

Nanotechnology in Medicine

Group 13

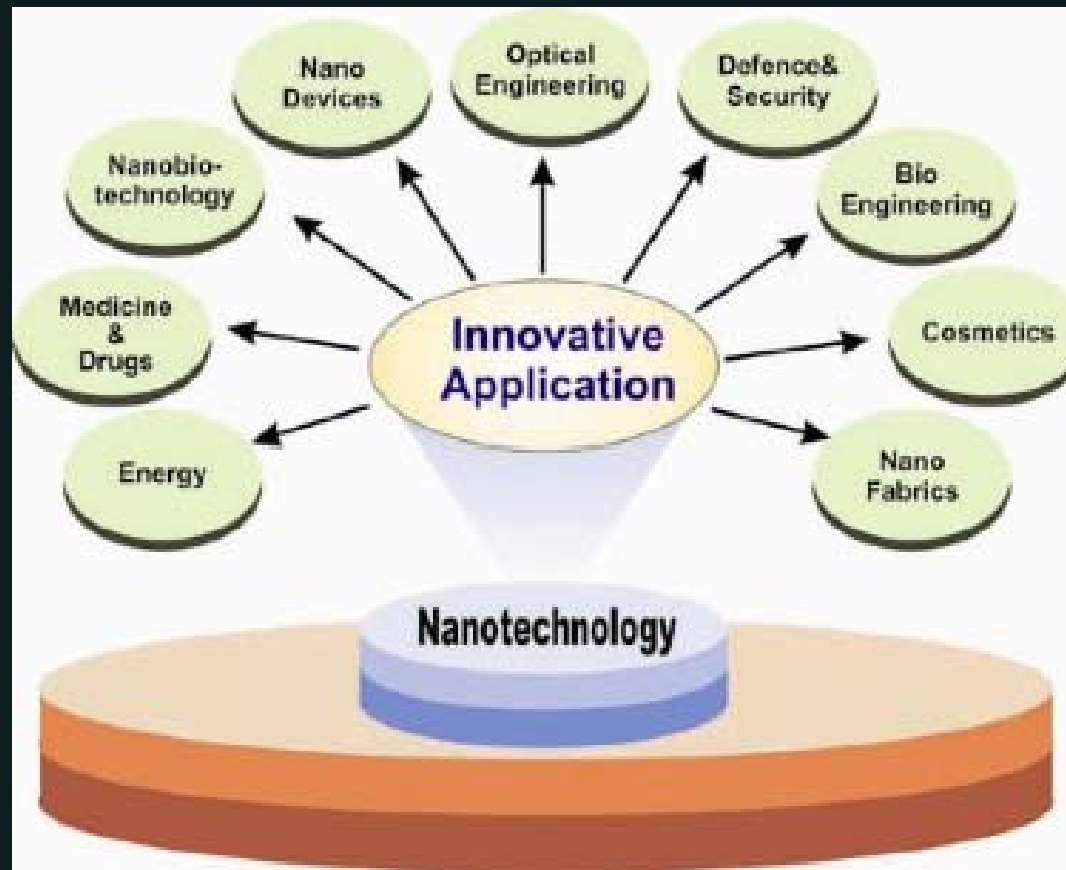
Alec Towle

Aaron Trask

Catherine Vanderhill

Nanotechnology is Rather New

- In 2004, the U.S. alone invested over \$400 million into nanotechnology research
- In a medical sense, we will utilize nanoparticles to bring light, heat, and substances to the human body
- This will help detect or cure diseases or injuries in specific cells

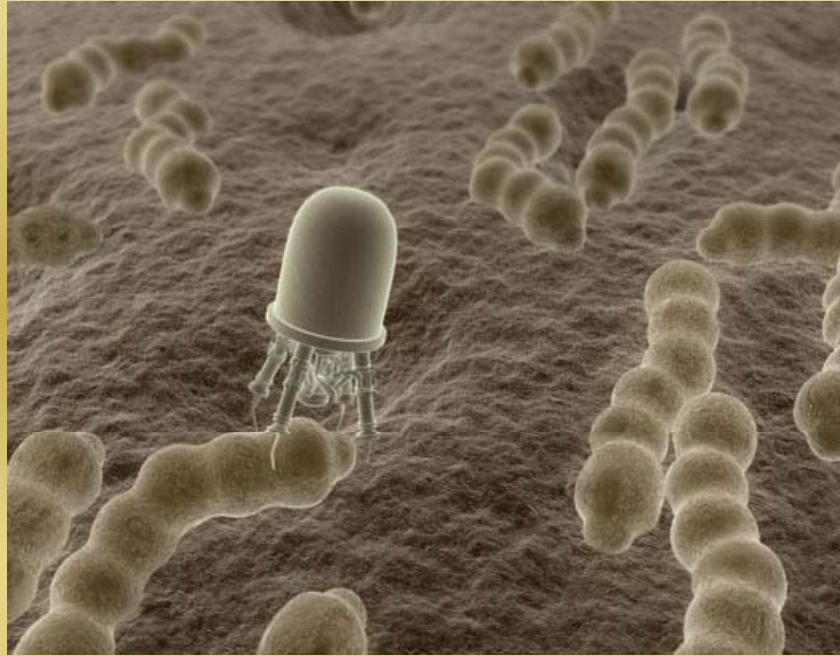


[://images.google.com/imgres?imgurl=http://www.nstc.in/%255CImage%255CArea%2520of%2520Nanotechnology.JPG&imgrefurl=http://www.nstc.in/NTBenefits.aspx&usg=__34Pnu9D7POCOuBBR_E2BMhiHLOU=&h=360&w=460&sz=83&hl=en&start=4&sig2=JwSei9krUqww6vCj99uG2A&um=1&tbnid=nP4ufbKQJLYlpM:&tbnh=100&tbnw=128&prev=/images%3Fq%3Dnanotechnology%2Bin%2Bmedicine%26hl%3Den%26client%3Dsafari%26rls%3Den%26sa%3DN%26um%3D1&ei=NmHHSrncB8yYIAe3-qmSAw](http://images.google.com/imgres?imgurl=http://www.nstc.in/%255CImage%255CArea%2520of%2520Nanotechnology.JPG&imgrefurl=http://www.nstc.in/NTBenefits.aspx&usg=__34Pnu9D7POCOuBBR_E2BMhiHLOU=&h=360&w=460&sz=83&hl=en&start=4&sig2=JwSei9krUqww6vCj99uG2A&um=1&tbnid=nP4ufbKQJLYlpM:&tbnh=100&tbnw=128&prev=/images%3Fq%3Dnanotechnology%2Bin%2Bmedicine%26hl%3Den%26client%3Dsafari%26rls%3Den%26sa%3DN%26um%3D1&ei=NmHHSrncB8yYIAe3-qmSAw)

Nanotechnology on a Global Scale

- In 2000, former president Bill Clinton announced the founding of the U.S. National Nanotechnology Initiative (NNI)
- NNI budget for fiscal year 2002 was \$604 million
- Governments in Europe, Japan, and other Asian nations have invested in national nanoprograms
- The European Union spent about \$180 million on nanotechnology in 2002
- Now a private company, Lux Research, has funded \$9.6 billion in 2008, while government investment was \$8.6 billion

What is Nanotechnology?



<http://thereadingroom.epsilonfoundation.com.au/wp-content/uploads/2009/01/nanotechnology-robot-530.jpg>

- “The ability to design and control the structure of an object at all length scales from the atom up to macro scale.” - Rolf Allenspach, IBM Zurich Research Laboratory in Switzerland
- “The core of nanotechnology consists of systems in the size range of nanometers” - George Robillard, director of the Biological Materials and at the University of Groningen in The Netherlands Devices

Complexity

7th FWP

In-Vivo Nano-Molecular Computing

Artificial Tissue and Organs

Nano-Bio-Robots

(Multi-) Functional Nano-Molecules
& Nano-Molecular DevicesTargeted Particles for
Molecular MedicineTherapeutic/
'Smart' ParticlesBasic
Particles

Materials

'Nanotechnology'
coined as term

1960

1970

1980

1990

2000

2010

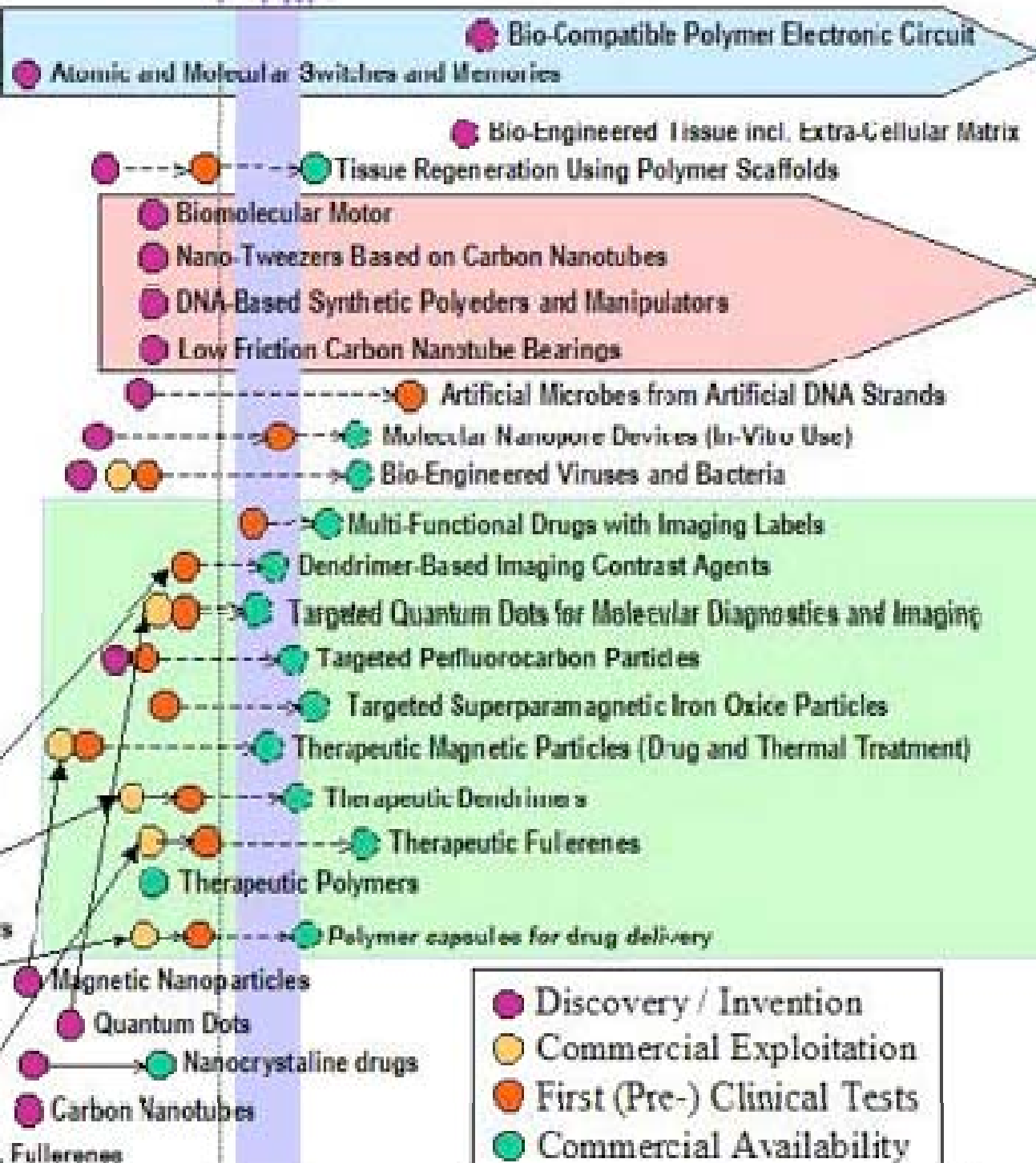
2020

2030

2040

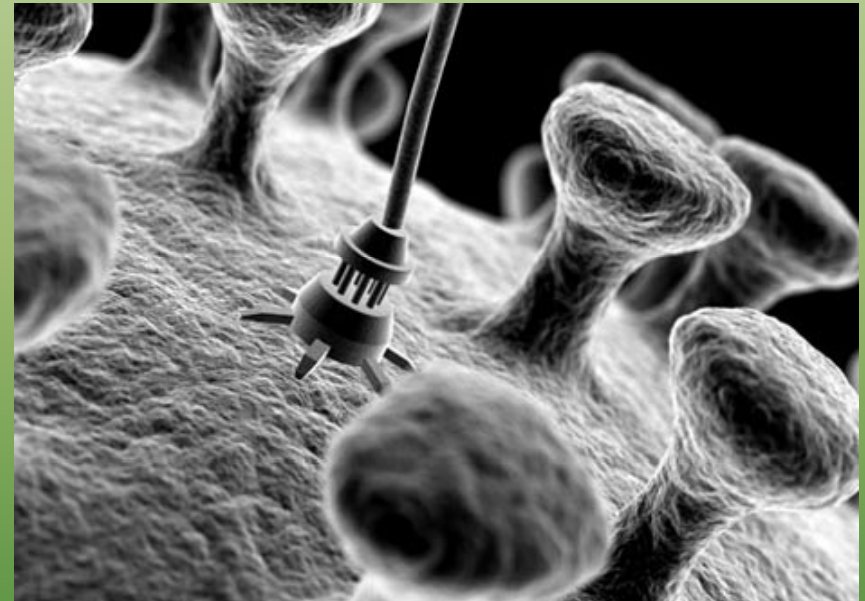
2050

Time



Ethical Dilemmas

- Nanomedicine enhancement will provide humans with improved functions and in a sense, “artificial” body parts
- There are toxicological risks associated with introducing nanoparticles into biochemical pathways
- Scientists will eventually be able to characterize each human cell
 - Will anyone be deemed healthy from this standpoint?
- Consider the privacy and confidentiality associated with knowing one’s entire medical database



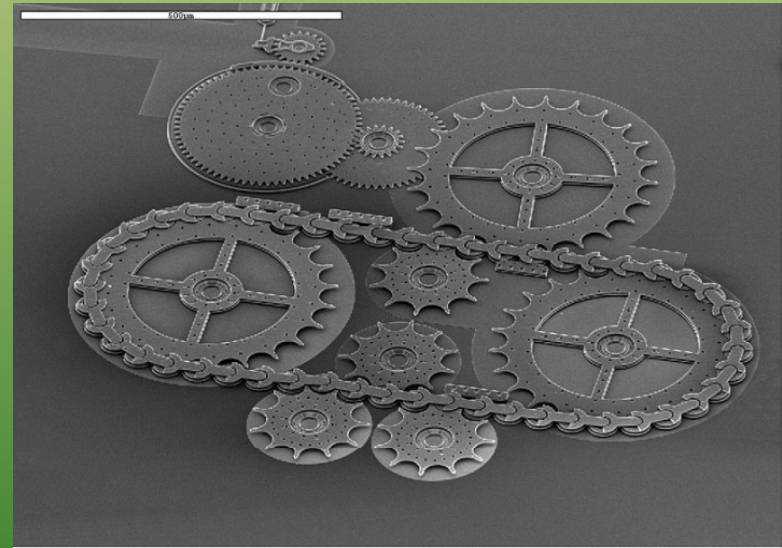
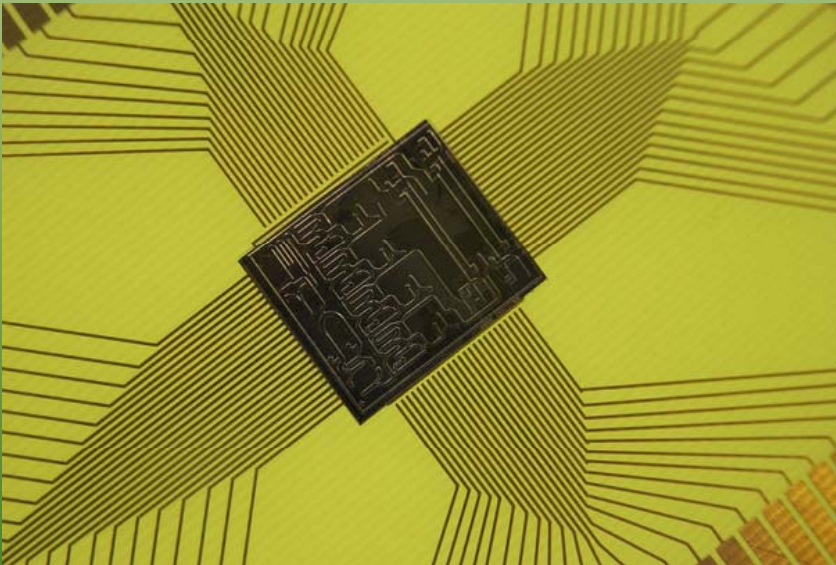
Ethical Dilemmas

- The way that nanotechnology is escalating, humans will eventually be able to control the movement of individual atoms, thereby controlling matter and the physical world around us.
- Some people see this as a new technological era.
- The possibilities of this new technology could go as far as making a car, beef, a computer chip, a t-shirt, a human organ, etc. by putting together the atoms one by one. Trash could be disassembled to be reassembled into useful matter. This is called nanofabrication.



Ethical Dilemmas

- An application already in use is microelectromechanical systems (MEMS), which are currently used in car airbags
- In medicine, nanotechnology is being used for pharmaceutical creation, disease treatment, and nano-machine assisted surgery



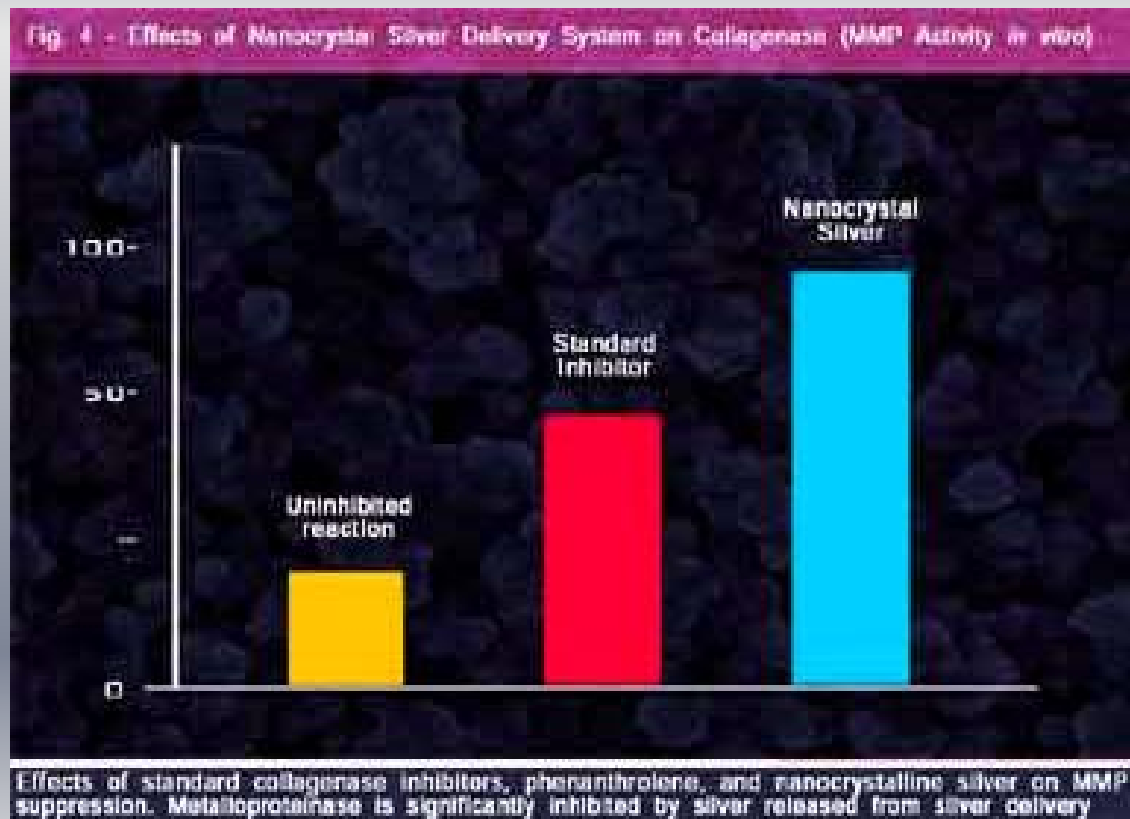
The white line is 500 nm

Ethical Dilemmas

- Questions asked of nanotechnology:
 - Who should create and enforce laws regarding research and development?
 - Does it have the ability to control other ethical issues?
 - Will it jeopardize the right to privacy?
 - What is defined as safe development of nanotechnology?
 - Who will create and enforce the laws to keep development safe?
 - Should we keep this technology secret or share it with the world?
 - If we share the technology, who and how will they monitor its use?

Current Applications - Silver

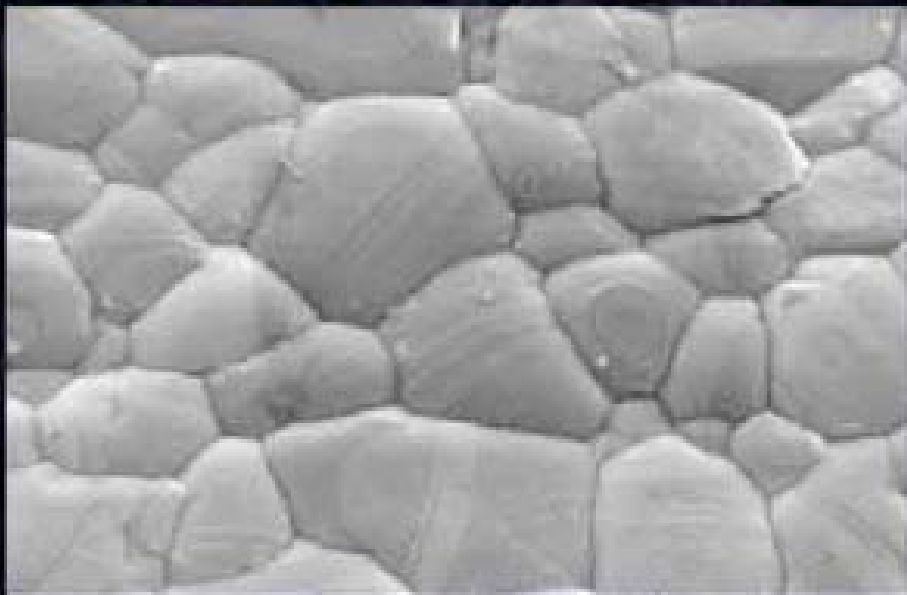
- Nanocrystalline Silver is utilized as an antimicrobial agent to treat wounds and infections
- This gives silver:
 - Antimicrobial Properties
 - Pro-Healing Properties
 - Anti-inflammatory Properties



Current Applications - Silver

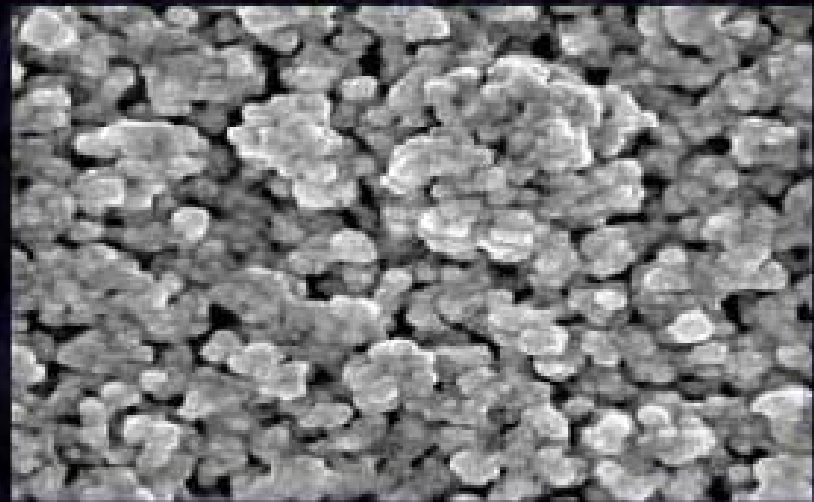
- Silver has been used to treat diseases in the past, but nanotechnology has made it possible to decrease the crystal size and thus increase surface area for potential reactions

Fig. 1 - Normal Silver Coated Membrane



When silver is sputtered under typical physical vapour deposition conditions, the resulting film, is very dense with virtually no pores, allowing limited access to water and for silver release. The crystals are smooth with crystal boundaries being the predominate feature. Crystal sizes range from 100nm to greater than 900nm with an average size of about 250nm.

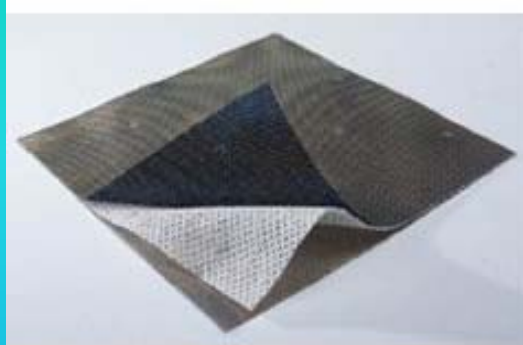
Fig. 2 - Nanocrystalline Silver Coating



The structure of silver antimicrobial delivery coating is evident in this. The physical vapour deposition process creates a material, which is very porous and consist of equiaxed nanocrystals, which allow for rapid exposure to water and subsequent silver release. These crystals are generally organized as aggregates in a columnar structure. The crystals range in size from about 10nm to 22nm with an average size of 15nm and rapidly release silver as ions, radicals and clusters when exposed to water. [13, 14]

Acticoat ®

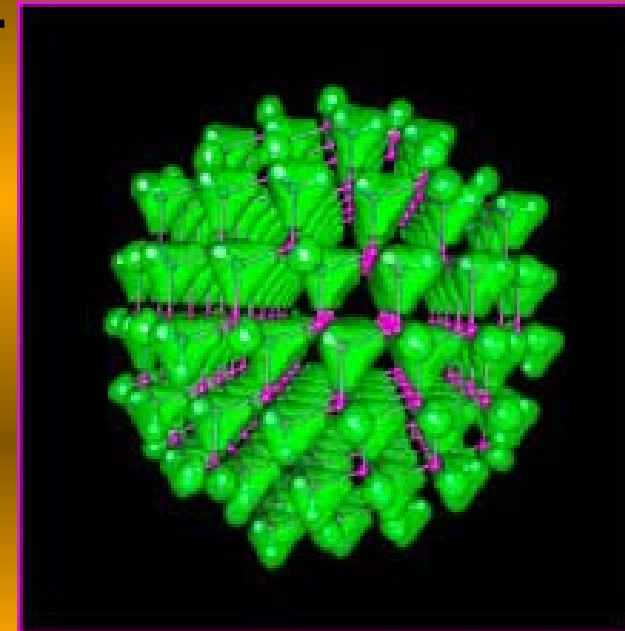
http://images.allegrocentral.com/3B/E6/Acticoat-Burn-Dressing-4-x-4-191609-PRODUCT-MEDIUM_IMAGE.jpg



- Uses SILVCRYST™ Nanocrystals
- These help create wound dressings for powerful antimicrobial barrier protection
- Related to Silver Antimicrobial protection
- Provides an effective barrier to over 150 wound pathogens
- Faster kill rates and longer wear times than other dressings

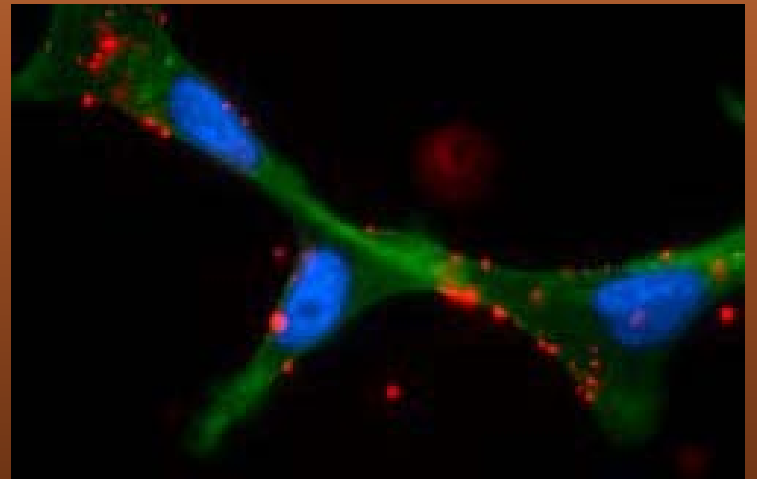
Future Applications - Quantum Dots (Qdots)

- These are fluorescent semiconductors
- Will allow scientists to study a single cell at a time
- This will help in the detection of cancer
- Can be color-coded for easy labeling
- Attaches to a protein and monitors:
 - What it comes in contact with
 - Signaling pathways
 - What cell it is in
 - Normal/abnormal cell functions



Future Applications: Nanoparticles

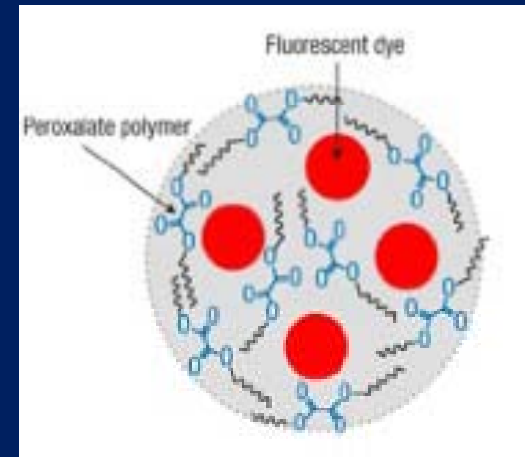
- Delivers chemotherapy drugs directly to cancer cells and tumors while not hurting healthy ones
- Reduces side effects of chemotherapy and makes drugs more effective
- They are attached with specific receptors to bind to a particular particle



Future Applications: Nanoparticles

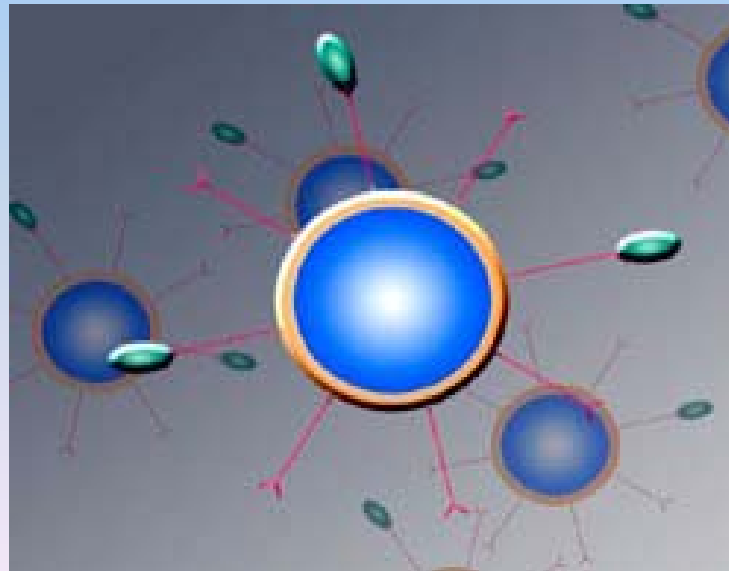
- Can attach to cells that are stricken with a variety of diseases
- Doctors can then identify, based on a blood sample, what is the particular disease
- For example, one can detect overproduced hydrogen peroxide in the body (this may be an early sign of disease)
- Detects cancer, Alzheimer's, arthritis, and heart disease

<http://www.gatech.edu/newsroom/release.html?id=1462>



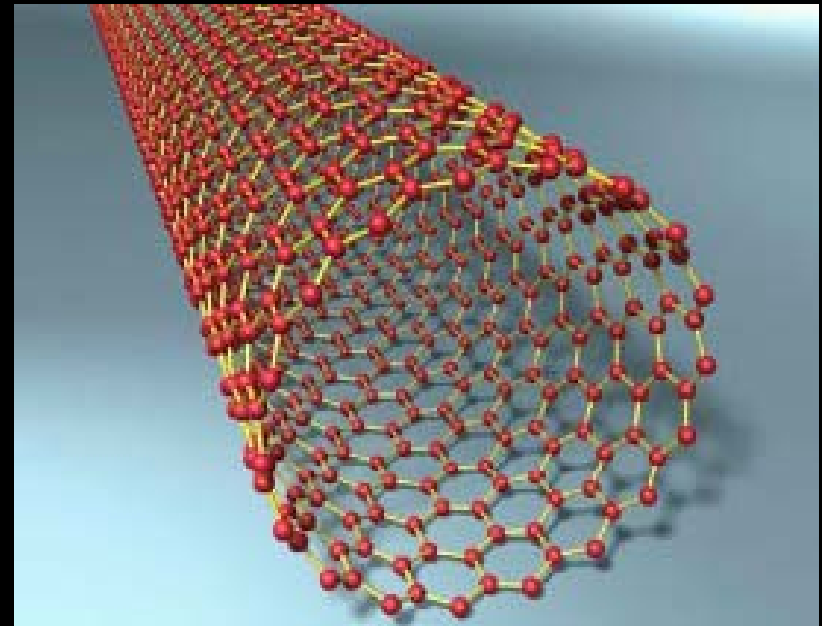
Future Applications - Nanoshells

- Concentrates heat from infrared light to destroy cancer cells without hurting healthy cells
- This could potentially eliminate chemotherapy
- Special coating binds them to cancer cells
- Captures lights and converts it to heat



Future Applications - Nanotubes

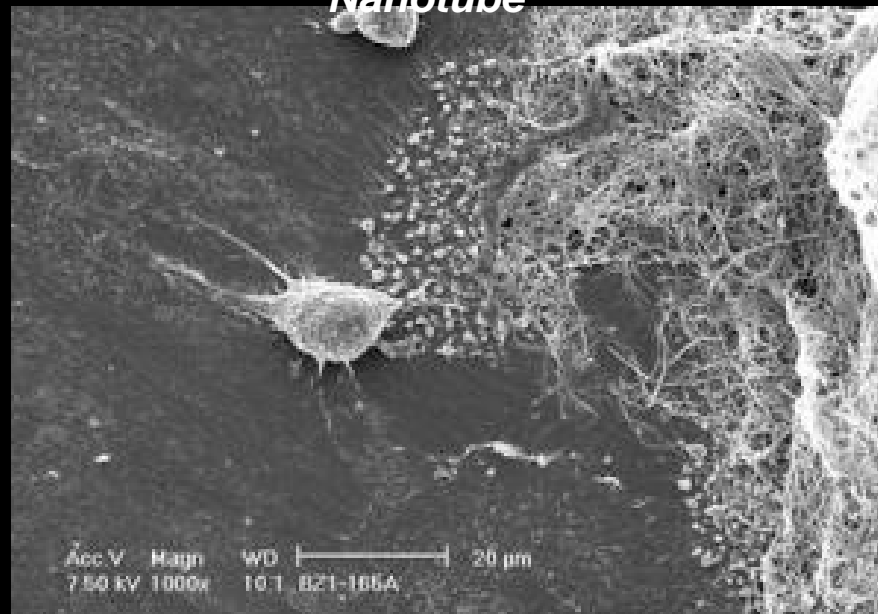
- Used to allow new material to grow from broken bones
- Carbon nanotubes give additional strength and stimulate more bone tissue
- In recent research, these nanotubes produced threefold the amount of bone growth than regular scaffolding



Carbon Nanotubes Grow Bone Cells

- Bone cells have found to grow and proliferate on carbon nanotubes
- Nanotubes are not biodegradable and cells can constantly attach to them
- The only question is how the body will react with its immune system to carbon nanotubes

Bone Growth on a Carbon Nanotube



Carbon Nanotubes as a Sensor

- These can be wrapped with DNA and placed inside living cells
- Can detect small amounts of harmful contaminants such as calcium, mercury, and sodium
- DNA changes shape when it comes in contact with these
- These optical sensors can be a great first step to diagnosing diseases

CellTracks®

http://www.nasatech.com/motion/applications/Images/apps1_0207.jpg

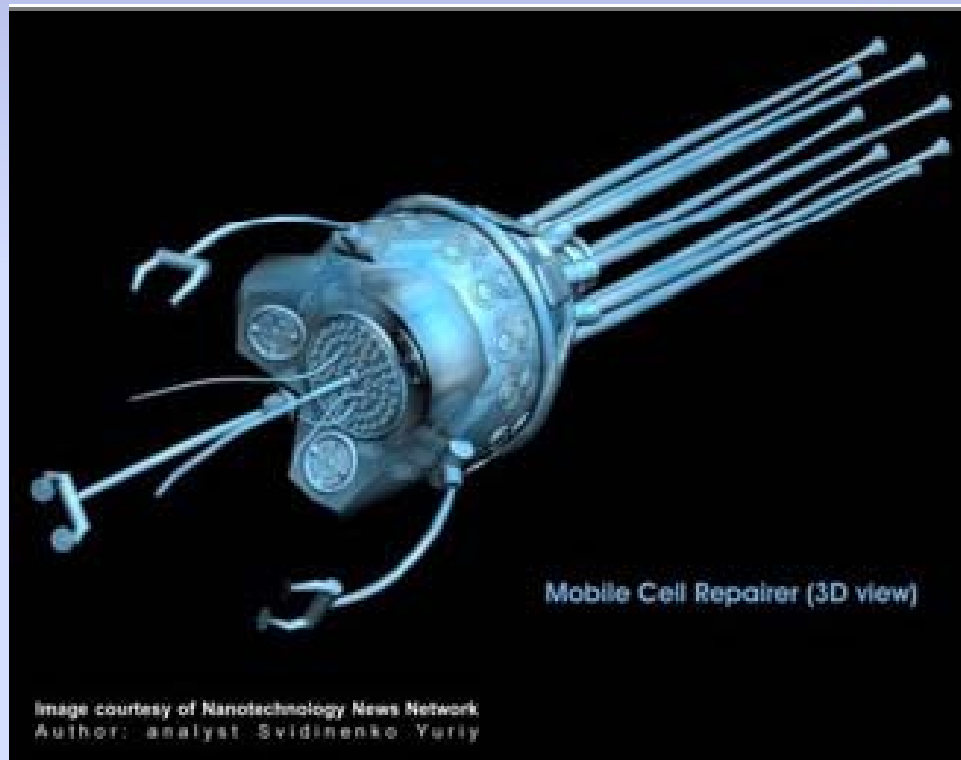


A technician monitors results from the CellTracks Analyzer II microscope.

- Magnetic nanoparticles, called ferrofluids, conjugate to antibodies directed against rare cells
- Attaches to circulating tumor cells and circulating endothelial cells
- The rare cells are then enriched from the patient sample and are fluorescently labeled
- This allows scientists to locate cancerous cells quicker

Nano-Robots

- These are manufactured to perform repairs at the cellular level
- Act similar to our naturally healing antibodies

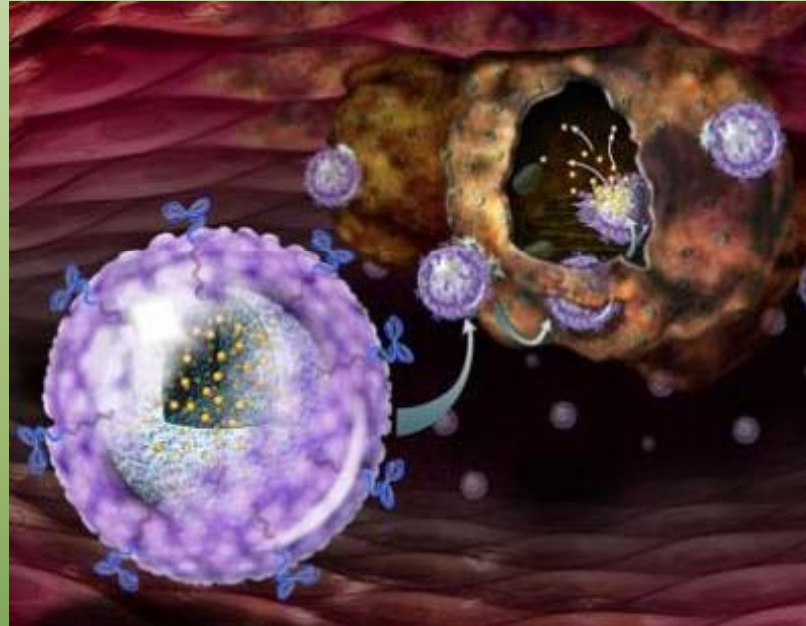


http://www.jabulela.com/files/media/nanorobot_1.jpg

Nanomedicine

- Building nano-robots for future development of medicine
- Examples:
 - Respirocytes
 - Microbivores
 - Chromalloyocytes

Future Potential: Treatment of Diabetes

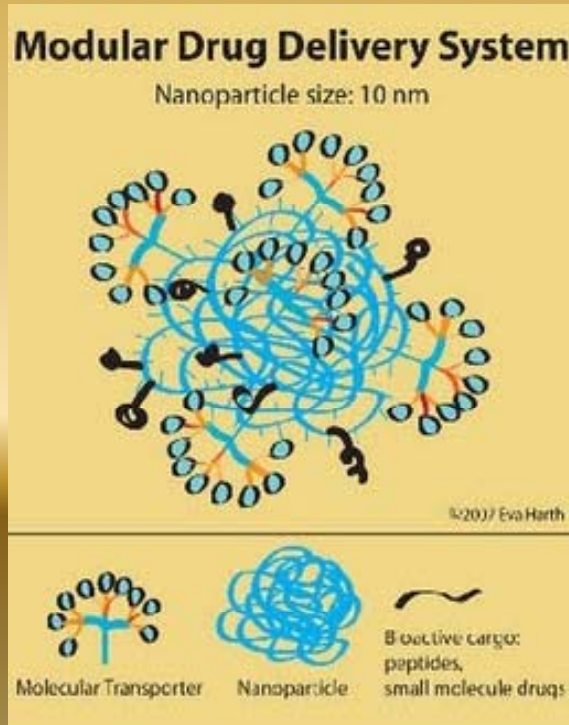


http://images.google.com/imgres?imgurl=http://www.pharmainfo.net/files/u2882/Slide3_0.jpg&imgrefurl=http://www.pharmainfo.net/santosh-kumar-jh/role-nanotechnology-drug-delivery&usq=__2BTVcHsVkBy2luoErN_y277tN6k=&h=300&w=400&sz=14&hl=en&start=6&um=1&tbnid=d0qPAFPAjDcmvM:&tbnh=93&tbnw=124&prev=/images%3Fq%3Dnanotechnology%2Bdispersion%26hl%3Den%26client%3Dfirefox-a%26rls%3Dorg.mozilla:en-US:official%26sa%3DX%26um%3D1

- The future of insulin treatment and regulation
- Nanoscale bio-sensors within the bloodstream determine local insulin and blood sugar levels
- Nanodrug delivery will occur automatically as a response to critical levels
- Entire process will occur as an involuntary body function, with no need for self-regulation and maintenance

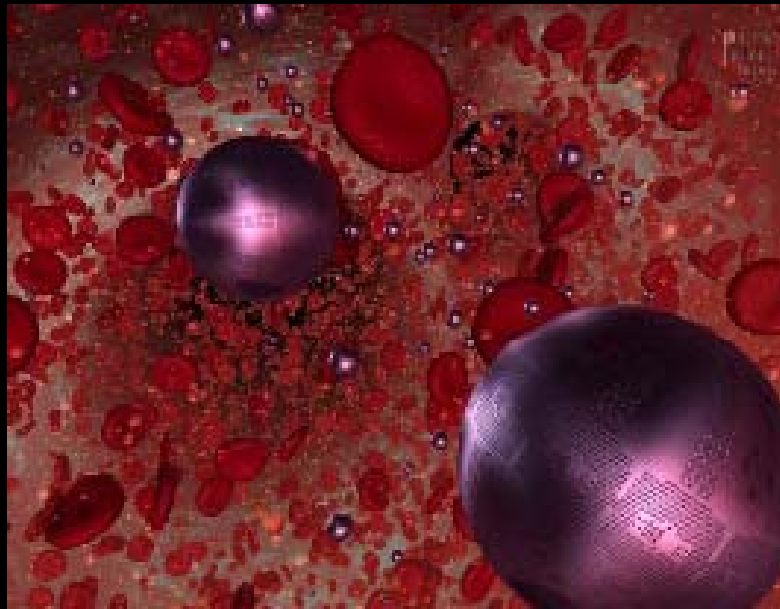
Current Techonology: Thresholds to Overcome

- At present 95% of all new potential therapeutics have poor pharmacokinetics and biopharmaceutical properties
- There is a need to develop suitable drug delivery systems that distribute the therapeutically active drug molecule only to the site of action, without affecting healthy organs and tissues
- Nanodelivery systems have shown to increase the stability of a wide variety of therapeutic agents



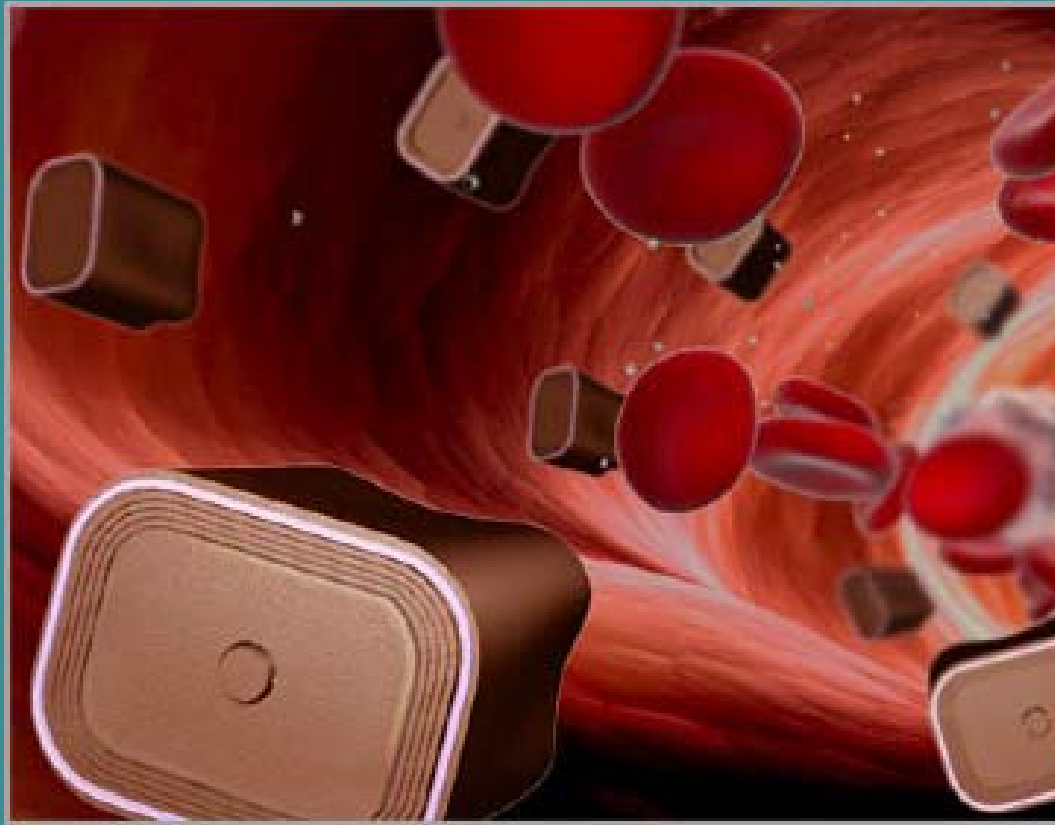
Artificial Red Blood Cell

- Known as respirocytes, will act as a mechanical erythrocyte
- Duplicates the function of carrying oxygen and carbon dioxide
- Mechanical nature will automatically monitor carbon dioxide levels
- Should deliver 236 times more oxygen than normal red blood cells
- Would run indefinitely as opposed to red blood cell's normal 4 year lifespan

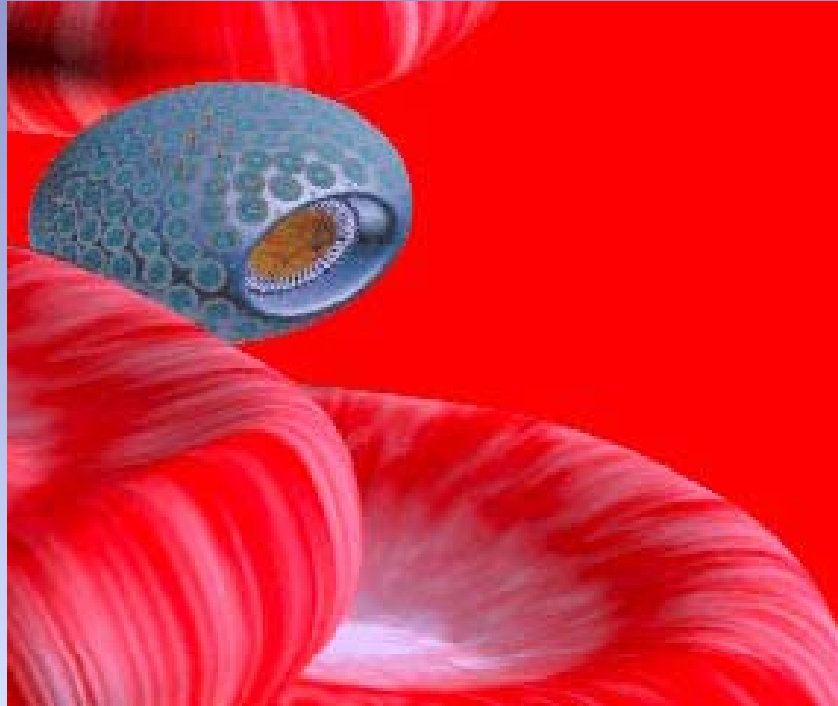


Chromalloytes

- Nanorobots for chromosome repair therapy (CRT)
- Chromatin in nucleus in a living cell is extracted and replaced with prefabricated chromosomes



Microbivores

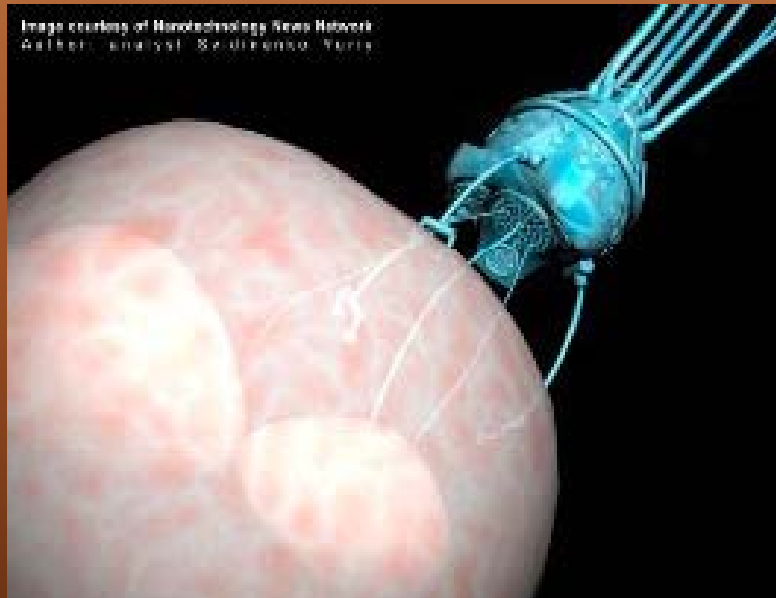


<http://www.foresight.org/nanomedicine/gallery/Images/Microbivore2.gif>

- Artificial mechanical phagocytes
- Destroy microbiological pathogens using digest and discharge protocol
- Binds to the pathogen and gets placed into a chamber
- Enzymes enter the chamber to break down the pathogen into simple molecules
- Those molecules are released into the environment
- Help eradicate bacterial and viral infections

Surgical Nanorobotics

- Could be programmed or guided by a surgeon with ultrasound signals
- With an onboard computer, could diagnose and nanomanipulate lesions
- Example: micropipette used to cut dendrites from single neurons
- Femtolaser, like “nano-scissors” vaporizes local tissue, even chromosomes, and leaves the rest unharmed
- Noninvasive organ and tissue transplants

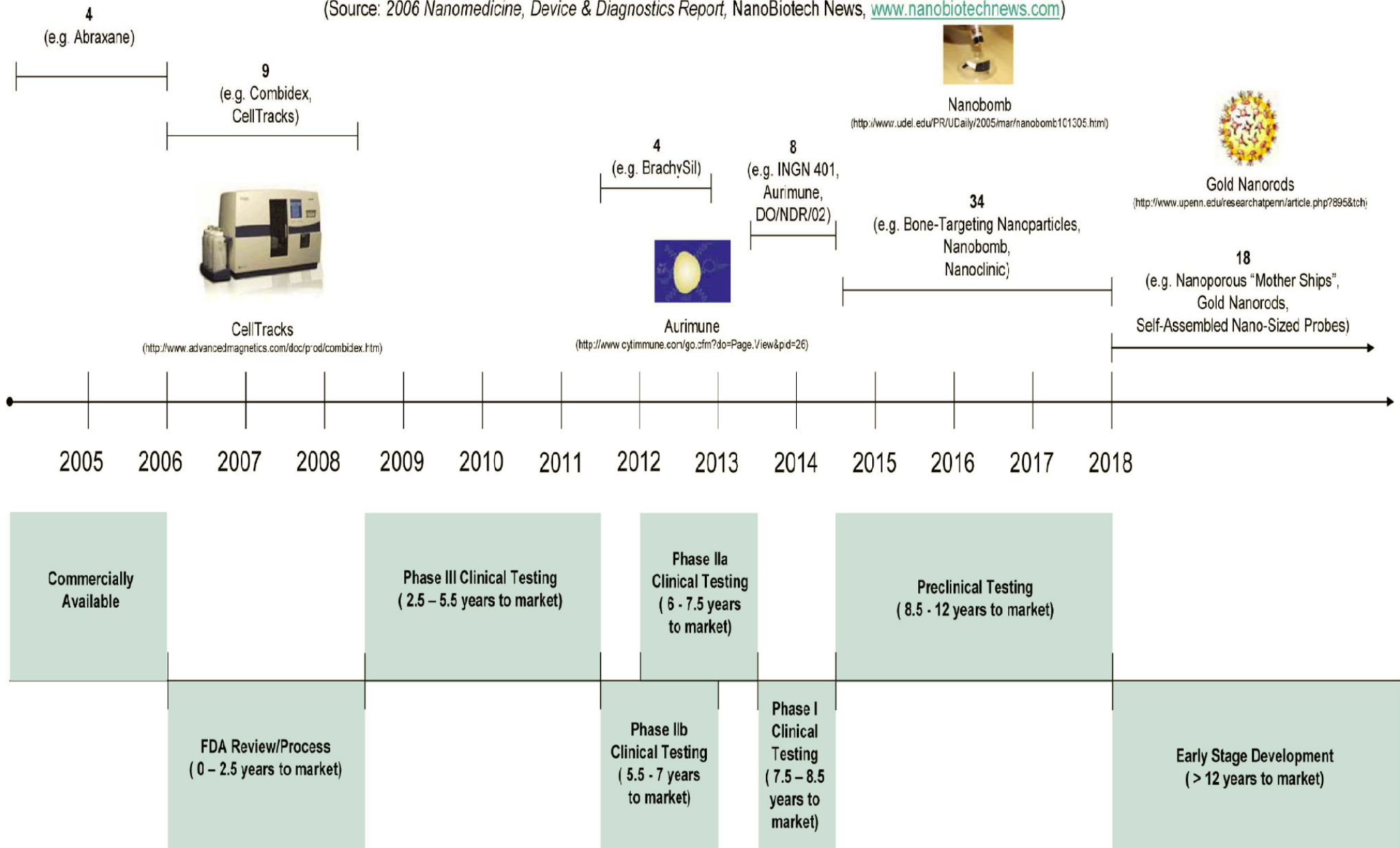


http://www.jabulela.com/files/media/nanorobot_8.jpg

Estimated Commercialization Timeline For Select Nanotechnology Cancer Applications

Total: 77

(Source: 2006 Nanomedicine, Device & Diagnostics Report, NanoBiotech News, www.nanobiotechnews.com)



4

(e.g. Nanocrystals used in Rapamune, Emend, TriCor, and Megace ES)



Emend

(<http://www.prestonhunt.com/hd/pics69%2CEmend.jpg>)

Estimated Commercialization Timeline For Select Nanotechnology Drug Delivery Applications

Total: 56

(Source: 2006 Nanomedicine, Device & Diagnostics Report, NanoBiotech News, www.nanobiotechnews.com)

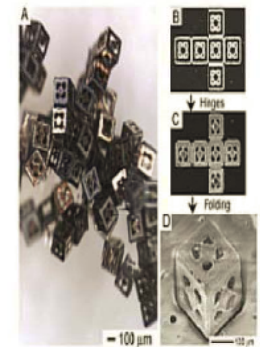
1
(e.g. PRNT)

1
(e.g. NPI 32101)

4

(e.g. Biological Nanoparticle,
Transferrin-Coated Nanoparticles)

30
(e.g. NX-300,
Nanocomposite Drug Carrier)



Self-Assembling Cubes

(<http://www.jhu.edu/news/home/05/dec/05/cubes.html>)

16
(e.g. Self-Assembling Cubes,
Fortifying Nanovehicles)



NPI 32101

(http://www.nucrys.com/product_pipeline.htm)



Commercially
Available

Phase III Clinical Testing
(2.5 – 5.5 years to market)

Phase IIa
Clinical Testing
(6 - 7.5 years
to market)

Preclinical Testing
(8.5 - 12 years to market)

FDA Review/Process
(0 – 2.5 years to market)

Phase IIb
Clinical Testing
(5.5 - 7 years
to market)

Phase I
Clinical
Testing
(7.5 – 8.5
years to
market)

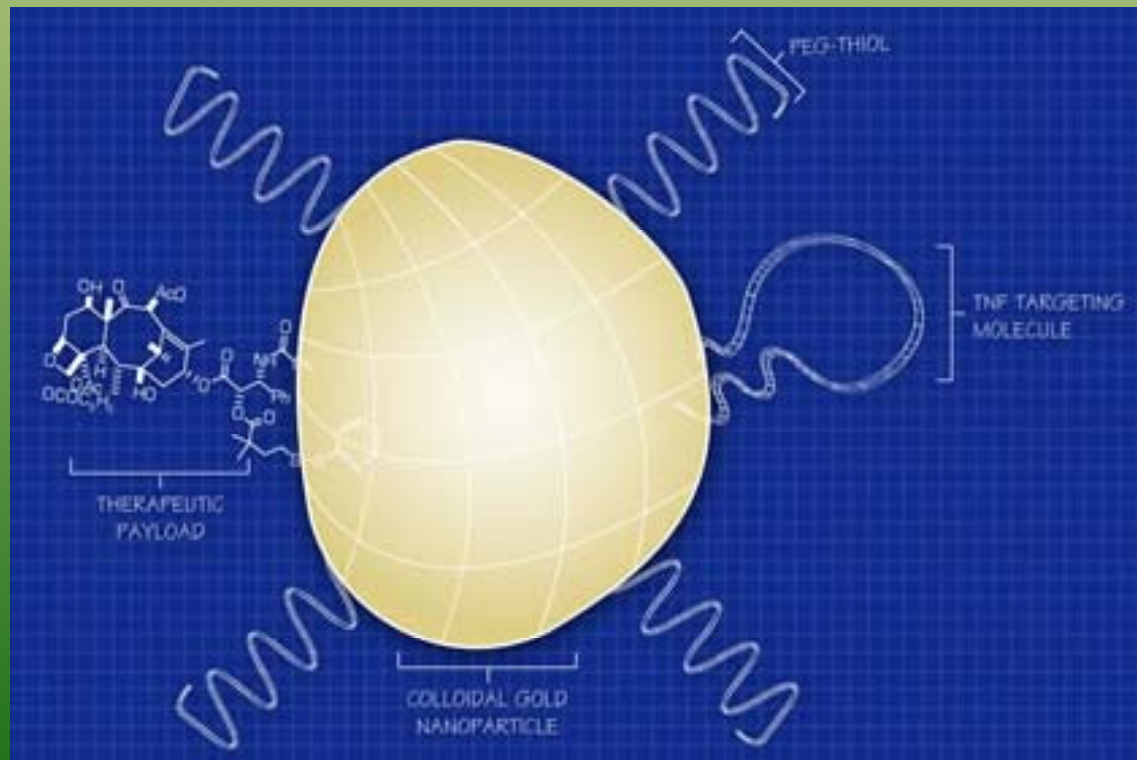
Early Stage Development
(> 12 years to market)

Medical Nanotechnology Companies

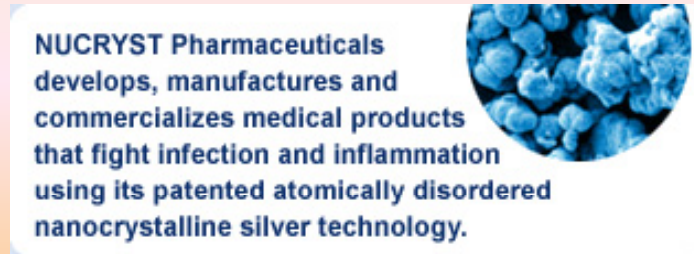
- CytImmune
- Nucrust
- Nanobiotix
- Oxonica
- Nanotherapeutics
- NanoBio
- BioDelivery Sciences
- NanoBioMagnetics

CytImmune Sciences Inc.

- Produce gold nanoparticles for targeted delivery of drugs to tumors
- The company is developing safe ways for drugs to be administered and go directly to the site of the disease
- These processes are meant to avoid build-up in healthy organs and tissue
- They are using colloidal gold based drug compounds to use the therapeutic potential of anti-cancer agents
- These nanomedicines act independently of the biochemistry of the tumors so that they can be used to treat multiple types of tumors.



Nucryst Pharmaceuticals

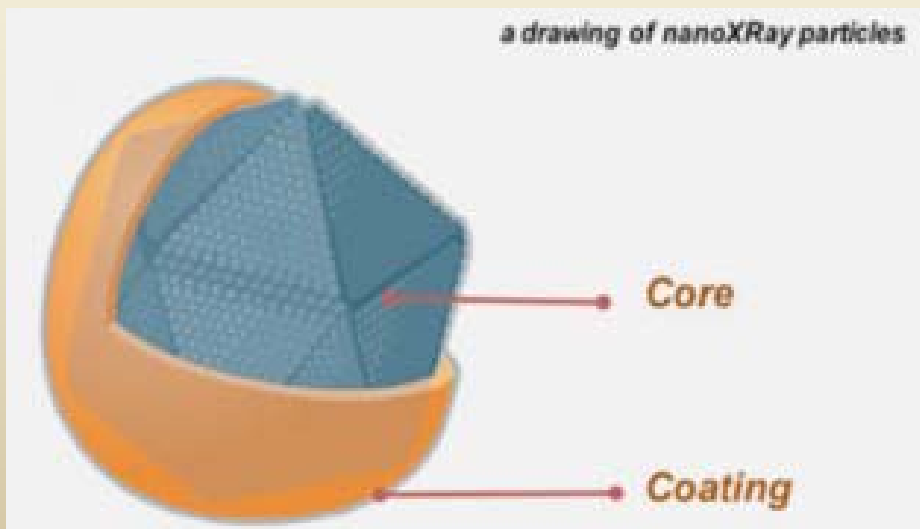


<http://www.nucryst.com/>

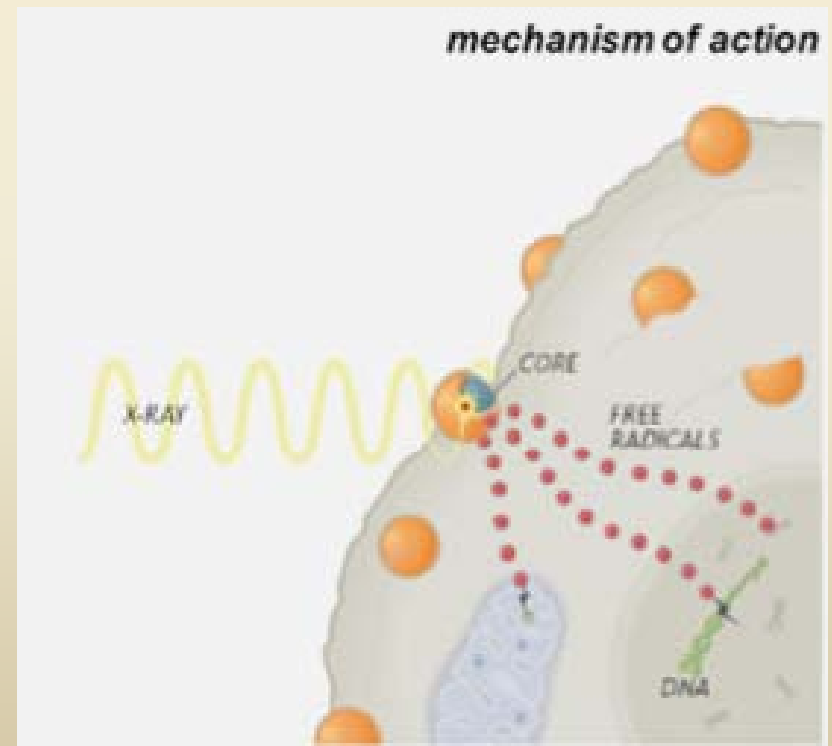
- Create antimicrobial wound dressings using silver nanocrystals
- This works in a number of ways:
 - Bacterial reduction (inhibits a wide range of pathogens)
 - Fluid management
 - Sustained release of silver ions
 - Non-adherent design (pain free removal)

Nanobiotix

- They create nanoparticles that target tumor cells.
- When irradiated by x-rays, the nanoparticles generate electrons which causes localized destruction of the tumor cells
- When the nanoparticles are not activated they are inert



<http://www.nanobiotix.com/technology-products/#nanoXray>



<http://www.nanobiotix.com/technology-products/#howdoes>

Oxonica

- Identify diseases using gold nanoparticles (biomarkers)
- Silica coated, surface enhanced Raman scattering (SERS)-active metal nanoparticles
- Allow robust, ultrasensitive, highly-multiplexed biomarker quantitation in any biological matrix, including whole blood.
- Provide diagnostics over a wide range of areas including infectious disease, cardiac and cancer, food testing for pathogens, and animal health.

Nanoplex Biomarker-
http://www.oxonica.com/diagnostics/diagnostics_home.php



Nanotherapeutics

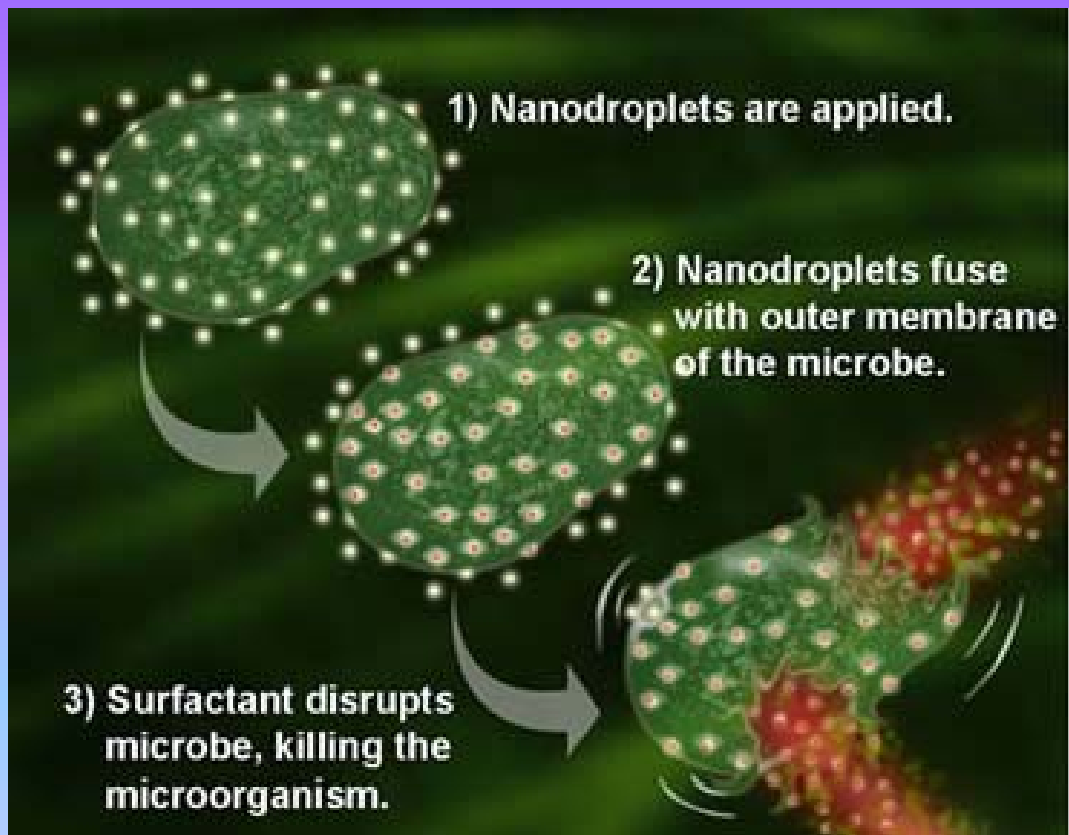


http://www.nanotherapeutics.com/technology_overview.php

- Create nanoparticles for improving the performance of drug delivery by oral, inhaled or nasal methods
- Innovative methods to manufacture nanoparticle formulations with controlled particle size, morphology and surface properties to improve handling, dispersion and absorption
- NanoDry - produces dry powder for efficient and reproducible delivery of large and small molecules.
- NanoCoat - solventless-encapsulation system for coating micron and sub-micron size powders. The coating is applied to slow the rate of release of an active component.
- Controls drug release kinetics

NanoBio

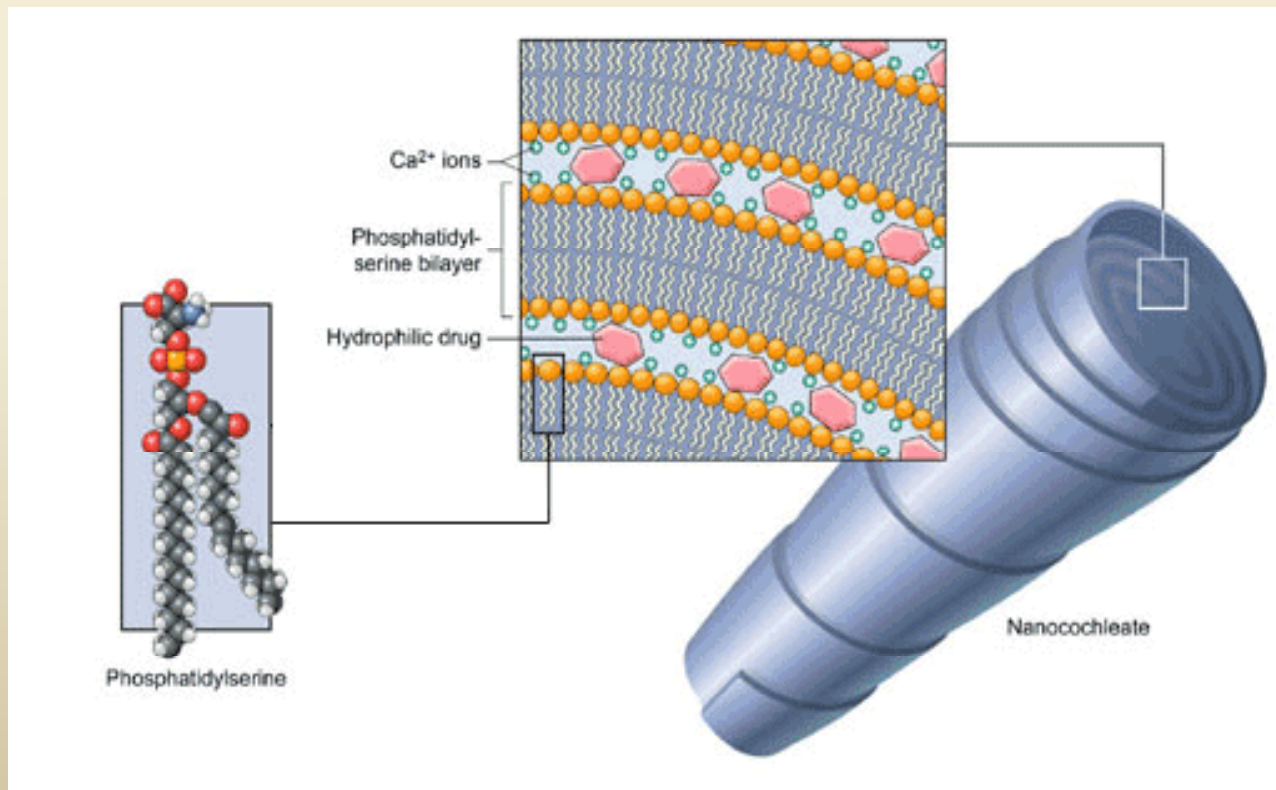
- NanoStat - proprietary oil-in-water emulsions, composed of nanometer-sized droplets that employ a physical process to disrupt the outer lipid membrane of pathogenic organisms.
- Droplets traverse the pores and hair follicles of the skin and mucosal membranes, without disrupting normal tissues



- The technology provides broad-spectrum antimicrobial activity against bacteria, enveloped viruses, fungi, spores and protozoa
- The nanoemulsion acts as a carrier for a vaccine antigen
- Are a big part of the mucosal vaccination process in the nose

BioDelivery Sciences International

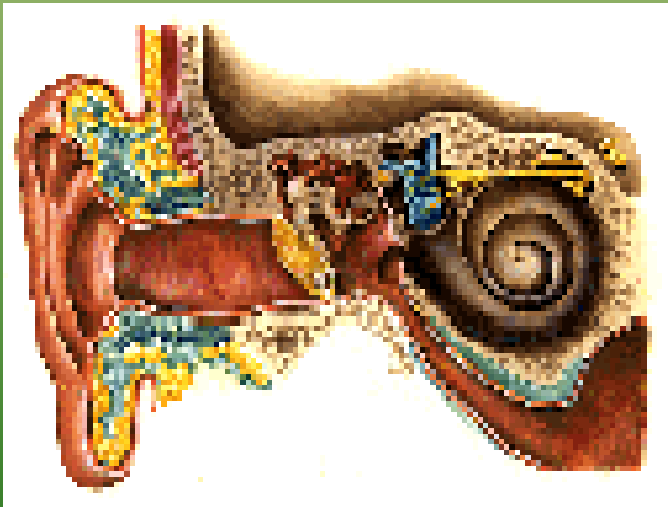
- Bioral - a novel drug delivery system
- Encapsulates a drug without chemically bonding to it
- Administered orally instead of by a needle into a vein
- The structure consists of layers of lipids surrounding the drug thereby protecting it from acid and enzymes in the stomach



<http://www.biodeliverysciences.com/Bioral.php>

NanoBioMagnetics, Inc.

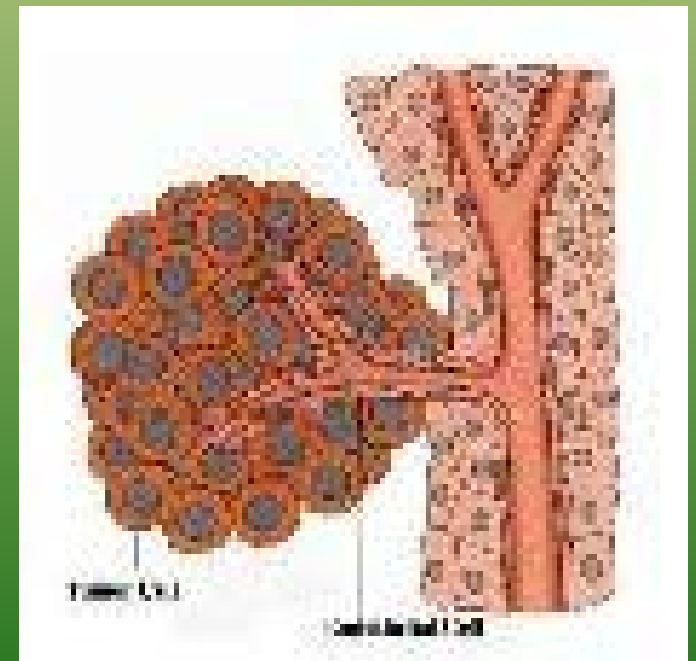
- Pioneering in an emerging area of Organ-Assisting-Device (OAD) technologies
- Nanoparticles are magnetically responsive and can drive a desired physiological event when under the influence of external magnetic field
- Includes biostable implants into tissue to nanomechanically drive tissue movements
- A site specific drug delivery.



Middle Ear Amplification-
<http://www.nanobmi.com/oadtechnologies.html>



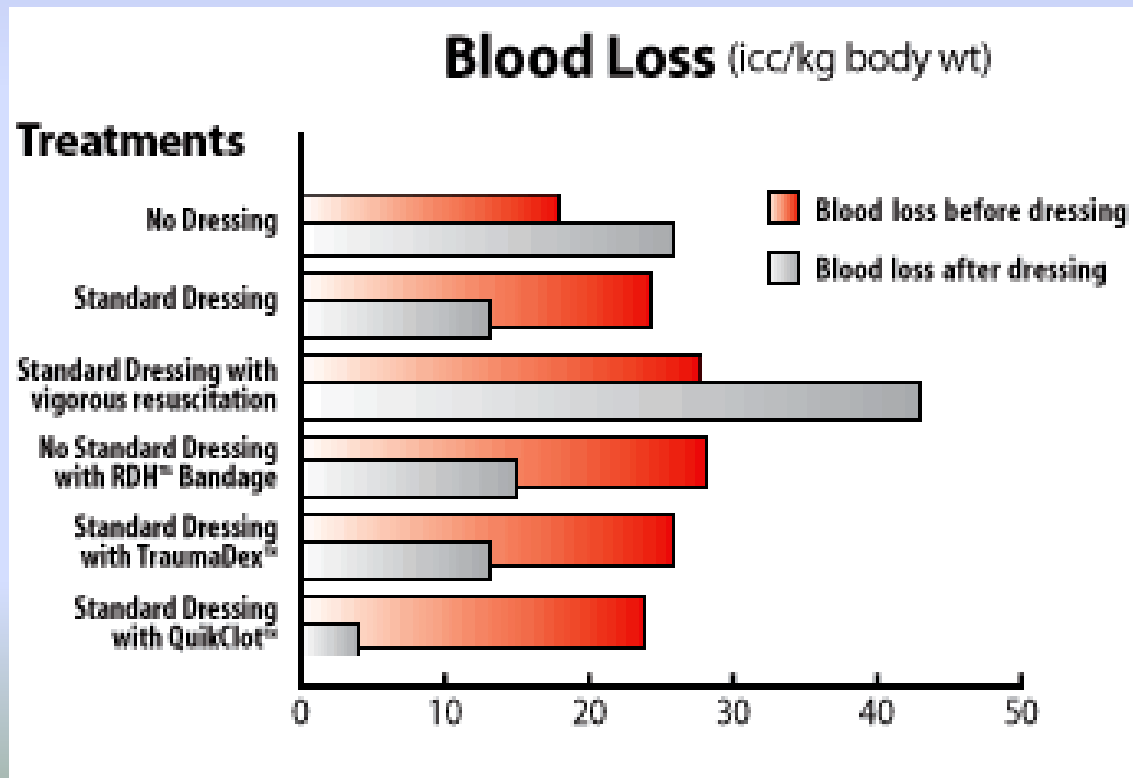
Inner Ear delivery-
<http://www.nanobmi.com/oadtechnologies.html>



Tumor Specific Delivery-
<http://www.nanobmi.com/oadtechnologies.html>

Z-Medica

- Creates medical gauze containing aluminosilicate nanoparticles which help blood clot faster in open wounds
- QuikClot hemostatic agent - a molecular sieve that promotes extremely rapid natural clotting
- Removes the smaller water molecules in the wound and allows the larger platelet molecules to remain in the wound in a highly concentrated form



http://www.z-medica.com/quikclot/hemostat_quikclot.asp

Estrasorb™

- Produced by Novavax, Inc. (USA)
- Soy-based Lotion used to treat hot flashes (vasomotor symptoms) associated with menopause
- Uses micellar nanoparticle drug-delivery platform to deliver 17β estradiol into bloodstream
- FDA approved in October 2003



<http://www.estrasorb.com/>

Megace® ES

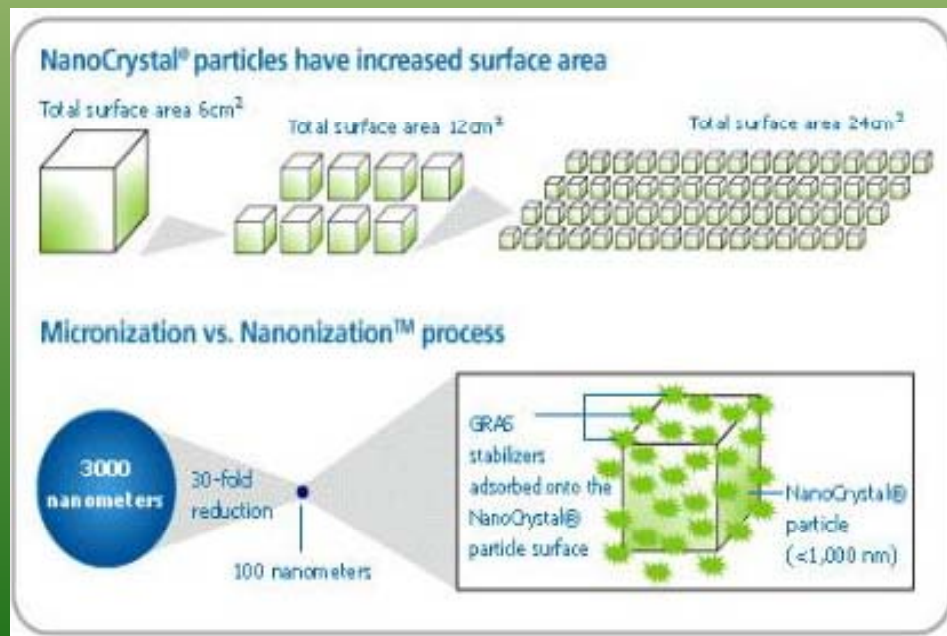


<http://www.megacees.com/megace-es.html>

- Produced by Par Pharmaceutical Companies, Inc. (USA)
- Utilizes Elan's NanoCrystal technology delivery system
- This improves the rate of dissolution and bioavailability of the original megestrol acetate oral suspension
- Stimulates appetite for those with anorexia, cachexia, or weight loss in patients with acquired immunodeficiency syndrome (AIDS)

Rapamune®

- Produced by Wyeth
- Is the first drug to use Elan's NanoCrystal Technology
- Was available before as an oral solution
- Now, nanotechnology has given the product more convenient storage and administration
- By increasing the surface area, the relative solubility has increased
- FDA approved in August 2000
- Used to help prevent organ rejection in patients aged 13 years or older receiving renal transplants



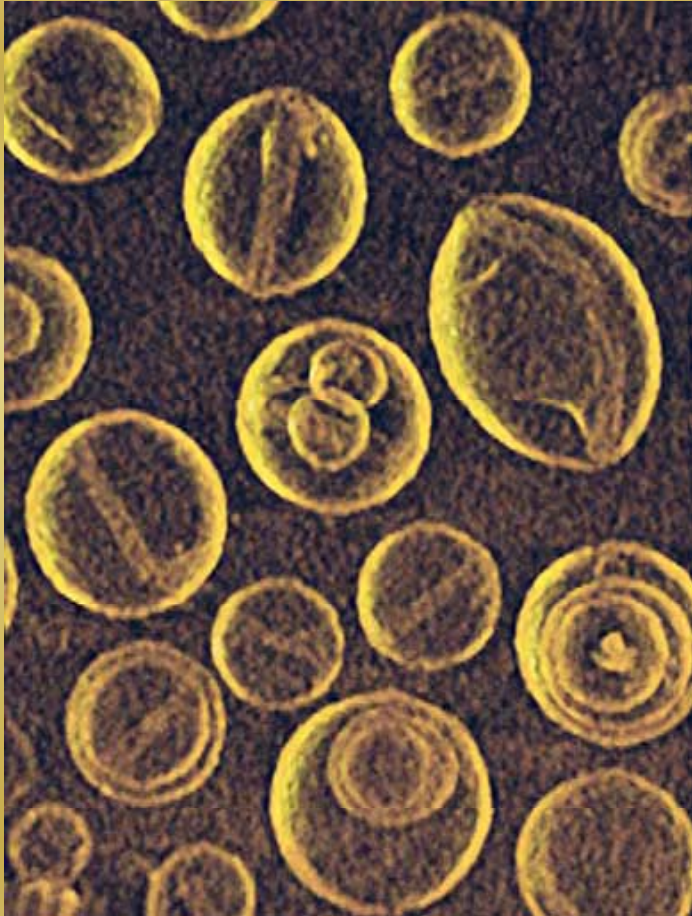
Emend®

- Produced by Merck & Co., Inc.
- Anti-nausea drug for chemotherapy patients
- Nanotechnology allows the product to formulate aprepitant as NanoCrystal drug particles
- GRAS (Generally Regarded As Safe) stabilizers keeps the NanoCrystals from agglomeration by surface adsorption
- The result is the product acts as a solution and is readily administered
- FDA approved in March 2003



Doxil®

Cryo-Tomogram of Vitrobot
frozen liposomes containing the
anti-cancer drug Doxil



http://www.tedpella.com/vitrobot_html/doxil.jpg

- Produced by ALZA corporation
- Anti-cancer drug for the treatment of refractory ovarian cancer and AIDS-related Kaposi's sarcoma
- Utilizes STEALTH® technology where lipid nanoparticles are coated with polyethylene glycol (PEG)
- This coating helps evade the potential impact of the immune system and delivers the drug to disease-specific sites
- Approved by FDA in February 2005

Abraxane®

albumin

paclitaxel

- Treats advanced forms of breast cancer
- Utilizes nanoparticles made of albumin, a human protein
- This protein releases the chemotherapy
- Can be administered in 30 minutes (as opposed to 3 hours for traditional chemotherapy)
- In a clinical trial, the tumor response rate was almost double for patients who received ABRAXANE compared to other treatments

Medicinal Nanotechnology

Medicinal Nanotechnology

Disease Treatment

Silver

Carbon
Nanotubes

Nanoshells

Disease Diagnosis

Qdots

Nanoparticles

Nanomedicine

Microbivores

Chromallocytes

Respirocytes

Nanotechnology is becoming an integral part of the diagnosis and treatment of diseases and the production of drugs.

Alec Towle; Aaron Trask; Catherine Vanderhill

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