

Nanomedicine: Prevention, Diagnosis & Treatment


Hossein Ghanbari, MD, PhD

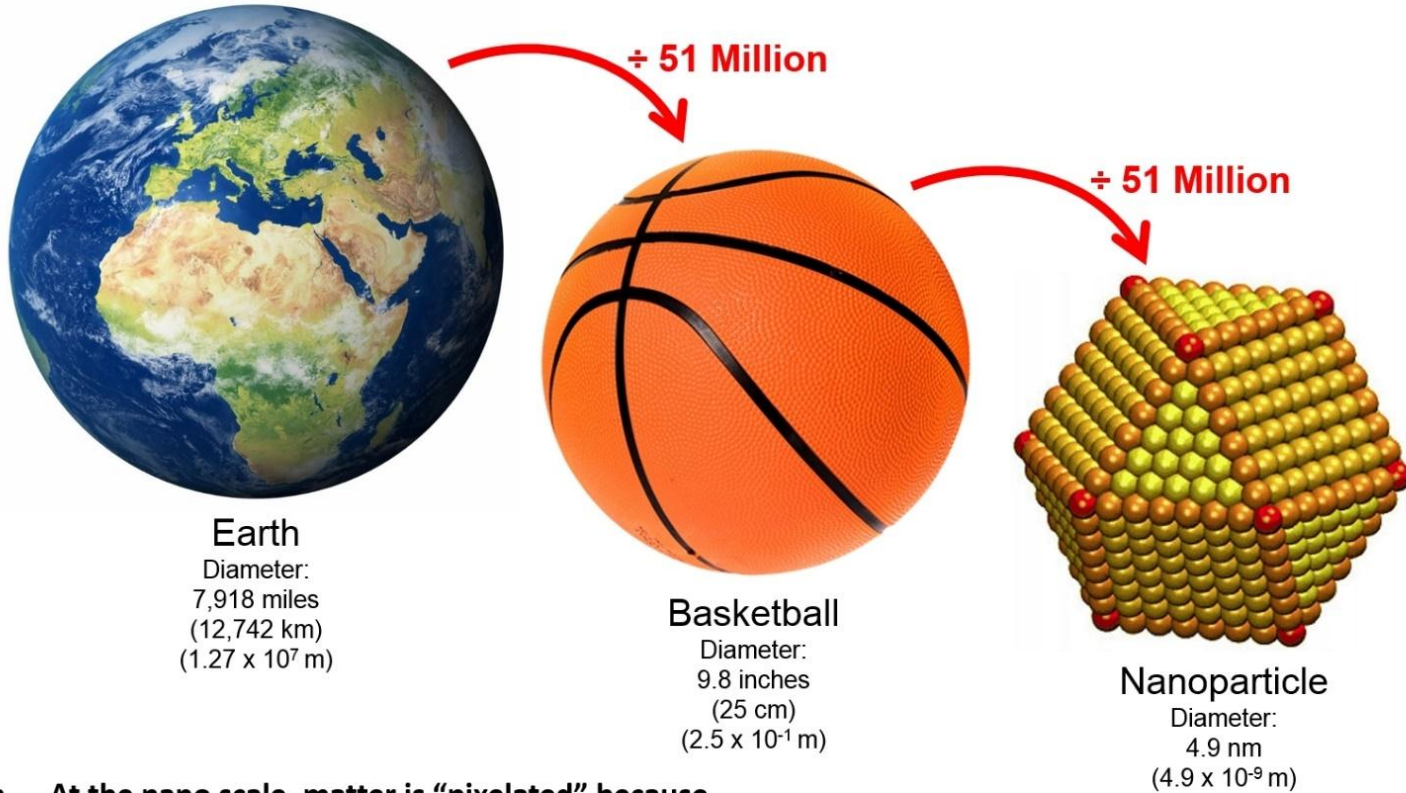
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Nanotechnology

How Small is Nano?

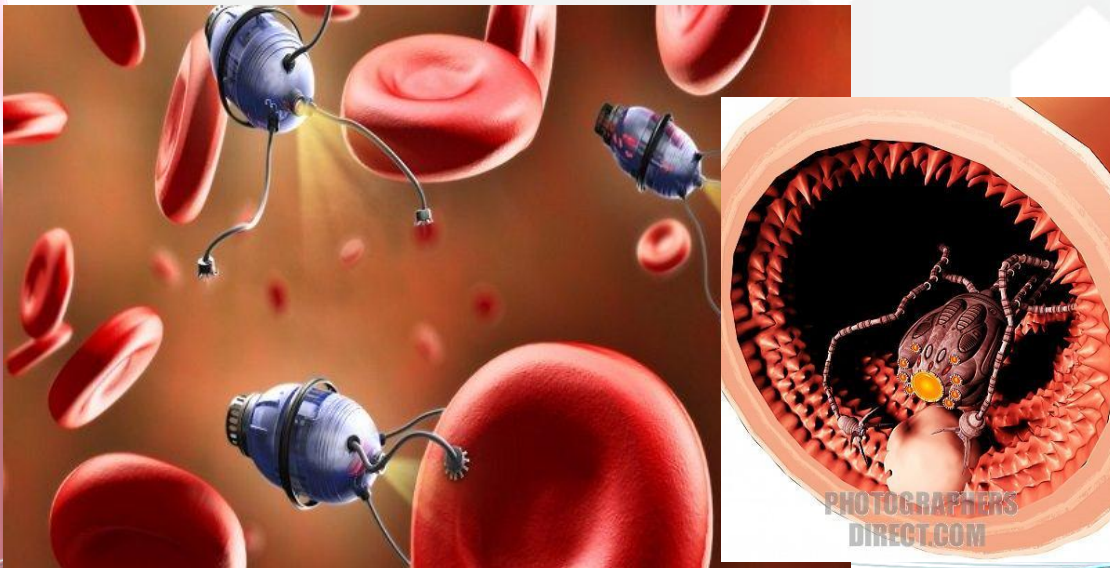
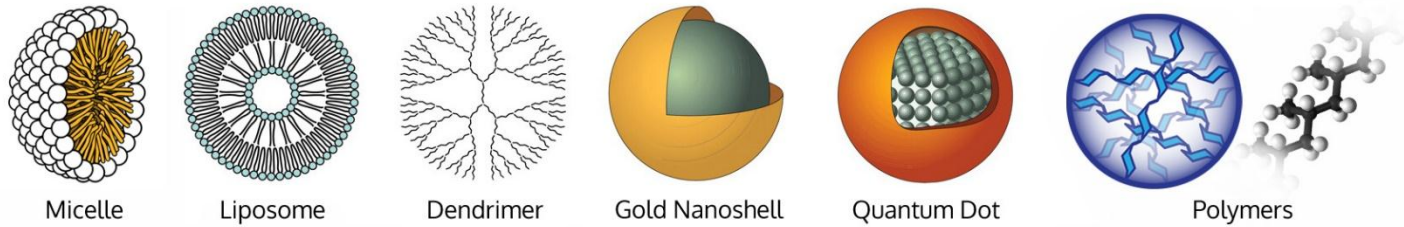
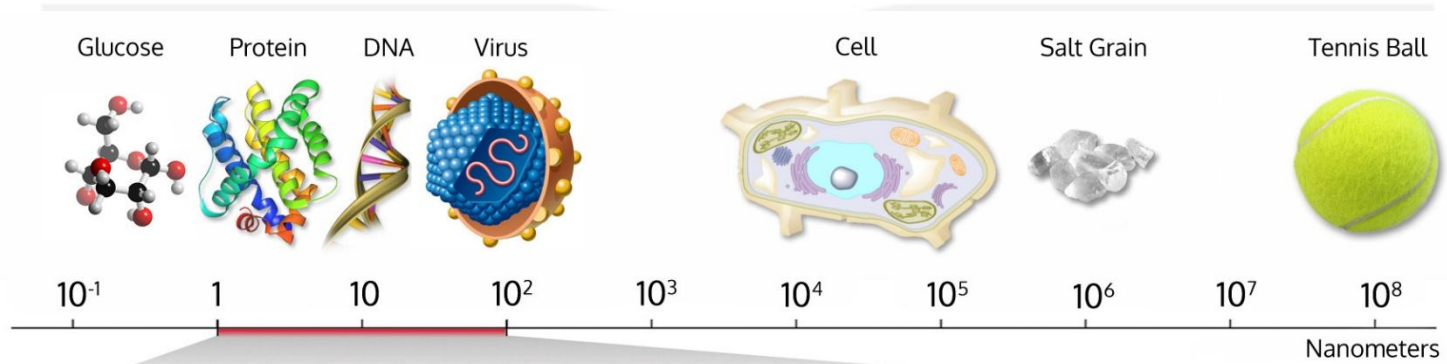
 NanoMan would only stand 36 nm tall on the basketball!



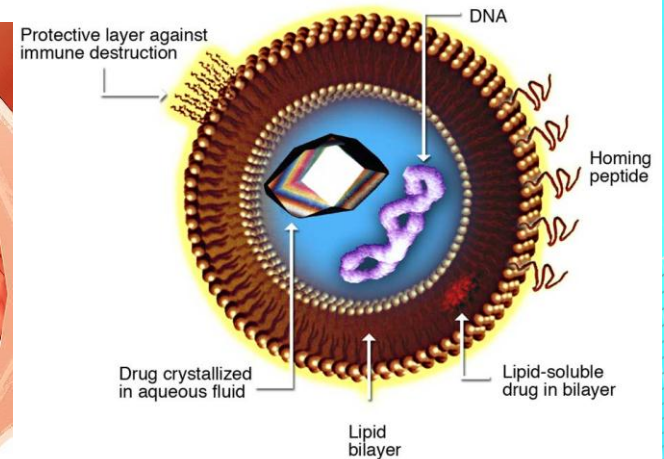
- **At the nano scale, matter is “pixelated” because you are approaching the size of atoms**

<http://www.redorbit.com/news/science/1112985219/gold-nanoparticles-convert-carbon-dioxide-to-carbon-monoxide-102513/>

NANOMEDICINE



Liposome for Drug Delivery

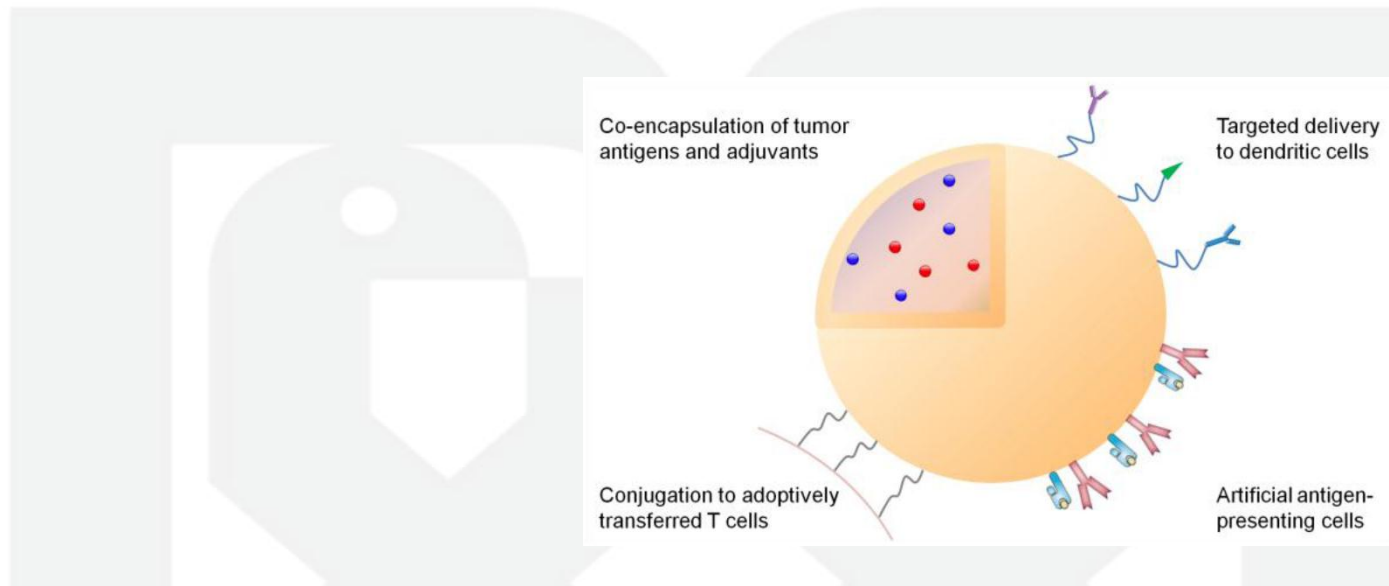


PHOTOGRAPHERS
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NANOMEDICINE

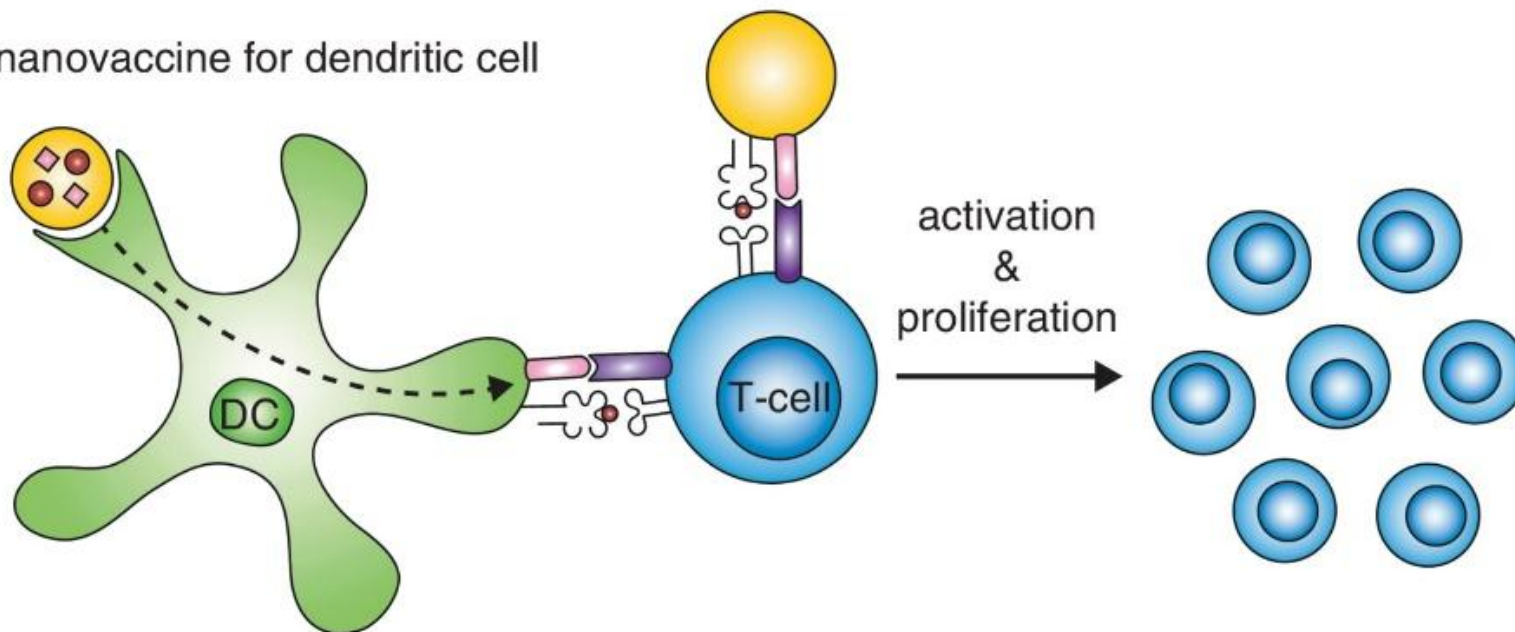
- Medical application of nanotechnology
 - **Prevention:** nanovaccines
 - **Novel diagnostics:** nanobiosensors, QDs, lab on a chip, imaging contrast agents,
 - **Novel therapeutics:** Targeted drug delivery systems, theranostics
 - Application of nanotechnology in **regenerative medicine**
 - Application of nanotechnology in **biomedical implants** and devices

PREVENTION: NANOVACCINES



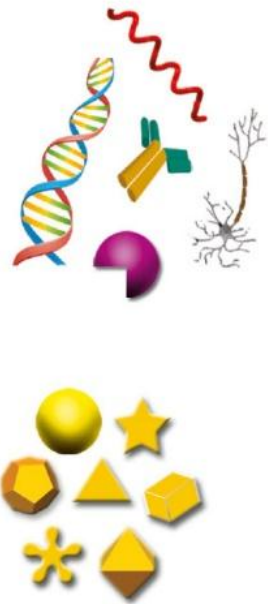
nanovaccine for T-cell

nanovaccine for dendritic cell

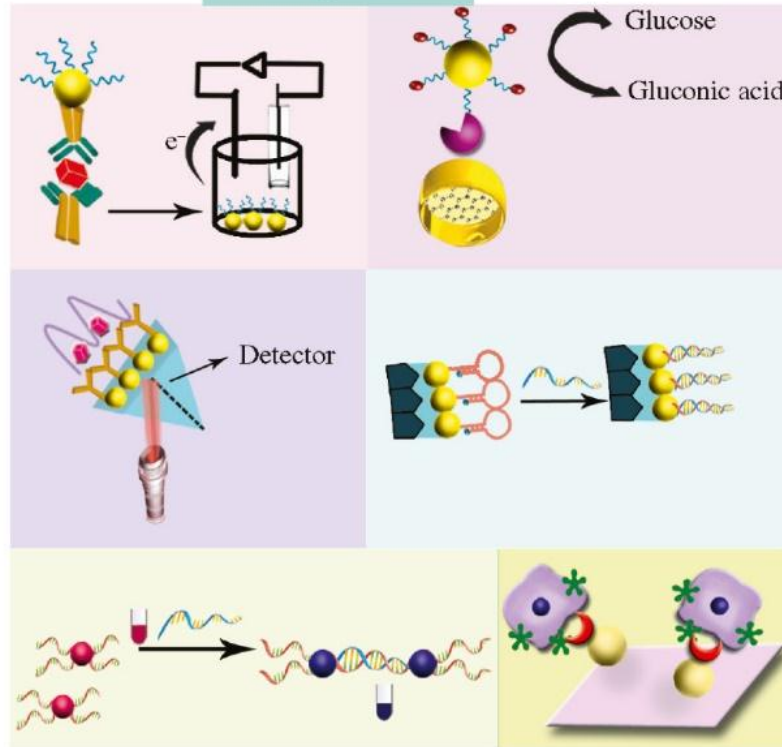


DIAGNOSTICS: NANOBIOSENSORS

Receptor



Recognition



Transduction

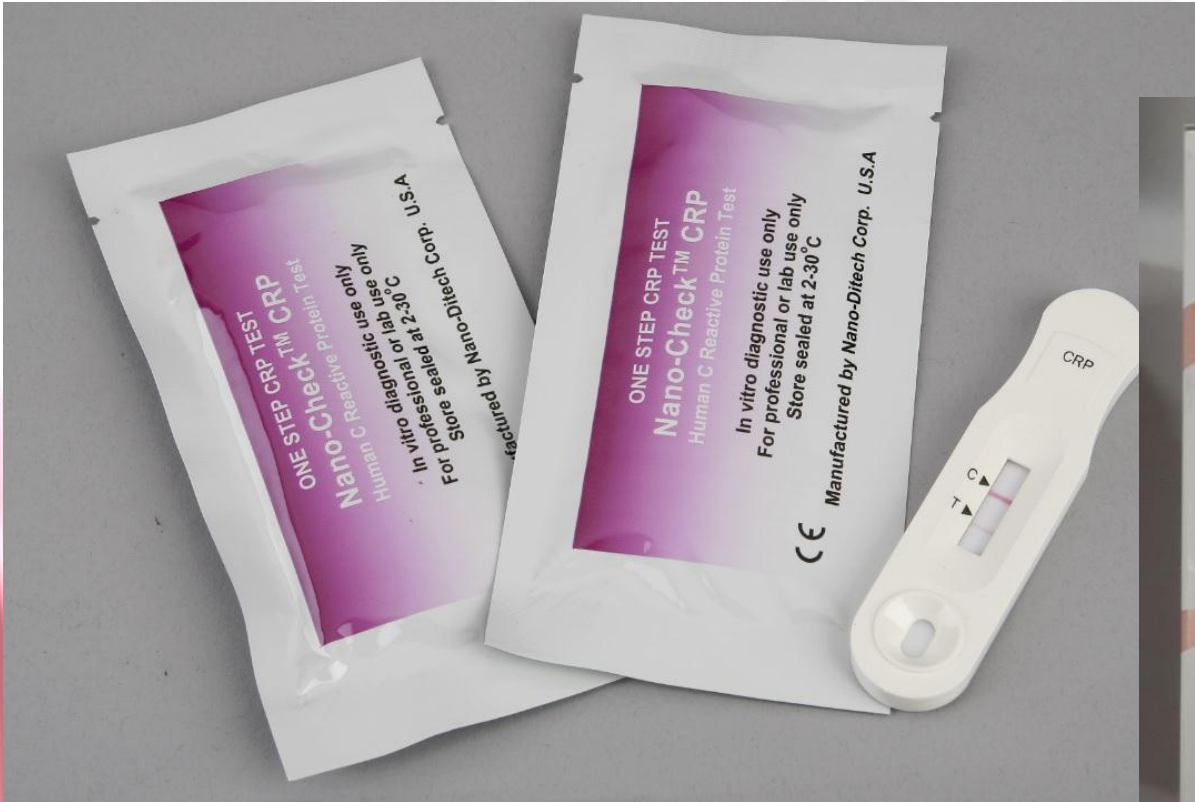
- ELECTROCHEMICAL
 - Amperometric
 - Potentiometric
 - Voltammetric
- OPTICAL
 - Plasmonic
 - Colorimetric
 - Chemiluminescence
 - Photoelectrochemical
- PIEZOELECTRIC

Measurable
signal

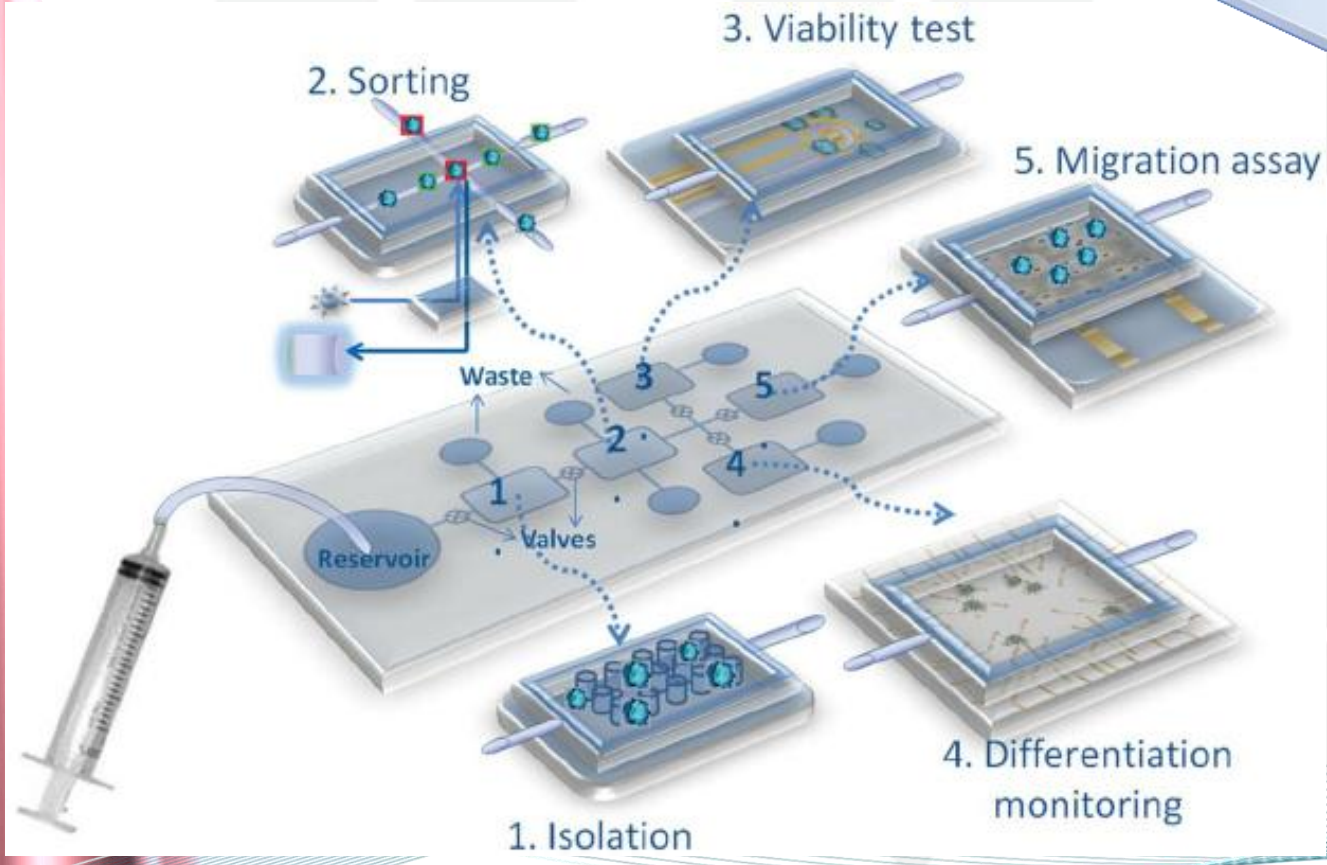
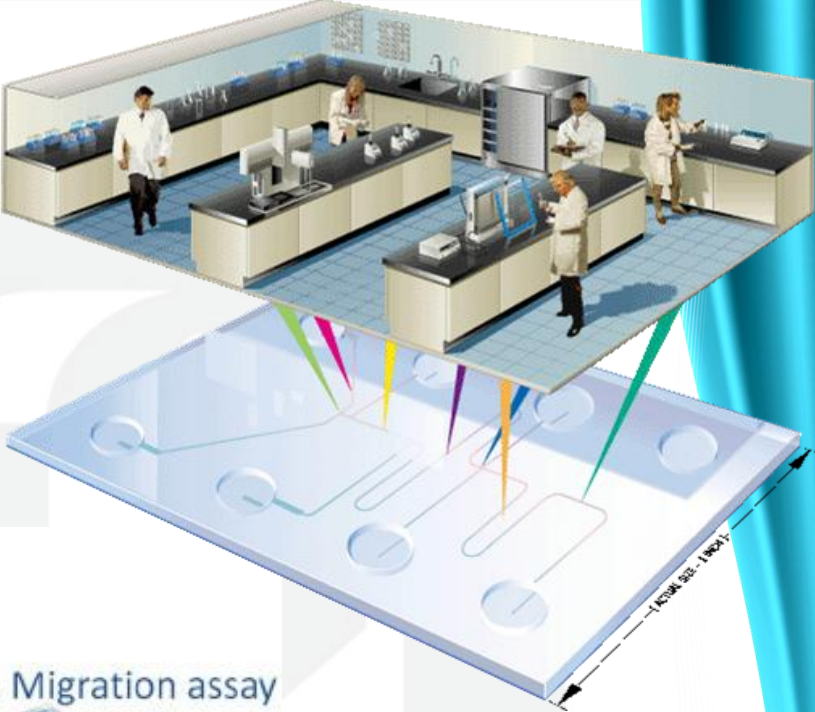
Signal
process

Signal
display

DIAGNOSTICS: RAPID TESTS



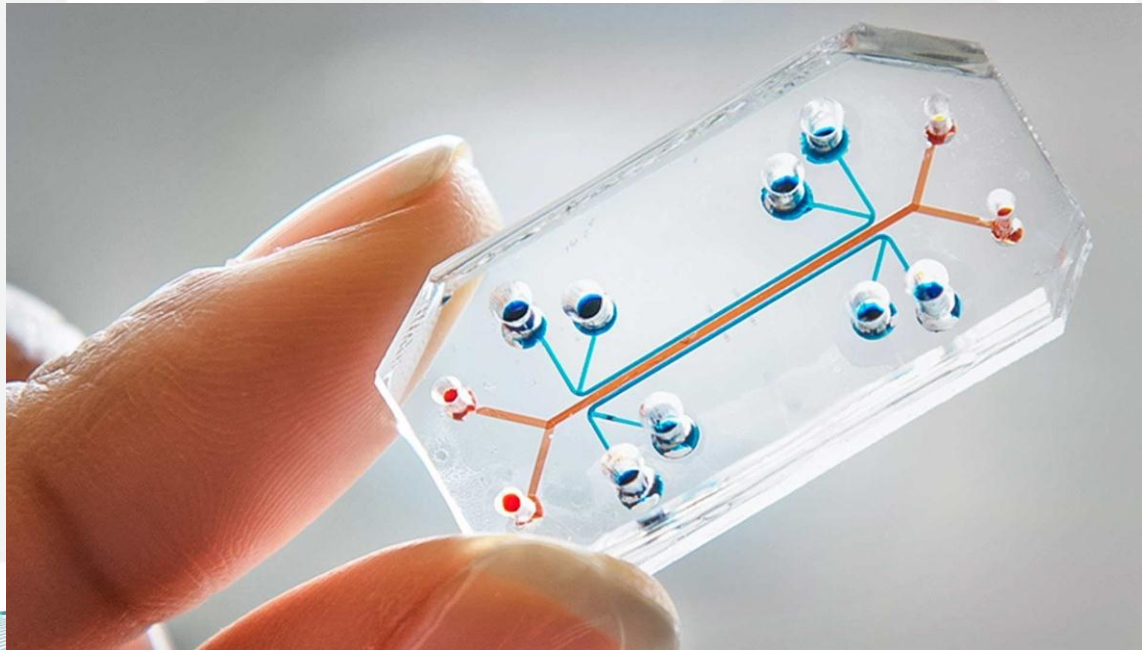
DIAGNOSTICS: LAB ON A CHIP



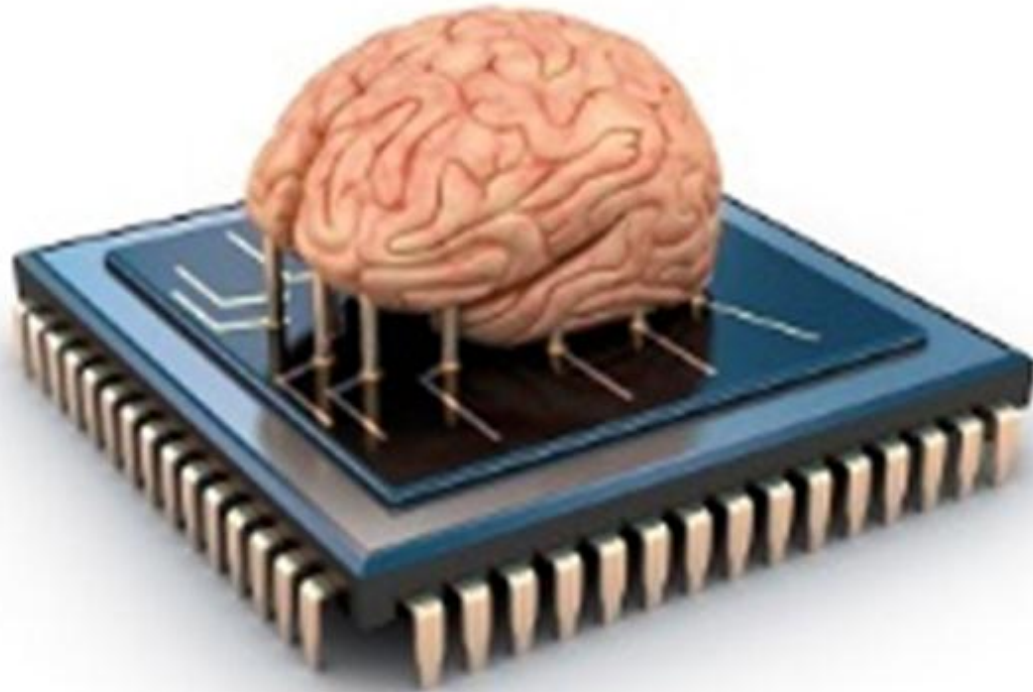
MICROFLUIDICS

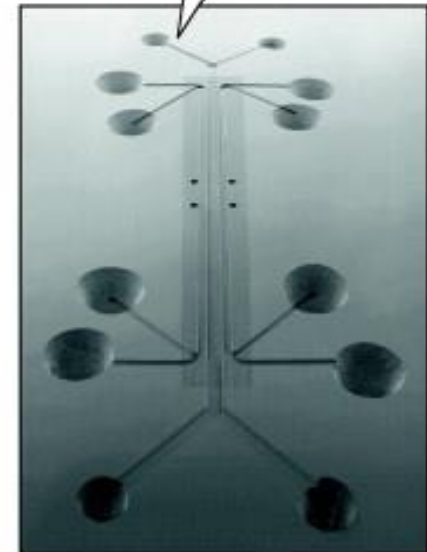
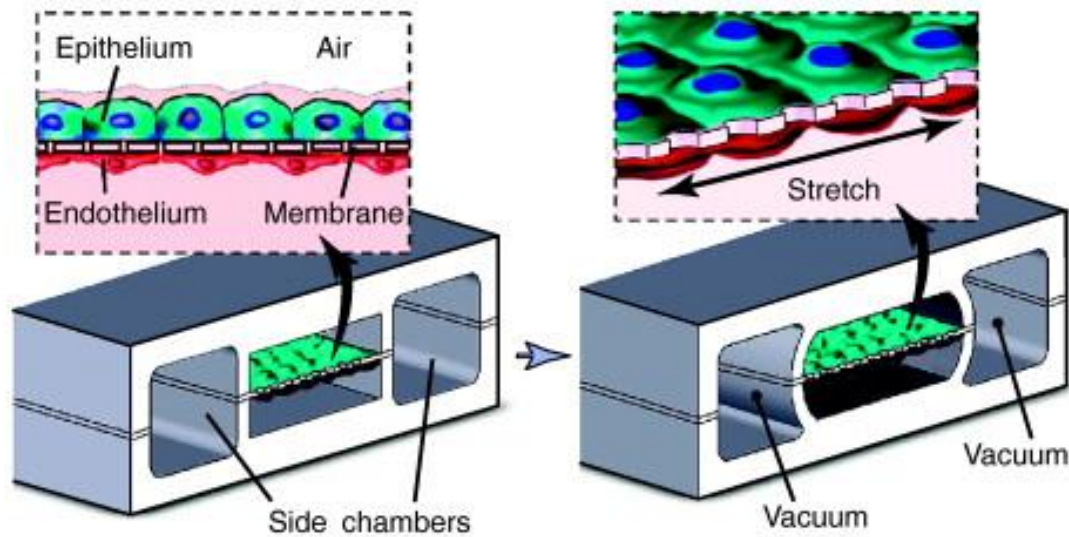
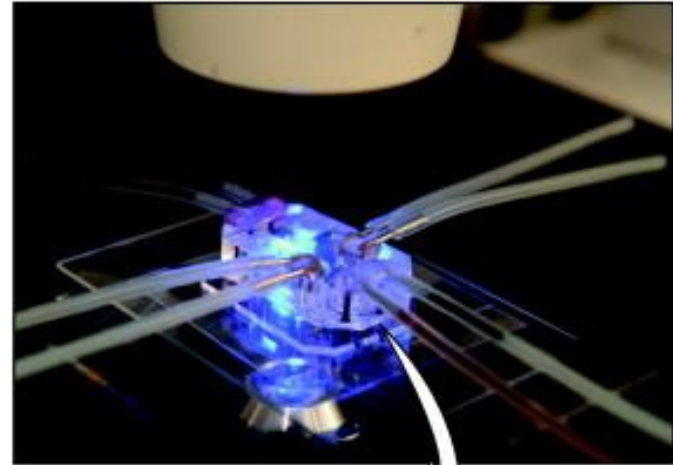
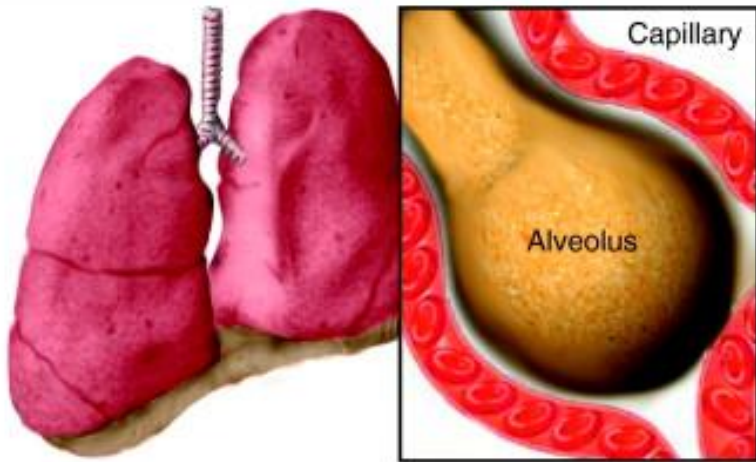
The science of manipulating small amounts (10^{-9} to 10^{-18} L) of fluids in microfabricated hollow channels:

- to generate and precisely tune dynamic fluid flows
- spatiotemporal gradients
- deliver nutrients and other chemical cues to cells in a controlled manner



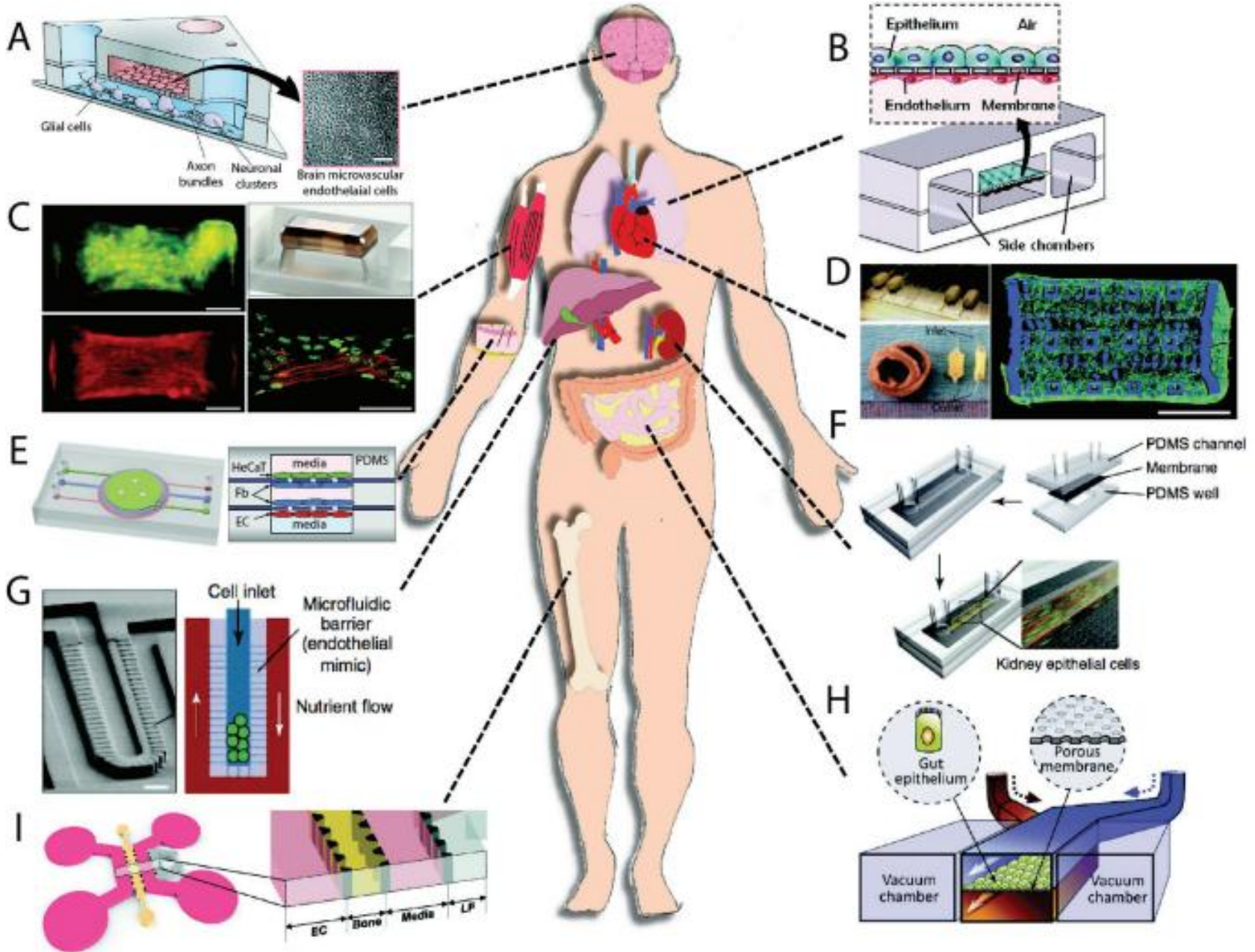
ORGAN ON A CHIP



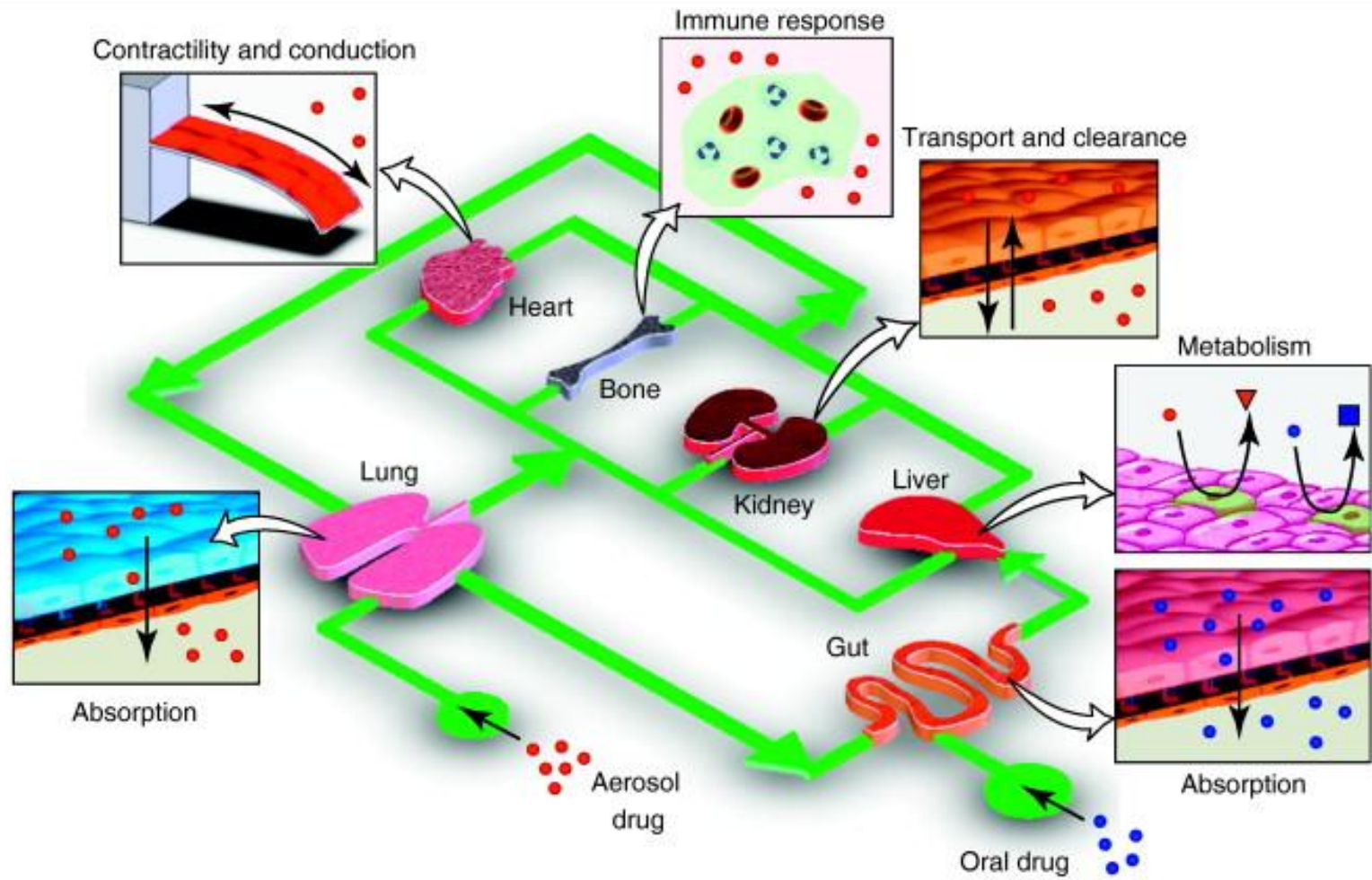


TRENDS in Cell Biology

A human breathing lung-on-a-chip



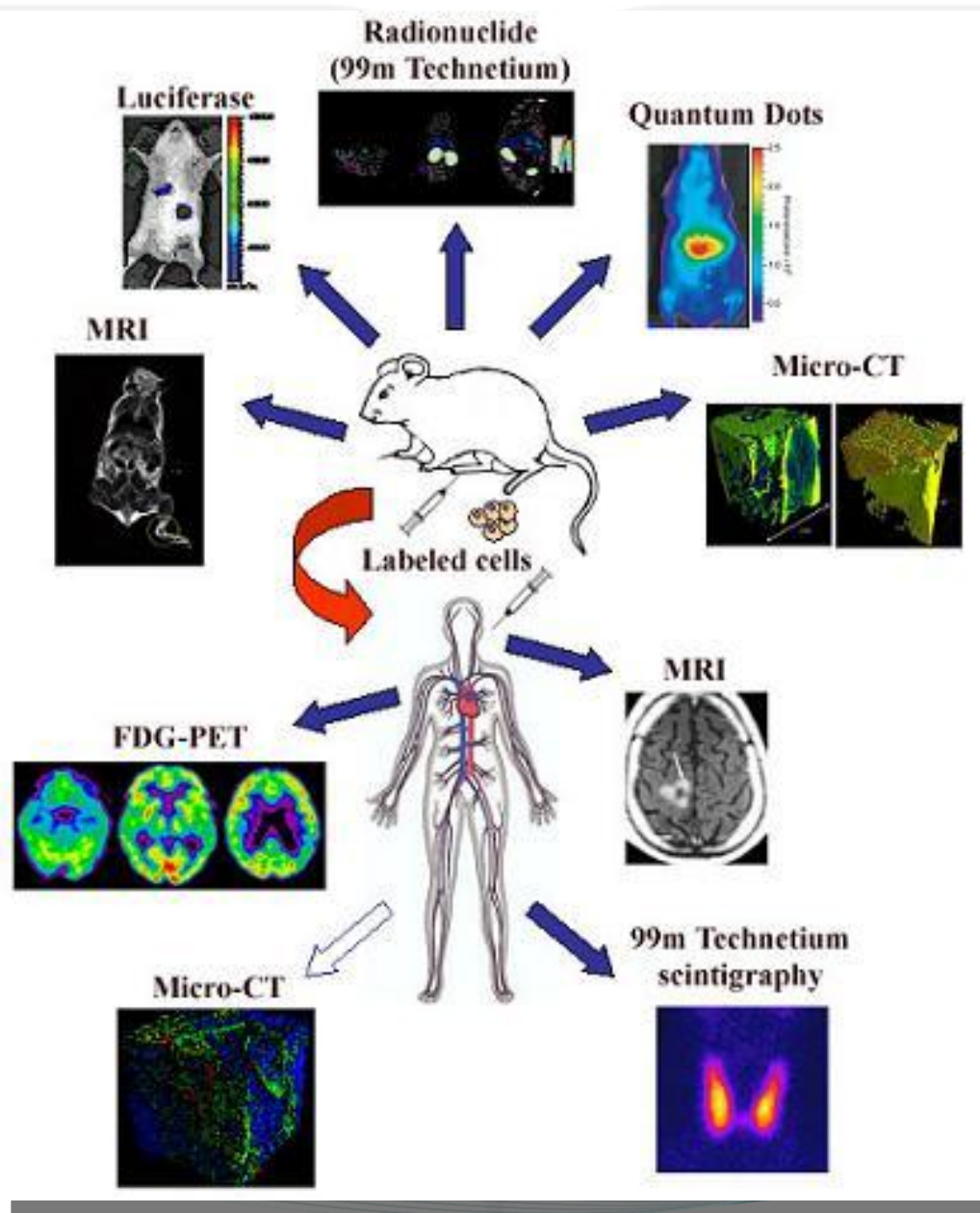
Different OOC models with their corresponding organs in the body.



TRENDS in Cell Biology

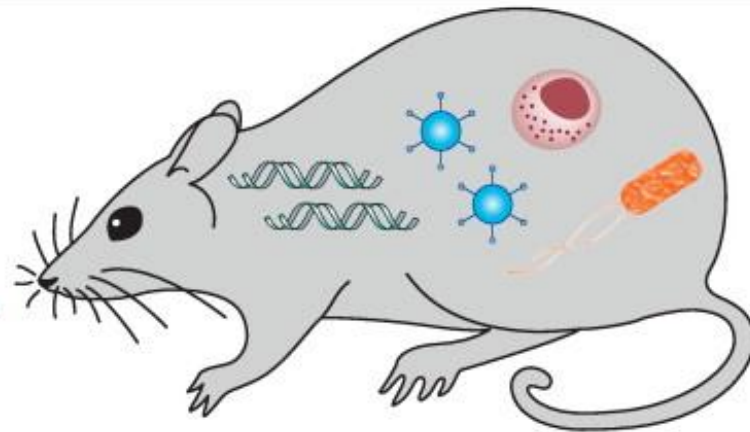
The human-on-a-chip concept

DIAGNOSIS: IMAGING

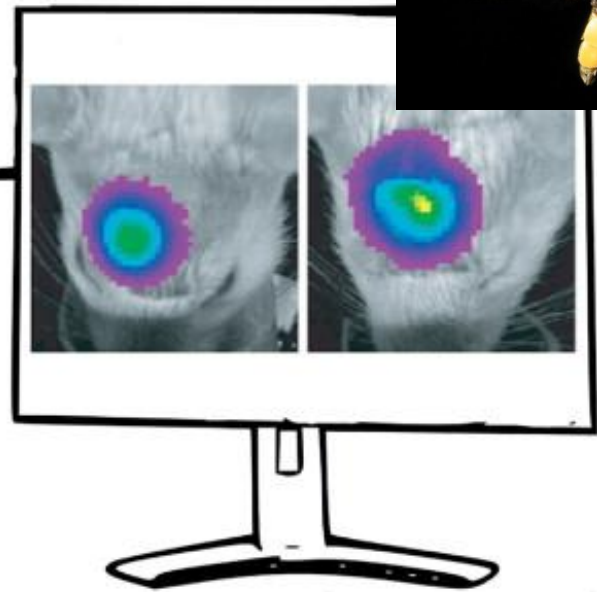
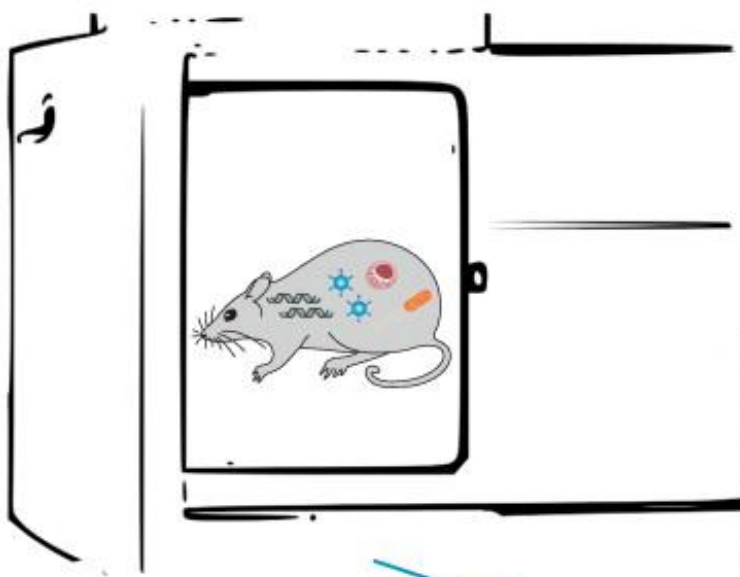


OPTICAL IMAGING BIOLUMINESCENCE

(a) Transgenic reporter genes, cells, or viruses expressing luciferase are introduced into animal models.

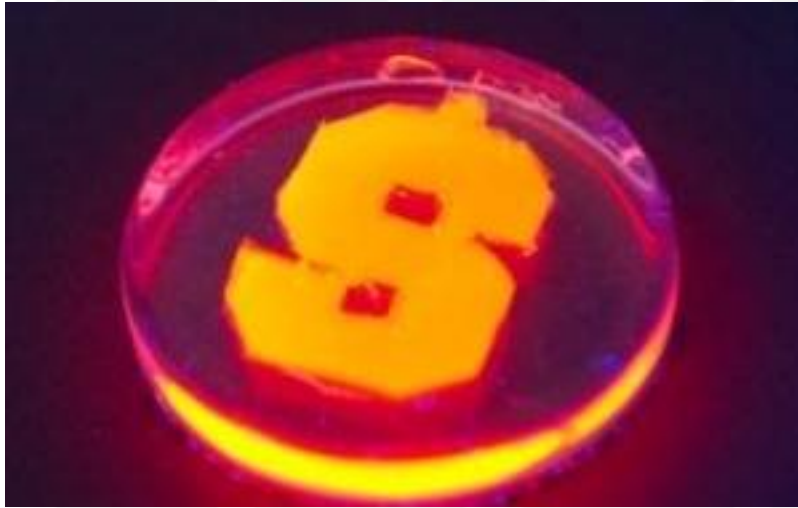


(b) Transgenic animals are positioned in a black box (light environment) and imaged using a CCD camera.

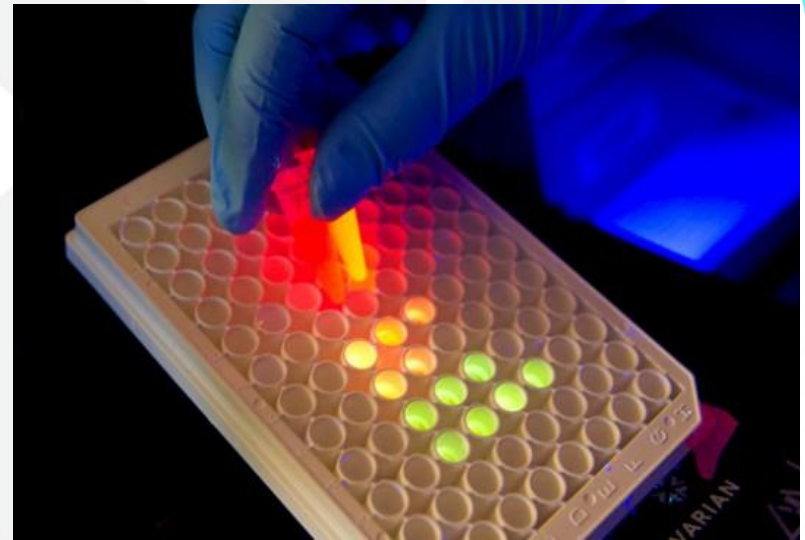


(c) Data is analyzed *in silico* and relative intensities can be calculated from the measurements.

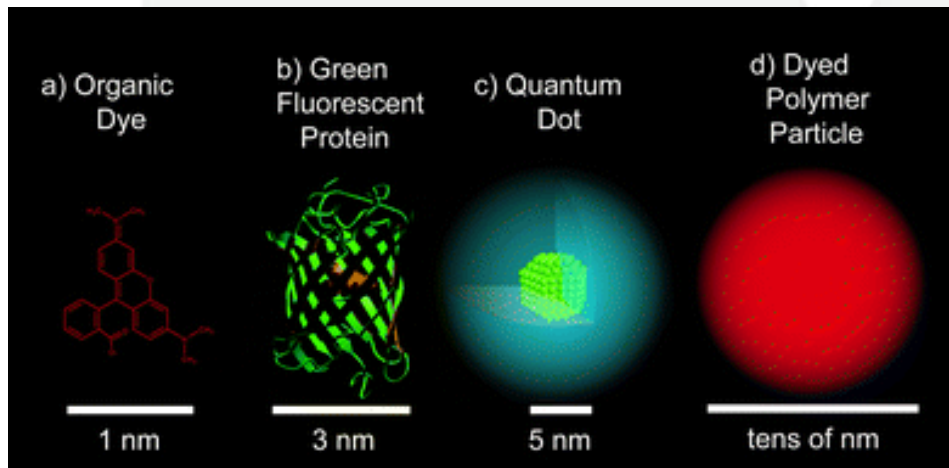
BIOLUMINESCENT NANORODS



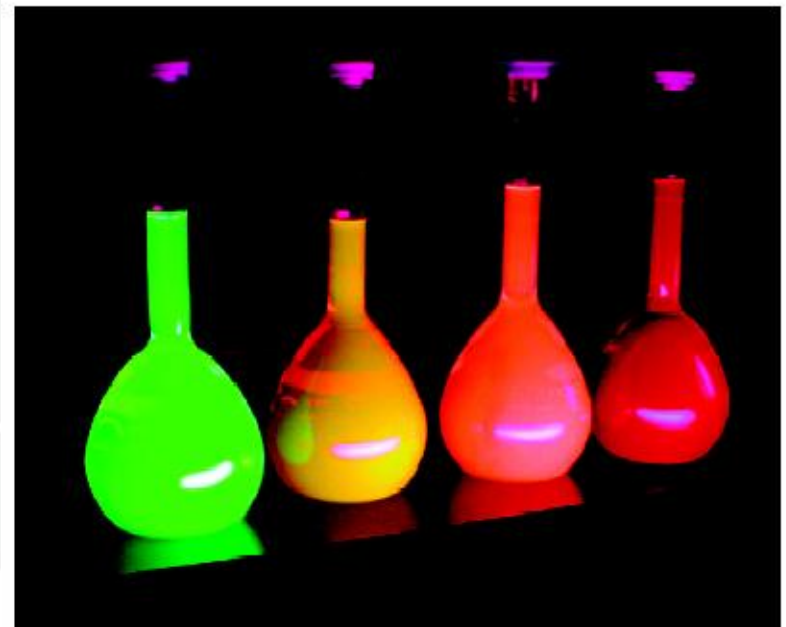
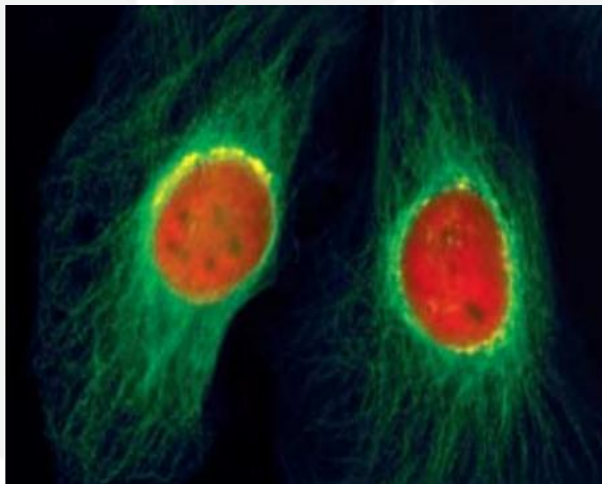
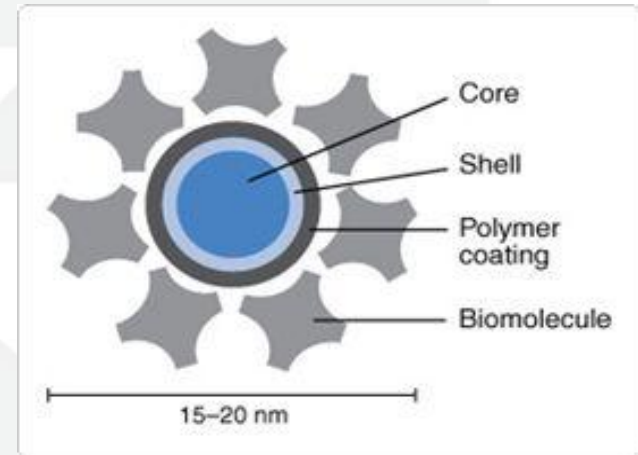
Nanorods (shell of cadmium sulfide and a core of cadmium selenide) modified with firefly enzymes glow orange.



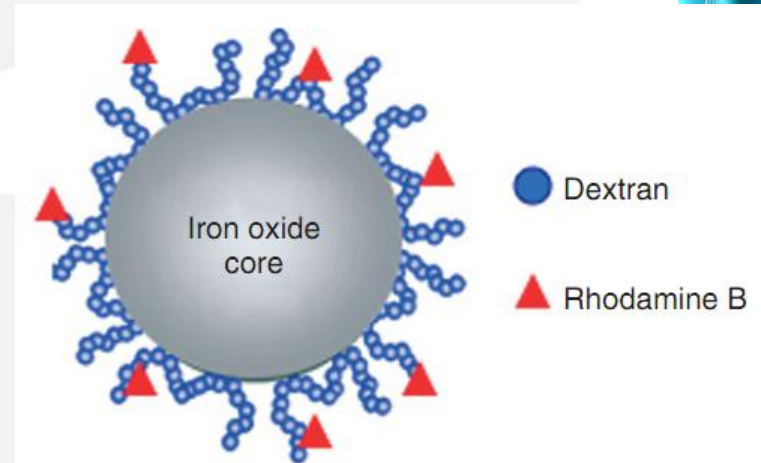
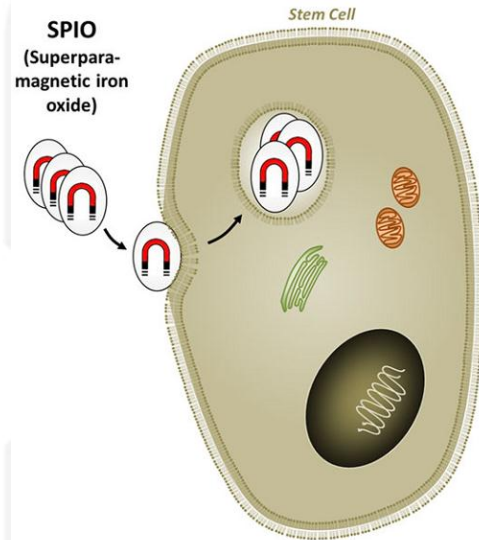
Fluorescent imaging



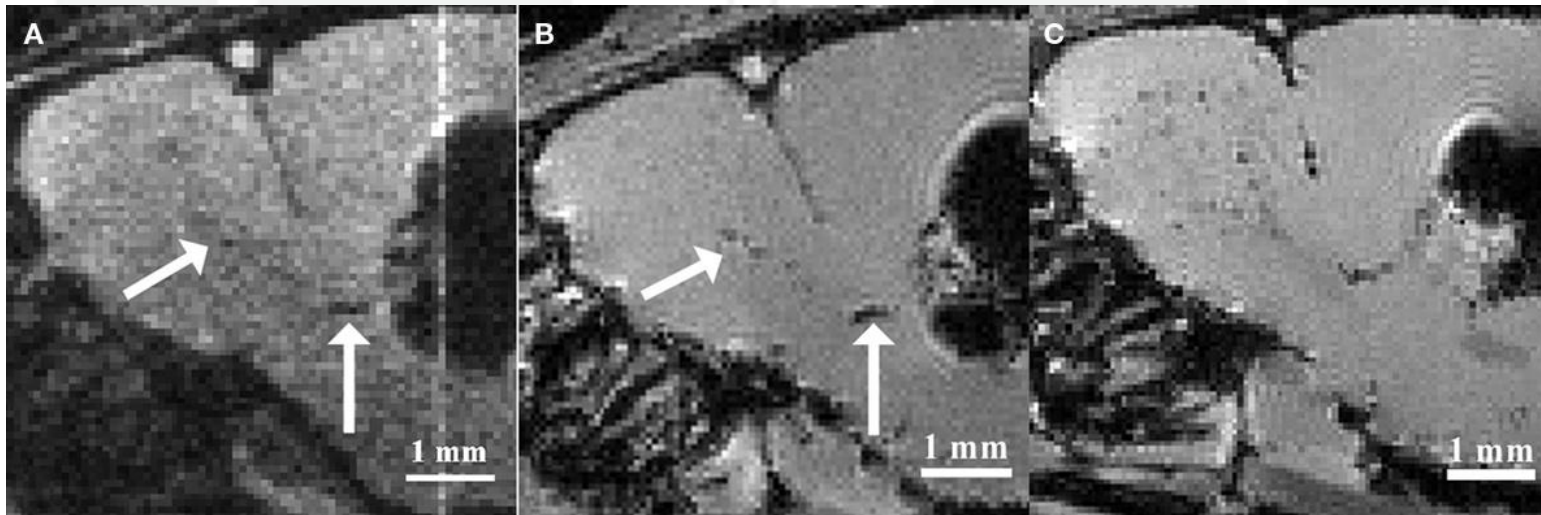
Quantum dot



IRON OXIDE NANOPARTICLES



- One of the most frequently used agents for cell tracking
- An MRI contrast agent (provides negative T2 contrast and T1 in ultra small nanoparticles)
- Enable the guidance and navigation of labeled cells after transplantation
- variety of sizes of iron oxide particles available for cell labeling



Magnetic resonance imaging of *in situ* labeled neural precursor cell migration.

NANOTECHNOLOGY IN NOVEL THERAPEUTICS

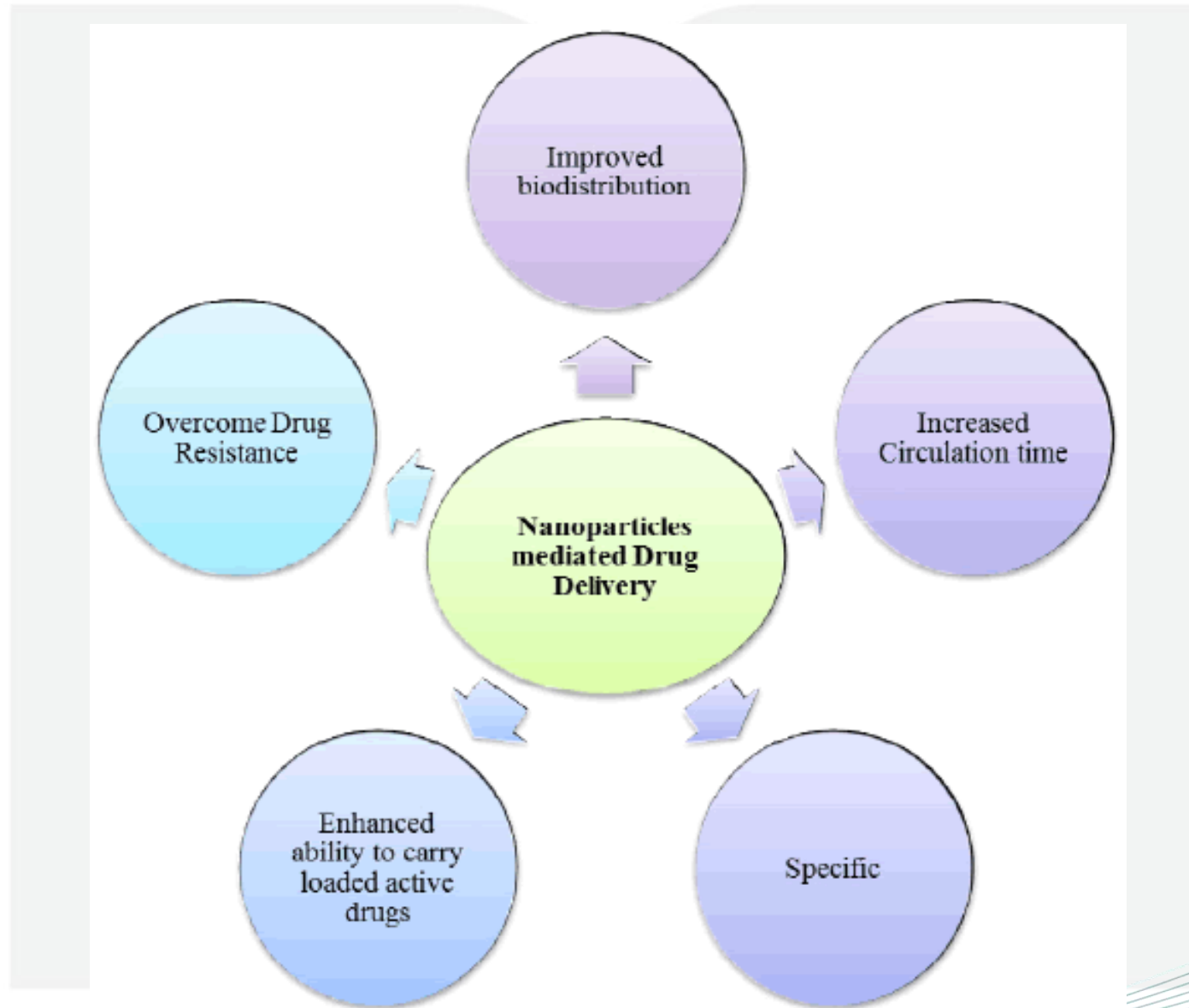
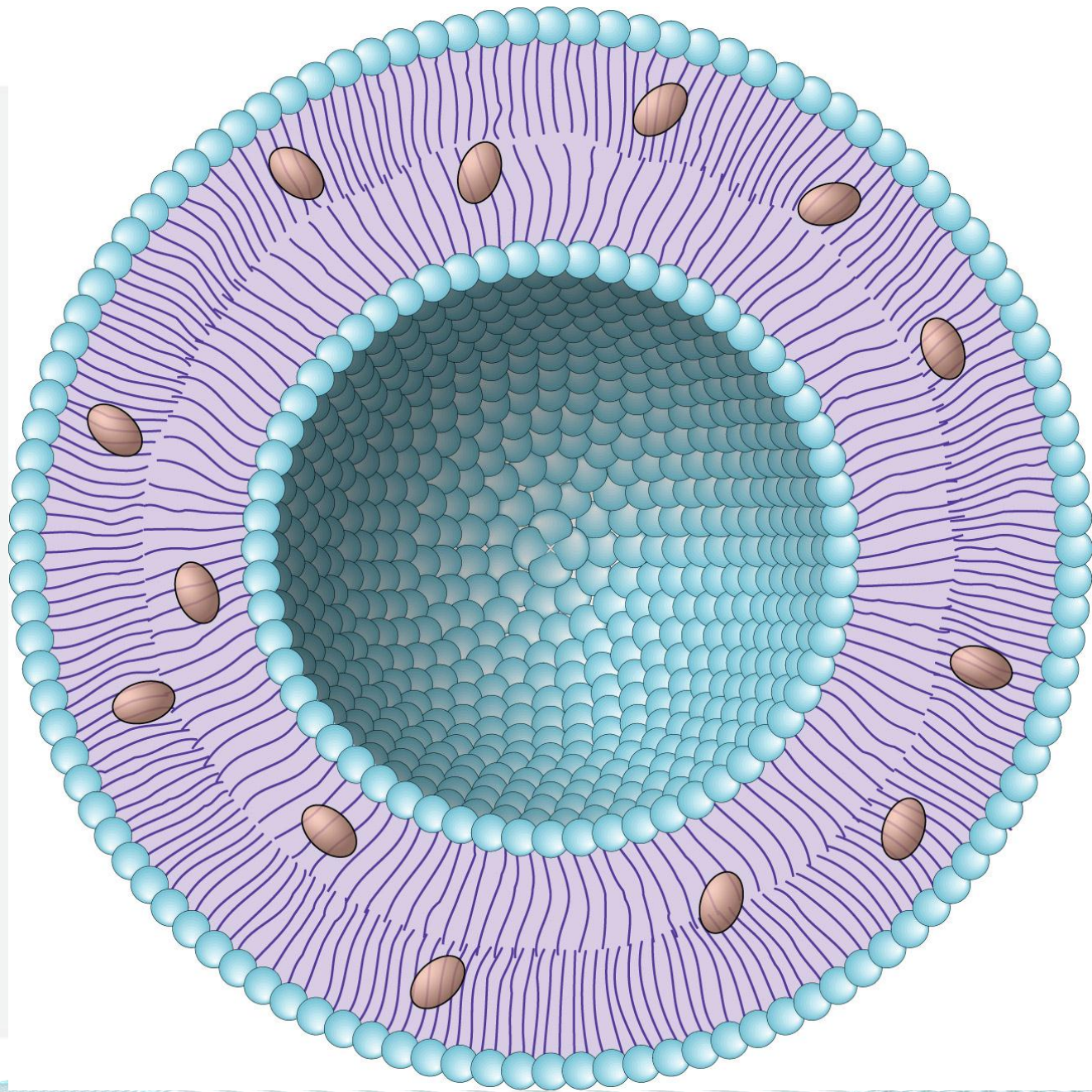


Figure 1: Advantages of Nanoparticles mediated drug delivery.

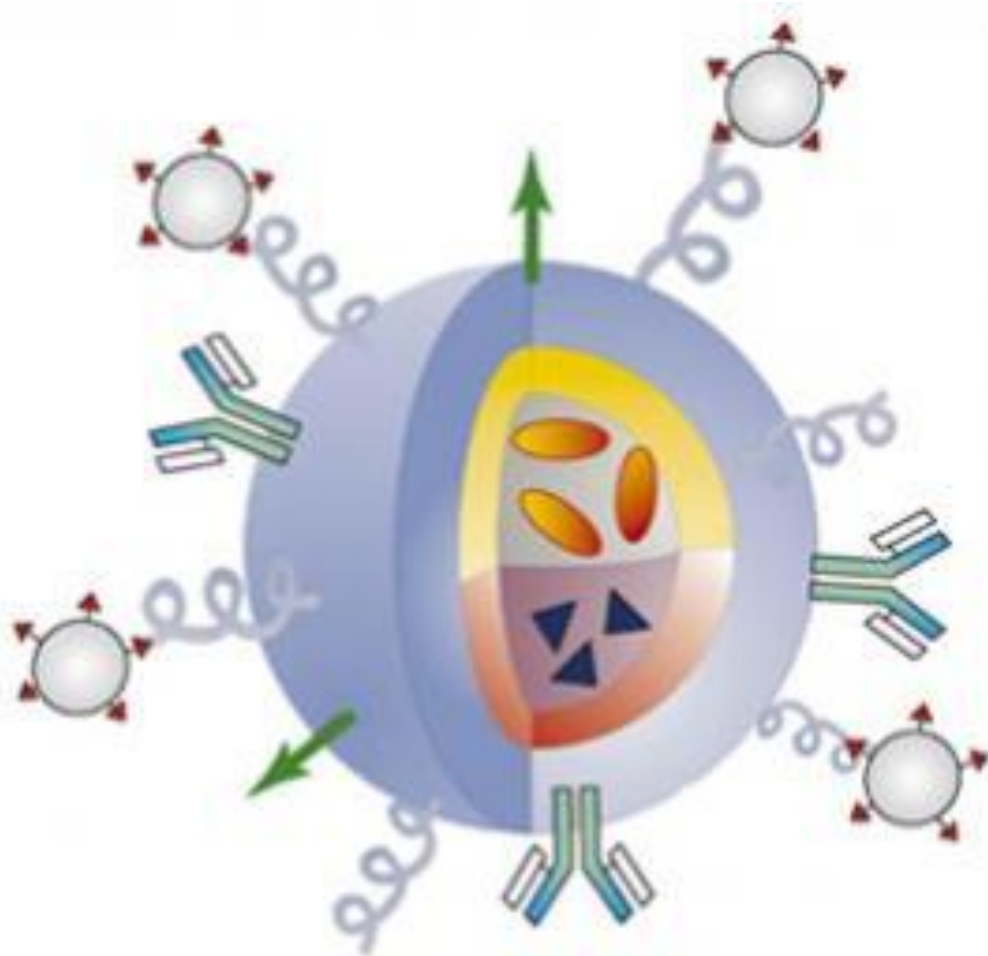
LIPOSOMAL NANOCARRIERS

- Liposomes remain one of **the first drug delivery carrier**
- more than 2000 papers and 200 reviews published in 2011 on the topic
- many liposomal drugs approved for cancer therapy:
 - **Doxil for doxorubicin** (Johnson & Johnson, New Brunswick, USA),
 - **Lipusu for paclitaxel** (Luye Pharma Group, Yantai, China),
 - **Marqibo for vincristine** (Talon Therapeutics, South San Francisco, USA)



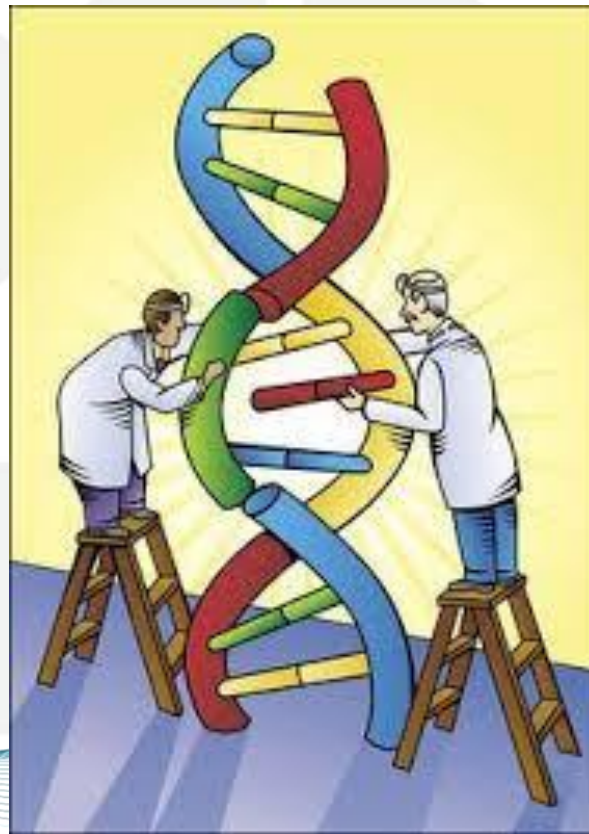
ANTI CANCER LIPOSOMES

- The **encapsulation of various types of anti-tumor drugs** has been extensively studied by many scientific research laboratories around the world.
- **Nonliposomal cisplatin** and **stealth liposomal cisplatin** were both effective antitumor agents but, at tolerable dose levels, stealth liposomal cisplatin was reported superior to nonliposomal cisplatin.
- **Doxorubicin liposomes (Caelyx, Doxil):** reduced dose and more efficacy
- **A thermosensitive liposomal taxol formulation:** significant reduction in tumor volume



A schematic illustration of an ideal multifunctional liposome with encapsulated drugs and genes, imaging agent, cell-penetrating agent and specific targeting moiety

NANOTECHNOLOGY IN GENE THERAPY



Non-viral and Viral Vectors for Gene Therapy

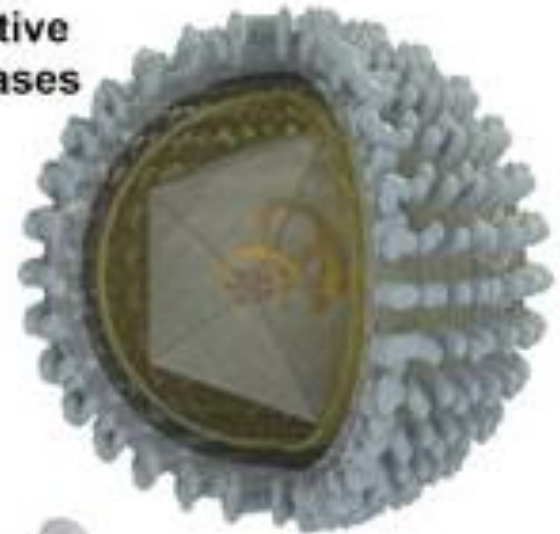


**Cancer
Vaccines
Neurodegenerative
Diseases**

**Therapeutic genes
miRNAs
siRNAs
Antisense oligonucleotides
Drugs**



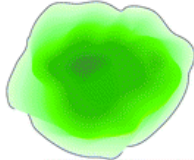
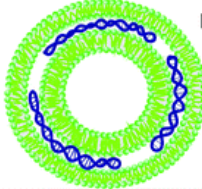
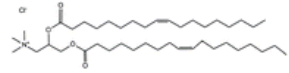
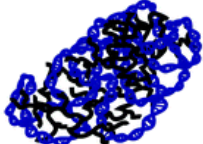
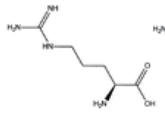
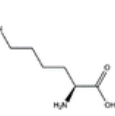
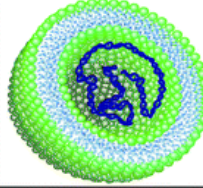
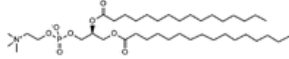
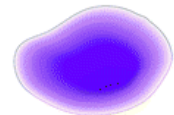
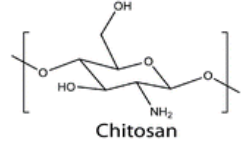

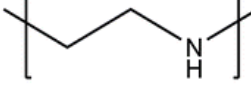
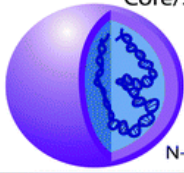
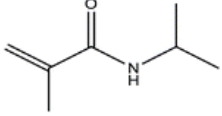
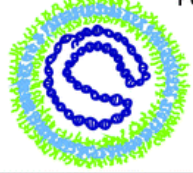
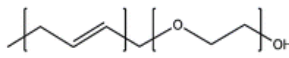
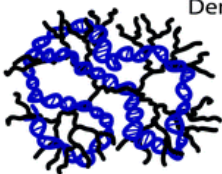
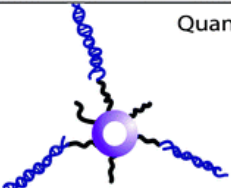
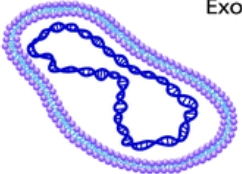
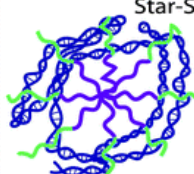
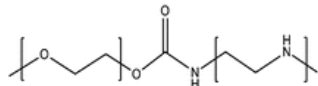
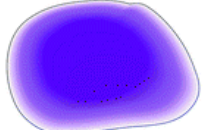
**Neurodegenerative
Diseases**



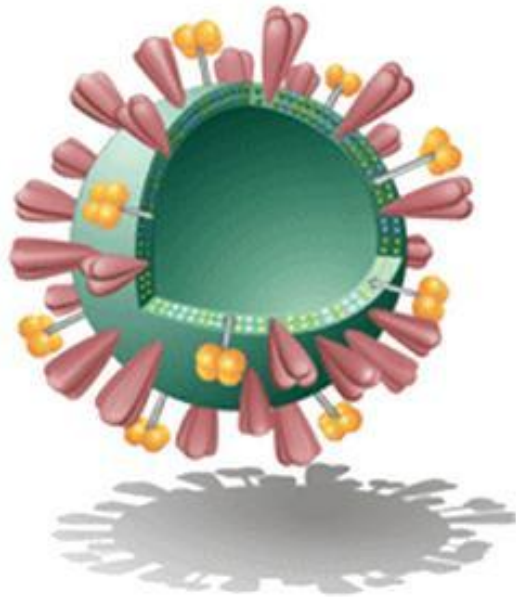
**Therapeutic genes
Models of disease**



Nanoparticle based gene delivery

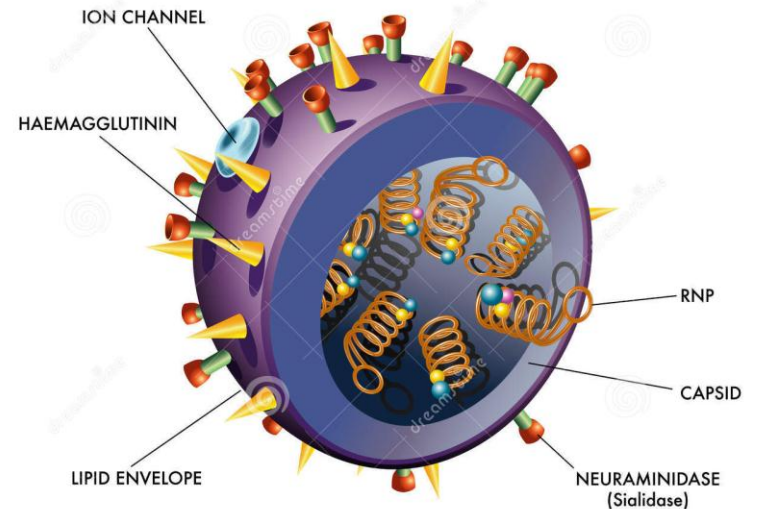
Gene Delivery Nanoparticle	Example Chemical Structure	Gene Delivery Nanoparticle	Example Chemical Structure
<p>Albumin Nanoparticle</p>  <p>Plasma protein</p>		<p>Lipoplex</p>  <p>Dioleoyltrimethylammonium-propane (DOTAP) lipid</p> 	
<p>Cationic Polypeptide</p>  <p>Arginine</p>  <p>Lysine</p> 		<p>Liposome</p>  <p>Dipalmitoylglycerophosphocholine (DPPC) lipid</p> 	
<p>Chitosan Nanoparticle</p>  <p>Chitosan</p> 		<p>Polyplex</p>  <p>Linear Polyethylenimine (PEI)</p> 	
<p>Core/Shell Nanogel</p>  <p>N-isopropylmethacrylamide (NIPMam)</p> 		<p>Polymersome</p>  <p>Polyethylene glycol (PEG) polybutadiene (PB) copolymer</p> 	
<p>Dendrimer</p>  <p>Several different polymers</p>		<p>Quantum Dot</p>  <p>Cadmium selenide (CdSe) core and zinc sulfide (ZnS) shell</p>	
<p>Exosome</p>  <p>Vesicle secreted from a cell</p>		<p>Star-Shaped Copolymer</p>  <p>Polyethylene glycol (PEG) polyethylenimine (PEI) copolymer</p> 	
<p>Gelatin nanoparticle</p>  <p>Collagen proteins</p>			

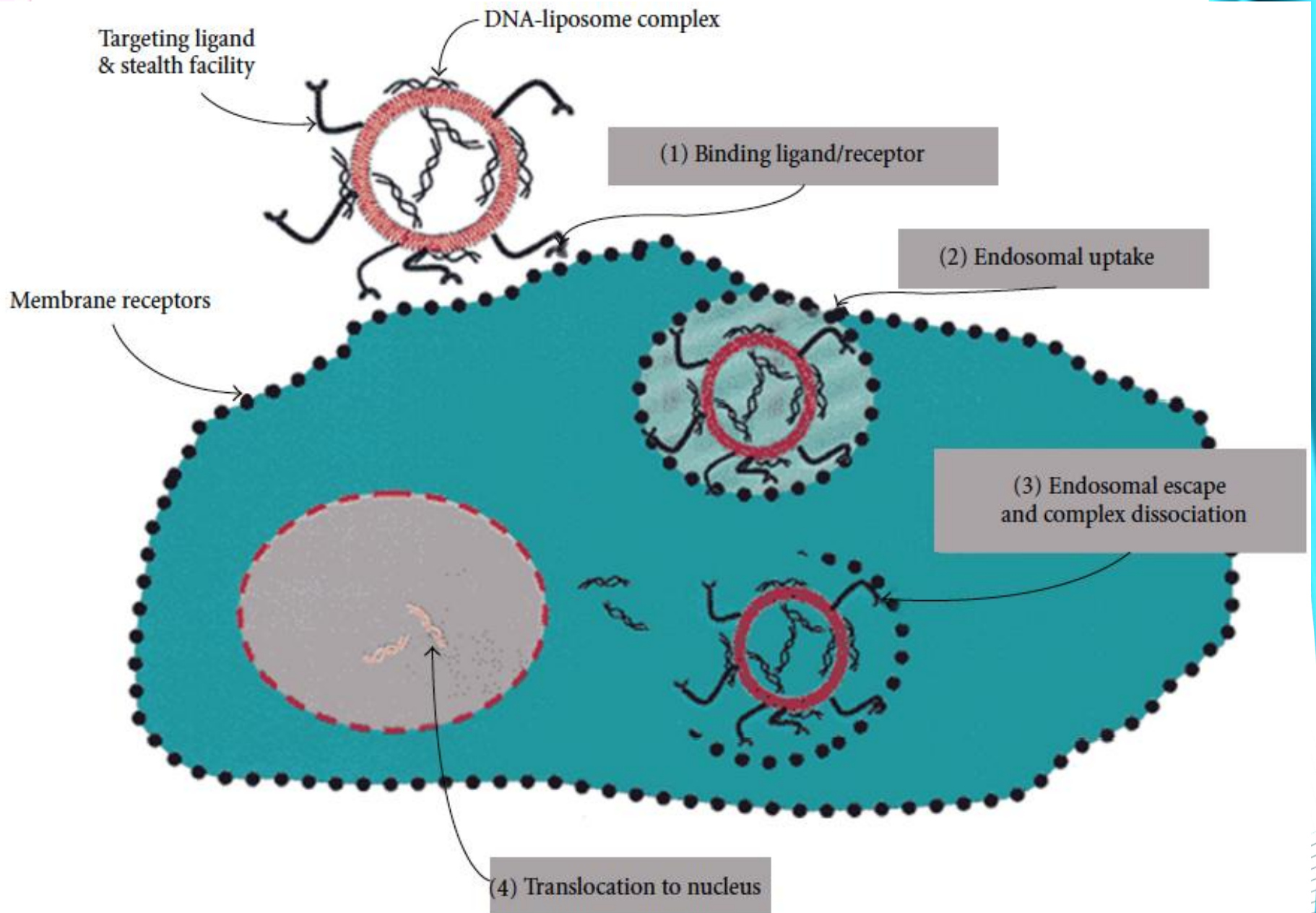
VIROSOME



-  Hemagglutinin
-  Neuraminidase
-  Phosphatidylcholine
-  Phosphatidylethanolamine

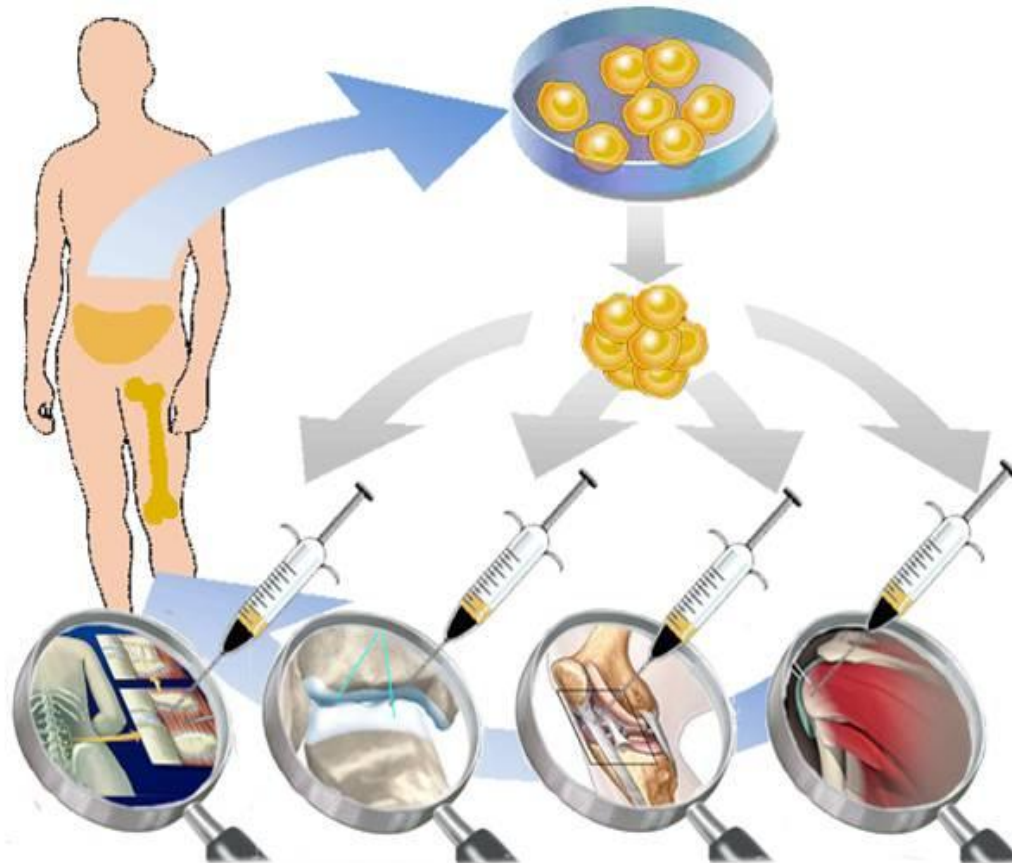
INFLUENZA VIRUS





A schematic depicting the optimization of liposomal gene delivery

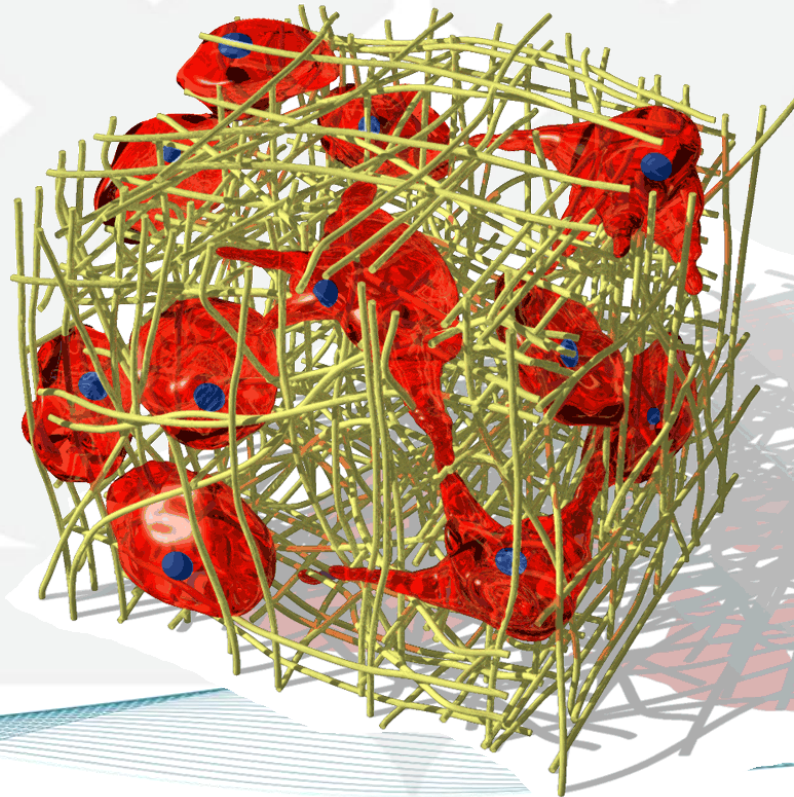
NANOTECHNOLOGY IN STEM CELL/CELL THERAPY



NANOTECHNOLOGY IN CELL THERAPY

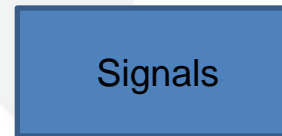
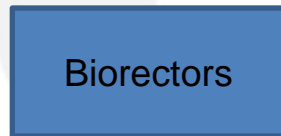
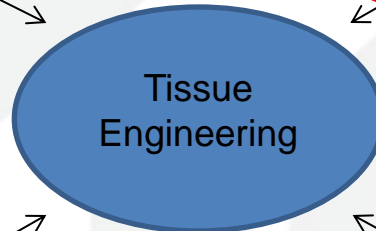
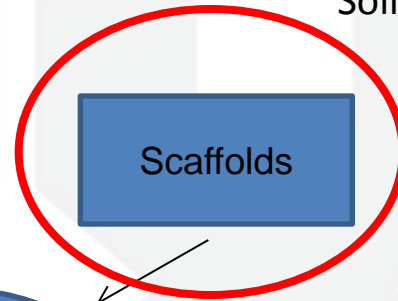
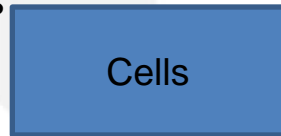
- In cell therapy it is important to guide the cells to specific locations.
- To monitor and evaluate the engraftment in the host, cells are labeled *ex vivo*:
 - to distinguish the implanted cells from the host tissue cells
 - to follow their survival, migration, differentiation
 - To track regenerative impact of the cells in living subjects
- Nanotechnology could help to track and localize transplanted cells.

NANOTECHNOLOGY IN TISSUE ENGINEERING



TISSUE ENGINEERING

Differentiated cells
Adult stem cells
Embryonic stem cells



Hydrogels

Nanofibrous scaffolds

Self-assembling scaffolds

Solid freeform fabricated scaffolds

Dynamic cell seeding
Improved mass transfer
Mechanical stimuli

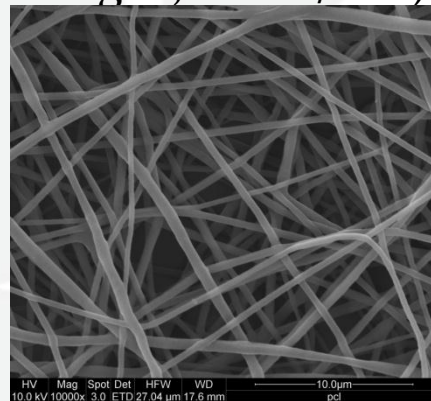
Small molecules
Growth factors/polypeptides
Nucleic acids (DNA, siRNA, and antisense oligonucleotides)

SCAFFOLD MATERIALS

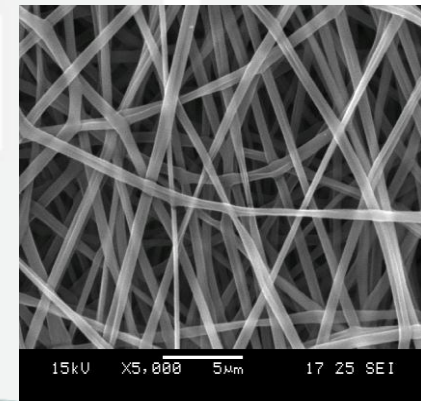
- Types of scaffold materials:
 - **Decellularised tissues** (e.g. heart valves)
 - **Natural matrix or protein** (such as collagen and fibrin)
 - **Synthetic polymers** (such as polyglycolic acid (PGA), Poly lactic acid (PLA), polylactic-co-glycolic acid (PLGA), poly-4-hydroxybutyrate (P4HB), polyhydroxy alkanate (PHA), Polycaprolactone (PCL))
 - **Hybrid scaffolds** (combination of synthetic and natural polymers like PLGA/Chitosan, PU/Collagen, PLGA/Silk)



Decellularised HV

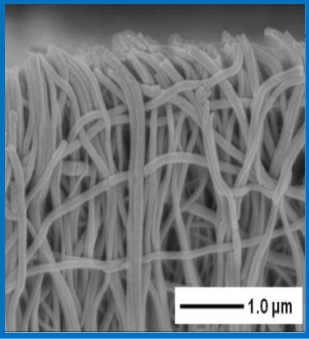
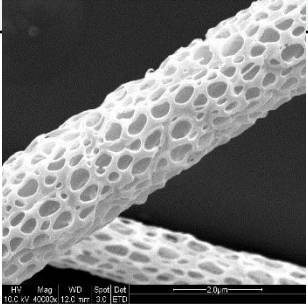
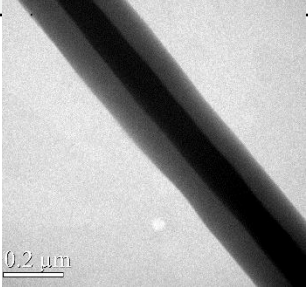
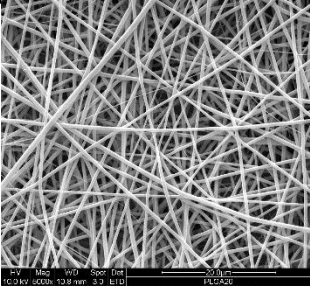
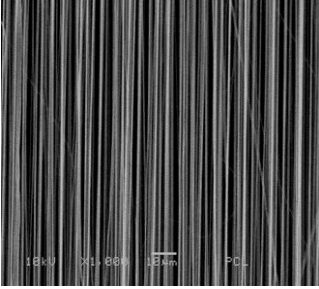
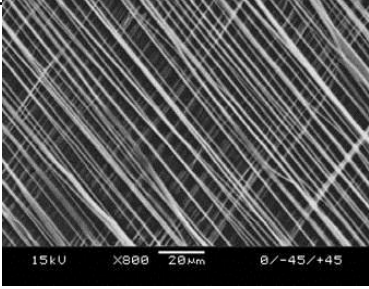
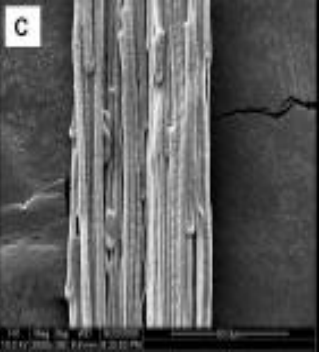
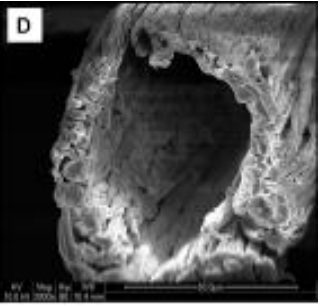
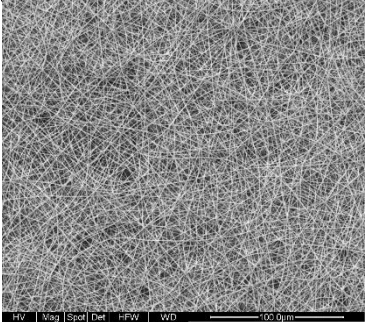


PCL



PLLA-Collagen

Variety of Electrospun Nanofibers

<p>Solid</p> 	<p>Porous</p> 	<p>Core-shell</p> 
<p>Random</p> 	<p>Aligned</p> 	<p>Layered</p> 
<p>Yarn</p> 	<p>Hollow yarn</p> 	<p>Membrane/Sheet</p> 

Nanofibrous tissue engineering bypass graft (PU)

