graphite or other carbon material wound on it. Carbon nanotubes can be functionalized with bioactive peptides, proteins, nucleic acids or drugs, and may release its cargo on a specific target cells. Functionalizing to the surface, carbon nanotubes show low toxicity and are not immunogenic what makes them good systems for controlled drugs delivery.

Polymer conjugates

drug delivery systems that are divided into two main groups, protein-polymer conjugates and polymer-drug conjugates. Both are made from a polymer consisting of repetitions of different chemical entities, as polyglutamics acids, polysaccharides, polyethylene and others. These polymers are covalently joined to form what will be the active agent through a link that must be stable during transport, but must also be able to degrade after reaching the target to which the drug is pointed.and size can be controlled very accurately. Dendrimers possess other characteristics such as its high stability and ability to functionalizing surface, which makes them good candidates for transporting drugs28. The investigations are not limited to the field of drug delivery, the Dendrimers are being studied as vectors for gene release, as contrast agents for different imaging techniques such as molecular and nano-supports29. Bioactive agents, which have to be transported, can be encapsulated inside the Dendrimers can join or to its surface by physical or chemical interactions.



Nanomedicine

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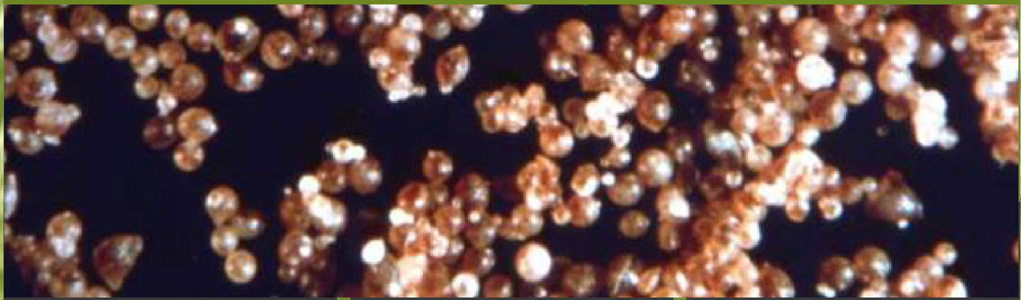


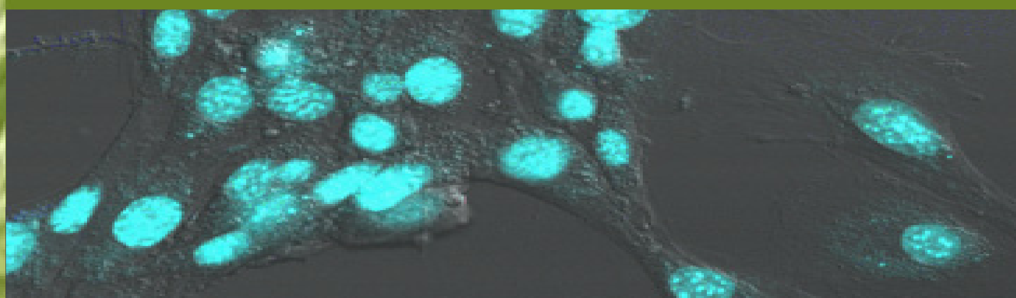
Nanomedicine

Regenerative medicine

The regenerative medicine is a discipline that seeks to maintain, improve or restore the function of cells, tissues and organs, by applying methods mainly related to cell therapy and tissue engineering.

Recent advances in nanotechnology are an impetus for Tissue Engineering, since they provide new materials and new techniques that allow a more efficiently integration of tissue by the possibility of generating microenvironments conducive to tissue regeneration.

The main contributions of nanotechnology to regenerative medicine are related to the production of new materials and support systems, the use of embryonic and adult stem cells and production of bioactive molecules that serve as indicators of cell differentiation.

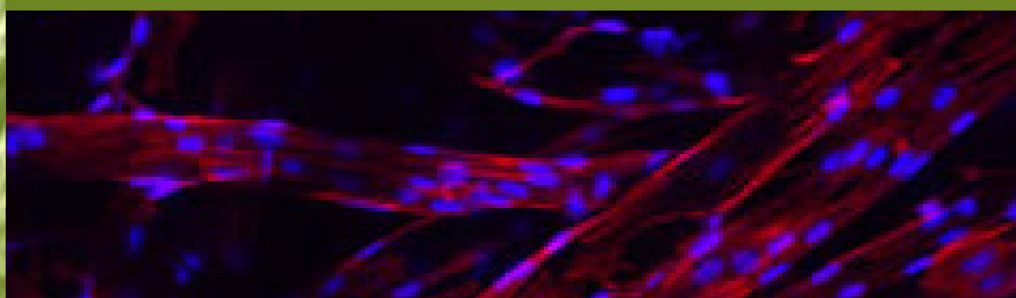


Nanomedicine

Biomaterials

All those materials those are likely to be used within a body for medical use.

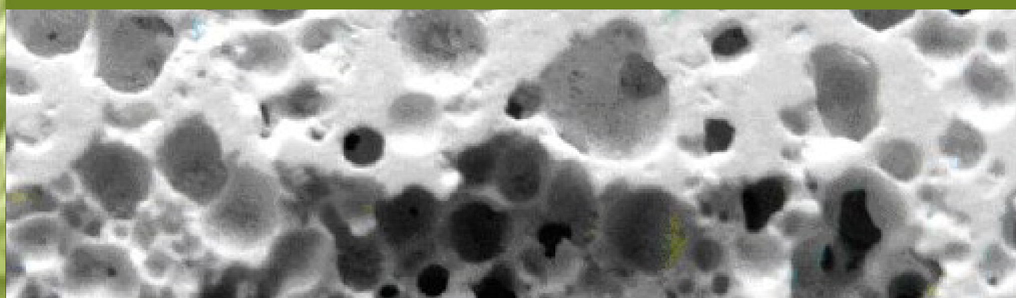
It is a common area to several applications of nanomedicine, being important not only for regenerative medicine but also for other applications of nanotechnology as the controlled release of drugs or diagnostic methods.



Classification of biomaterials used in Nanomedicine

Nanomedicine

The materials of the third generation, unlike those above, are both bioactive and biodegradable, which is a breakthrough because for a part are capable of stimulating regeneration tissue and at the same time, reducing the need for surgery.



Classification of biomaterials used in Nanomedicine

First generation of biomaterials

Type of materials	Clinic applications	Advantages	Disadvantages
Glass ceramics	Dentures Orthopedic prostheses	Low toxicity	Limited life of the implant Not absorbable Inactive Lack of response to external changes

Second generation of biomaterials

Type of materials	Clinic applications	Advantages	Disadvantages
Bioactive silicon crystals Ceramics Composites Hydroxyapatite	Dentures Orthopedic prostheses	Low toxicity Bioactive or biocompatible	Inability to be both biocompatible and bioactive Lack of response to external changes

Third generation of biomaterials

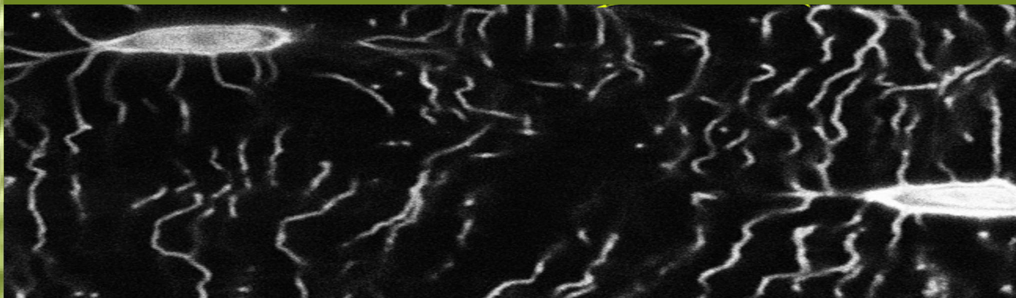
Type of materials	Clinic applications	Advantages	Disadvantages
Nanofibers Stands and porous nanofibers Nanospheres Nanocomposites Carbon nanotubes Hydroxyapatite Nanozirconium	Cardiovascular problems Epidermis Cartilage Bone Alzheimer Neurodegenerative diseases of the nervous system resulting focused Diabetes Cancer	Low toxicity Bioactive or biocompatible Ability to respond to external changes	Need to control the material's structure at the nanoscale Toxicity questionable Regulatory Issues

Nanomedicine

Bioactive signalling molecules

They are defined as those molecules naturally found in cells that cause regenerative events in them, such as cytokines, growth factors, receptors and second messengers.

Nanotechnology contributes with the design of smart biomaterials that incorporate within them for signalling molecules that, once inserted into the patient, would be released gradually and triggered tissue regeneration in vivo.



Nanomedicine

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