PURDUE UNIVERSITY

Weldon School of Biomedical Engineering

The Convergence of Differences, The Future of Excellence

BME 695 – August 23, 2011

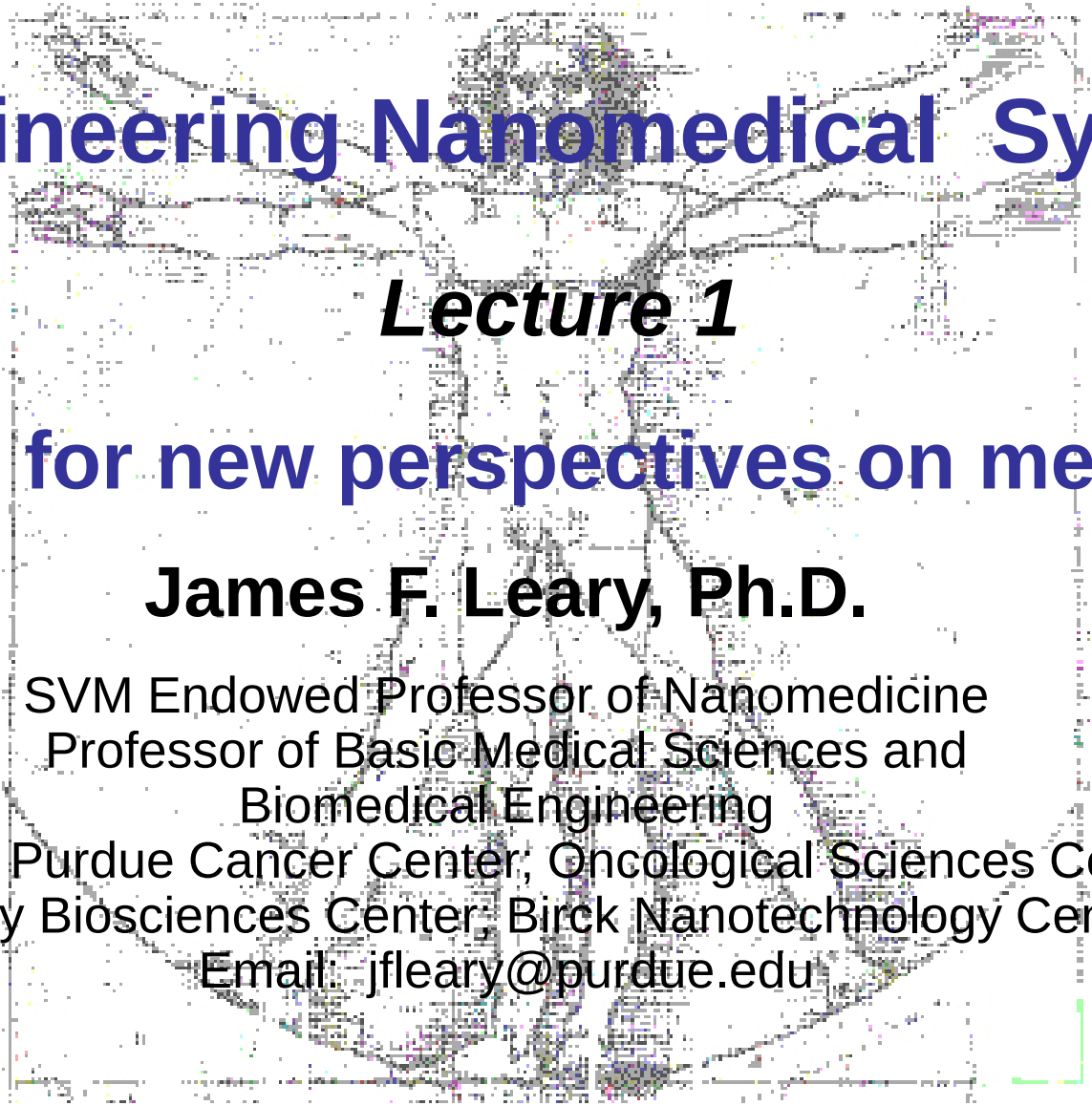
Engineering Nanomedical Systems

Lecture 1

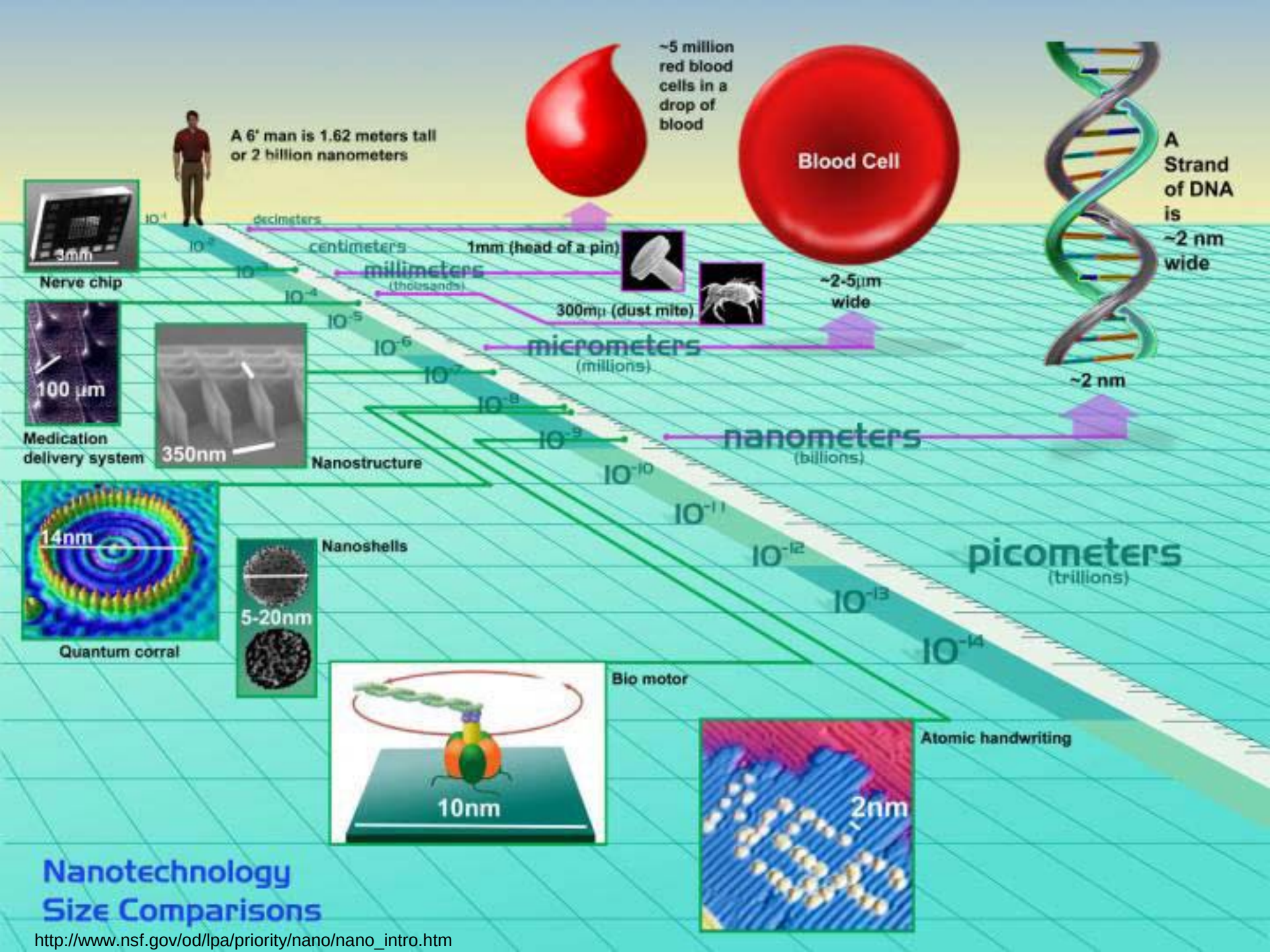
"Need for new perspectives on medicine"

James F. Leary, Ph.D.

SVM Endowed Professor of Nanomedicine
Professor of Basic Medical Sciences and Biomedical Engineering
Member: Purdue Cancer Center; Oncological Sciences Center; Bindley Biosciences Center; Birck Nanotechnology Center
Email: jfleary@purdue.edu



1.1 Nanotechnology: Why is something so small so big?



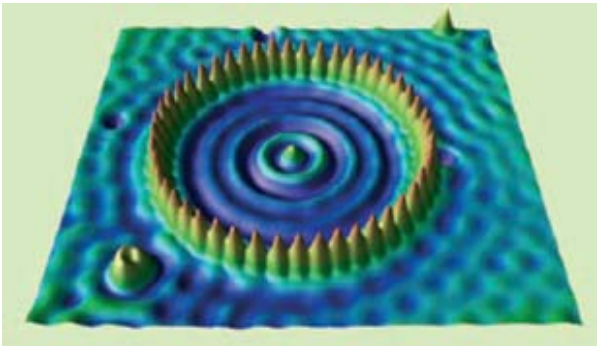
http://www.nsf.gov/od/lpa/priority/nano/nano_intro.htm

Nanotechnology represents a major paradigm shift

For most of human history manufacturing came from sculpting bigger objects down into smaller objects

OLD paradigm

NEW paradigm



Nanotechnology represents a “bottoms up” atom-by-atom assembly

Examples of Nanotechnology Basic Applications

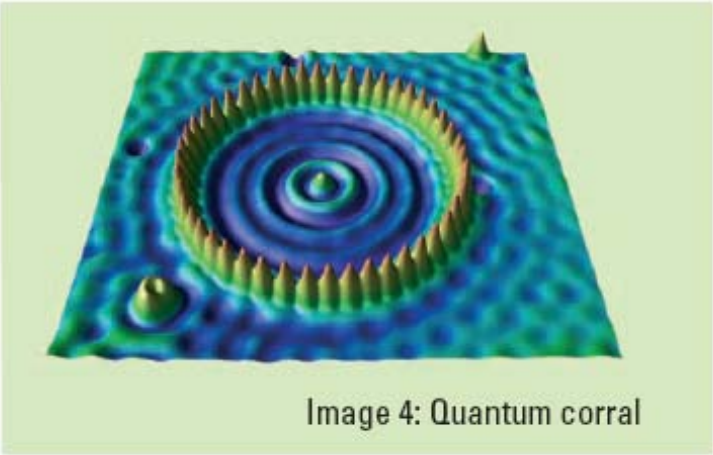


Image 4: Quantum corral

http://www.colorado.edu/physics/phys3220/phys3220_sp06/mainPage3.html *Science 262, 218-220 (1993).*

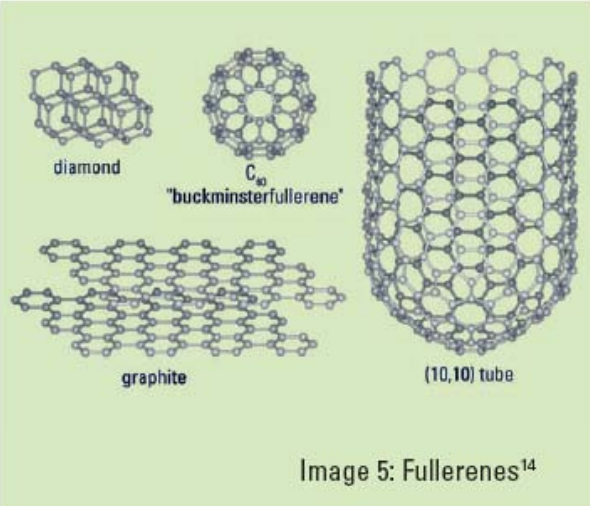


Image 5: Fullerenes[14]

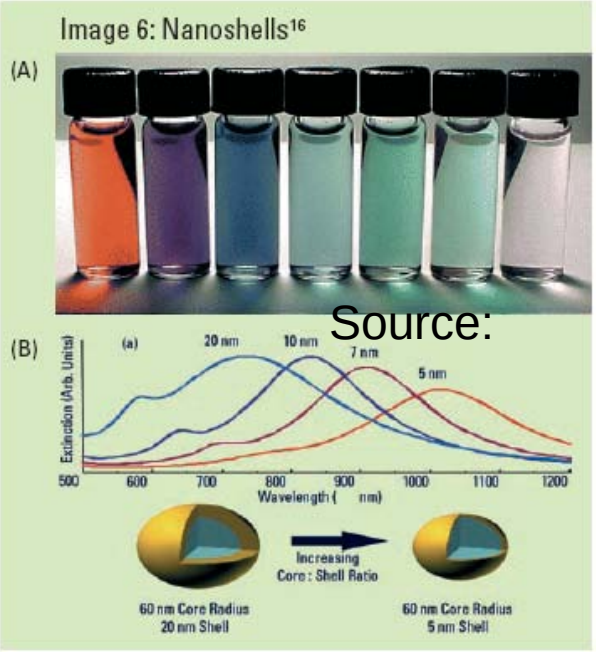
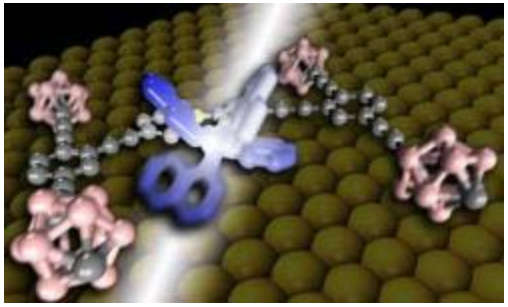


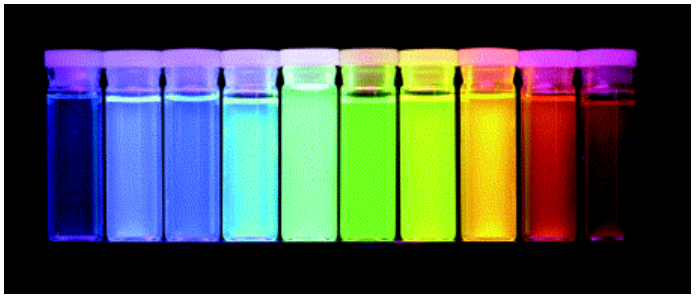
Image 6: Nanoshells[16]

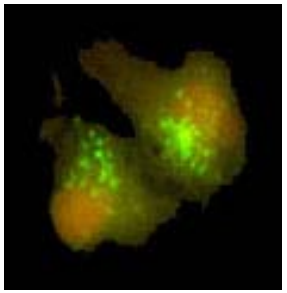
Source:



"Nano-cars" by Dr. Tour's group at Rice University

Source: Tour Lab website





"Quantum dot" nanocrystals… Nie, 2002

The nanoworld challenges our perspectives on size – if you lived in a nanoworld…

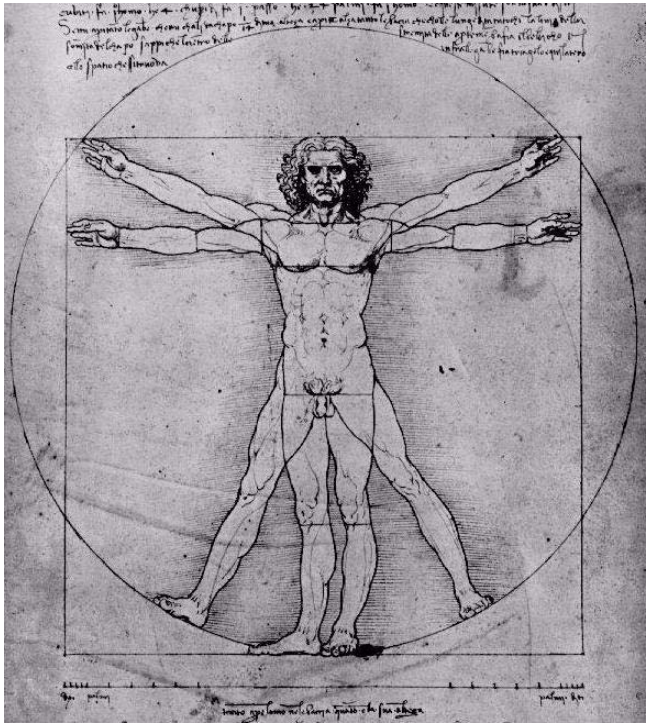
You would need to think about nanoparticles as sometimes smaller than the molecules attached to them (antibodies are quite large) and the cell would be proportionately the size of a very large banquet room!

nanoparticle

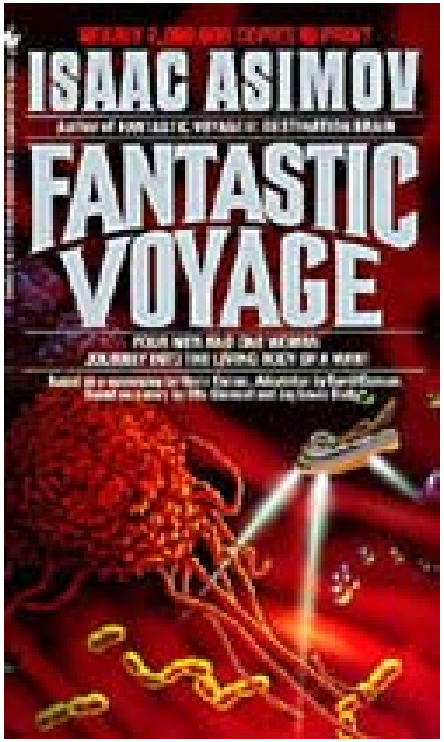
DNA molecules

1.2 The Progression of Medicine

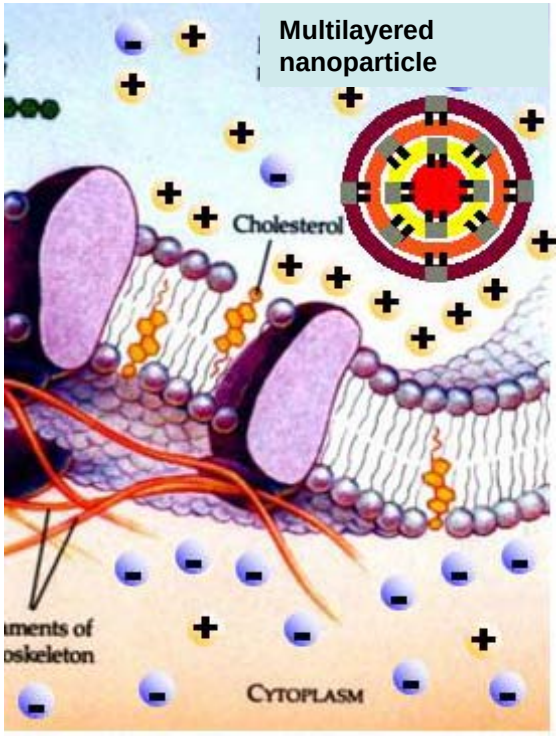
Concepts of Medicine
In 1490, 1966 and 2009



Art: Da Vinci's "Vitruvian Man" 1490



1966 science fiction



2009 science

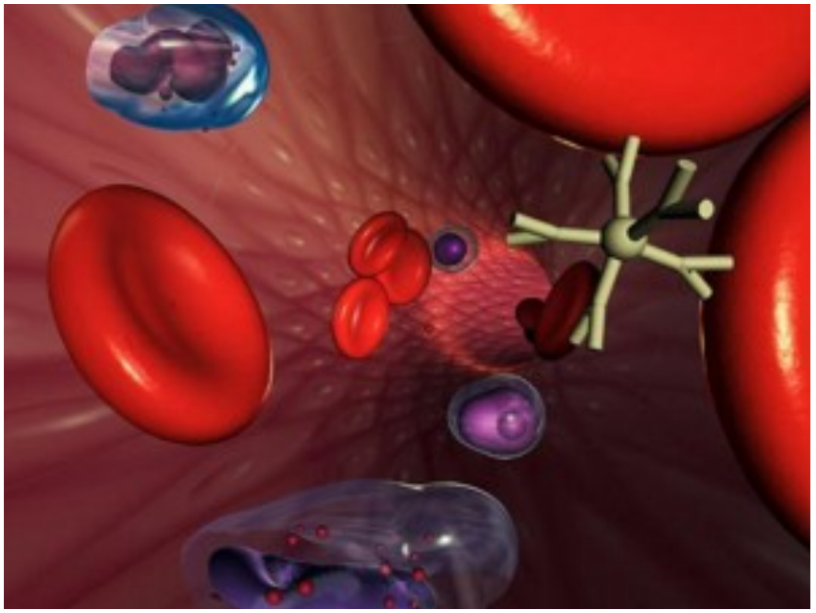
Voyage of the Nano-Surgeons

NASA-funded scientists are crafting microscopic vessels that can venture into the human body and repair problems – one cell at a time.

http://science.nasa.gov/headlines/y2002/15jan_nano.htm

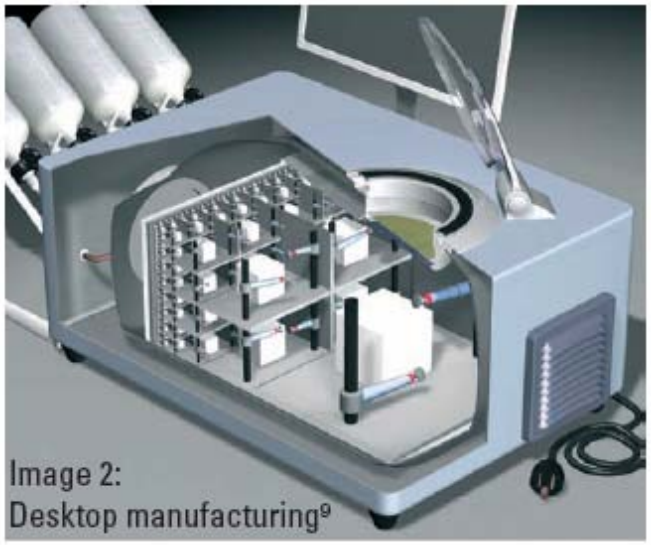
January 15, 2002: It's like a scene from the movie "Fantastic Voyage." A tiny vessel -- far smaller than a human cell -- tumbles through a patient's bloodstream, hunting down diseased cells and penetrating their membranes to deliver precise doses of medicines.

Only this isn't Hollywood. This is real science.

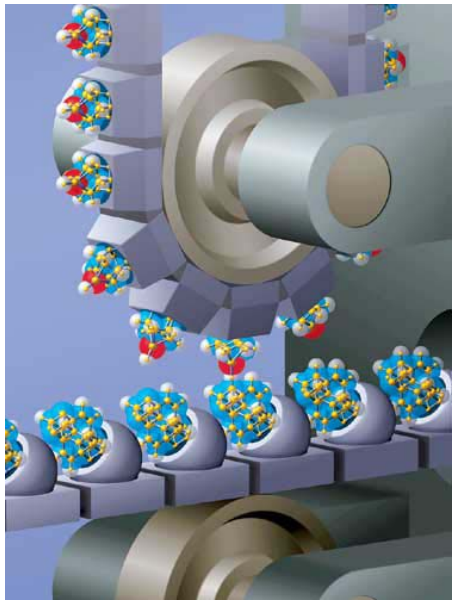


Right: Tiny capsules much smaller than these blood cells may someday be injected into people's bloodstreams to treat conditions ranging from cancer to radiation damage. Copyright 1999, Daniel Higgins, University of Illinois at Chicago.

Nanoscience or Nanoscience Fiction?



Source:

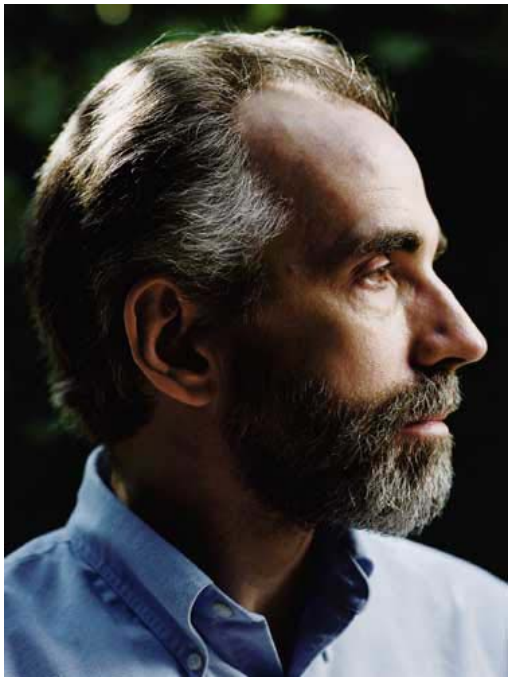


Source:

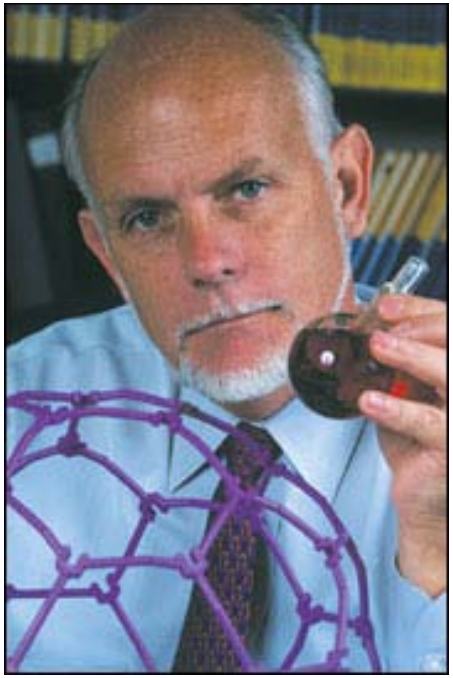
The concept of nanotechnology, as first mentioned by Nobel Laureate Richard Feynman in his famous 1959 “nanotechnology” lecture on “Plenty of Room at the Bottom”, proposed that atom-by-atom assembly of materials might someday be possible. Many people think that “molecular manufacturing” proposed by futurist Eric Drexler in his 1991 MIT PhD dissertation is science fiction. Unlike conventional chemical batch synthesis of finished products from raw materials, “molecular manufacturing” would create products in an atom-by-atom assembly in a form of “desktop manufacturing”. As of 2007 this has not yet been accomplished to the degree of real “molecular manufacturing”.

Due to its controversial status, Drexler’s “molecular manufacturing” was overtly removed from the National Nanotechnology Initiative passed by Congress and signed into law in 2001. But it is a topic that will probably not go away. If it were indeed possible it would revolutionize manufacturing as we know it.

An Ugly Debate About the Feasibility of "Molecular Manufacturing"



Eric Drexler

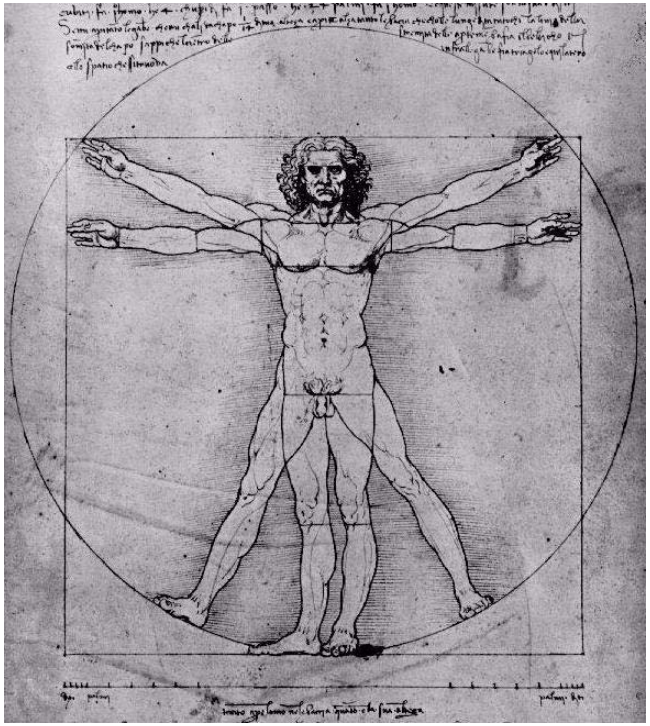


Richard Smalley

In a rather heated series of back-and-forth debates, Eric Drexler and Richard Smalley argued about the feasibility of "molecular manufacturing". Smalley contended that it was impossible due to the inability to pick up and position atoms quickly enough while Drexler countered that smaller components could self-assemble and then be positioned as larger pieces later in the process.

Nanotechnologies and Healthcare

We have come a long way…



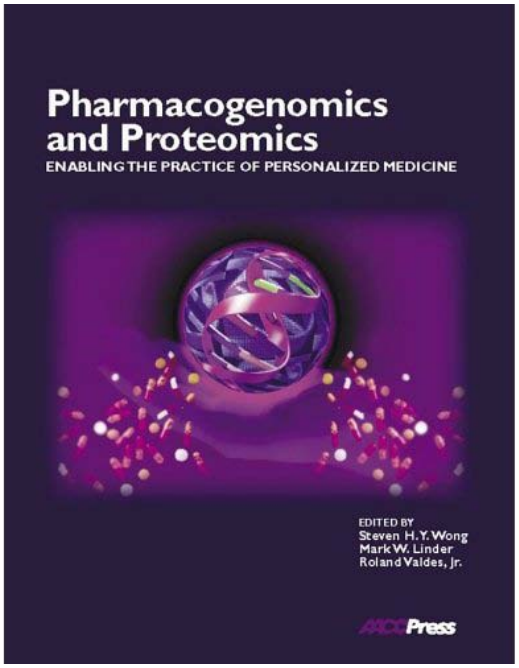
Art: Da Vinci's "Vitruvian Man" 1490

but we still have so far to go!

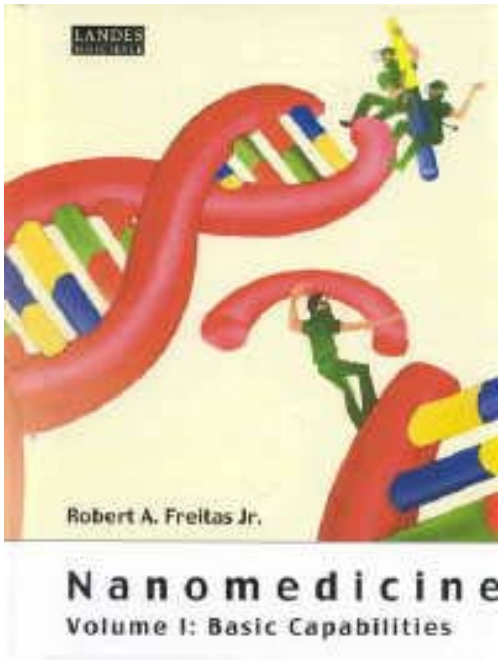
The Progression of Medicine

Conventional "Modern" Medicine

"Personalized" or "Molecular" Medicine



Nanomedicine Single-cell Medicine



Bionanotechnology at Discovery Park

Bindley Bioscience Center

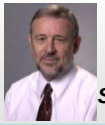
Birck Nanotechnology Center

Important question: Can nanomedical systems be "bionanomanufactured" in Indiana?

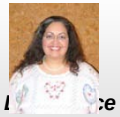
INDIANA UNIVERSITY

PURDUE UNIVERSITY

IndianaCTSI | ACCELERATING CLINICAL AND TRANSLATIONAL RESEARCH



Bio-Nano Core Facility



Scientific Core Director: James F. Leary, Ph.D. Staff Leader: L ce

OVERVIEW

Bio-Nano Core Mission

- Provide bionanotechnology expertise
- Provide access to and help coordinating core facilities

Bio-Nano Core Vision

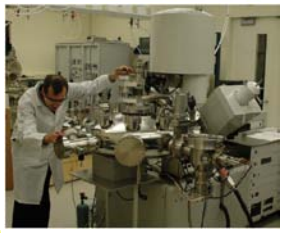
- Provide world-class resources to CTSI participants
- Continue to expand bio-nano capabilities for cutting edge research

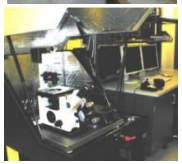
RESOURCES

Expertise: Bionanotechnology faculty and staff come from multiple departments and programs at Purdue University. Many of these faculty are housed at Discovery Park in the Birck Nanotechnology Center or at the Bindley Bioscience Center or at the Weldon School of Biomedical Engineering across the street from Discovery Park.

Discovery Park - Birck Nanotechnology Center

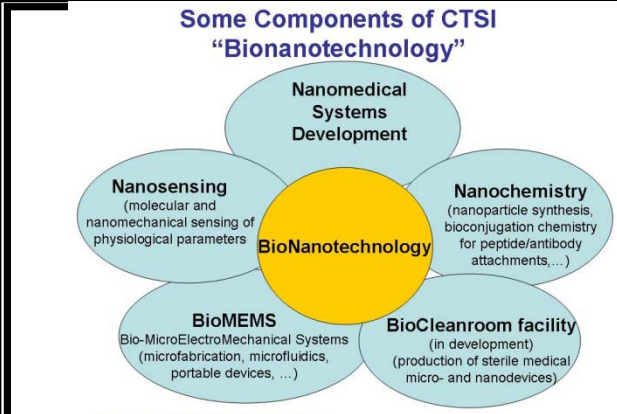
Discovery Park - Bindley Bioscience Center



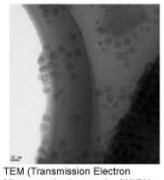


BME Medical Device Design,Prototyping, and Evaluation
Contacts: Jim Jones (jones@purdue.edu), electrical/computer; Kirk Foster (foster@purdue.edu), mechanical

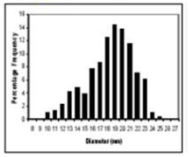
SOME RESEARCH CONTRIBUTION HIGHLIGHTS



Nanoparticle Synthesis for Nanomedical Applications



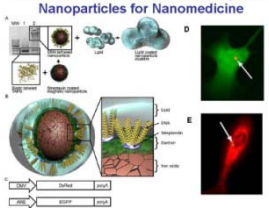
TEM (Transmission Electron Microscopy) micrograph of MION (Magnetic Iron Oxide Nanoparticles) particles deposited from acetone onto a holey carbon TEM grid.

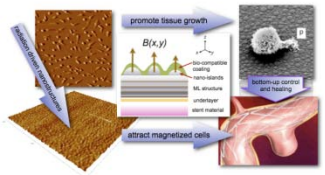


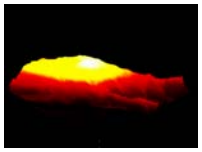
Particle size distribution for MION particl identified in TEM micrographs.

http://docs.lib.purdue.edu/cgi/viewcontent.cgi?article=1021&context=nanoposter

Tethered Gene Expression on Magnetic Nanoparticles for Nanomedicine

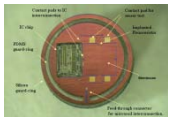




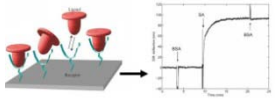


Atomic Force Microscopy (AFM) for Nanomedical Systems (cells and nanoparticles)

BioMEMS and medical devices
Small, portable microfabricated devices can be designed and built for biomedical application by BME and BNC engineers



A microfabricated transponder for wireless measurement of intra-ocular pressure



Nanomechanical sensors

LIST OF SERVICES

- BioMEMS design, construction, and testing
- Nanomedicine, including drug/gene delivery systems using polymers, liposomes, multilayered nanomedical systems
- Nano- and micro-manufacturing of delivery systems for bioactive agents;
- Nanoparticle design, construction and characterization
- Atomic-level characterization of nano and micro surfaces
- Biomolecular Imaging; including AFM,
- Nanodevice design and construction including biosensors; microfluidics; bioMEMs, actuators;
- Neuroengineering
- Nanoscale Tissue Engineering

CONTACT INFORMATION

James F. Leary, PhD, Scientific Director
jfleary@purdue.edu 765-494-7280
For specific research expertise see faculty website at:
http://web.ics.purdue.edu/~jfleary

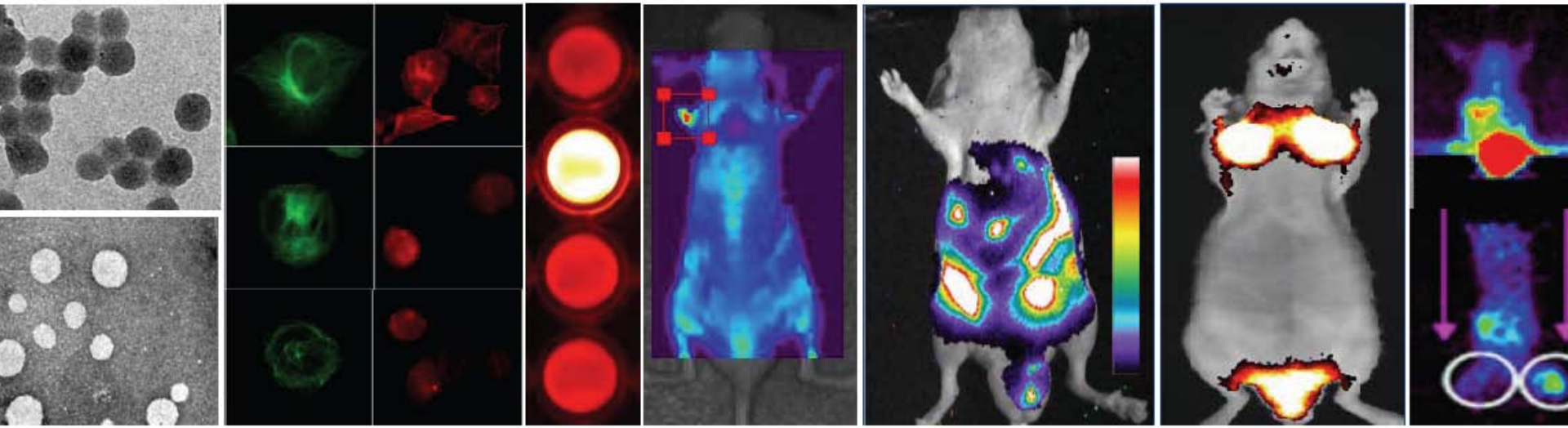
Lisa M. Reece, Staff Leader & Biosafety Officer
lreece@purdue.edu 765-496-6786

Monica Allain, PhD., Managing Director
mallain@purdue.edu 765-494-5138 Fax: 765-496-8299

PURDUE UNIVERSITY

Global Research Lab Program

Molecular Imaging and Nanomedicine for Theragnosis using Nano-Biomaterials



KPI: Kuiwon Choi (KIST)

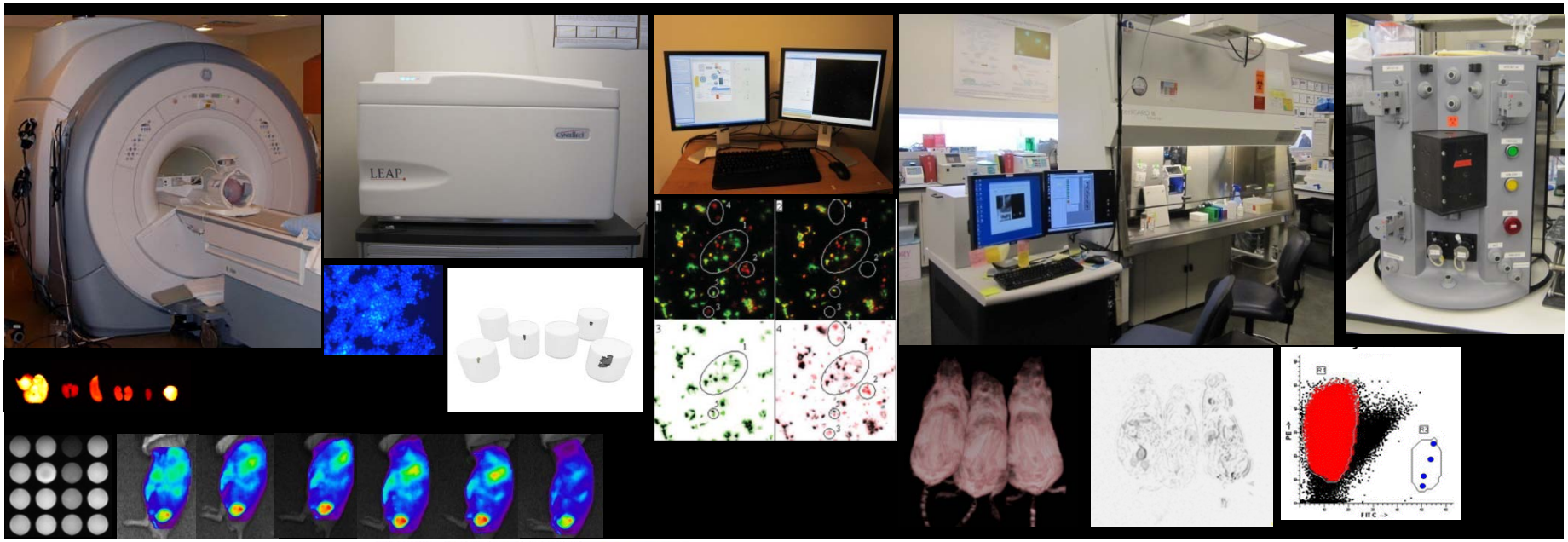
FPI: James F. Leary (Purdue Univ.)

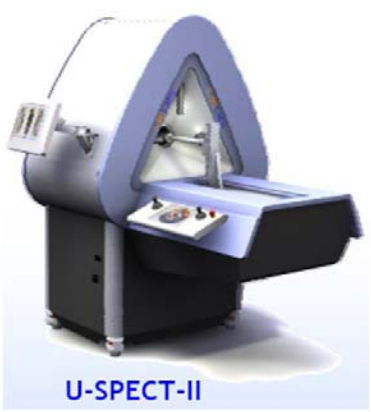
2007-2016

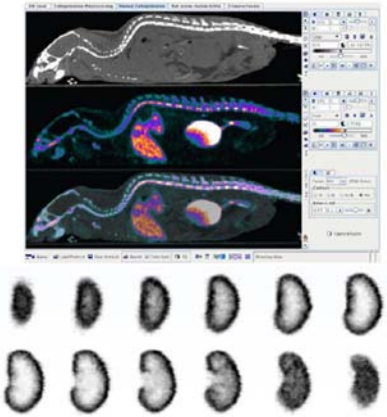
Korea Institute of Science and Technology

PURDUE

“Nanotools” for Development and Evaluation of Nanomedical Devices







1.3 How Conventional Medicine Works for Diagnosis of Disease

How Conventional Medicine Works for Diagnosis of Disease

• Identification of a “diseased state” by a patient who doesn’t “feel right” and then goes or is taken to a clinic or emergency room of a hospital

• Attempts by nurses and doctors to collect simple measurements (e.g. temperature, blood pressure, heart beat rate, palpitation to find where it hurts and/or is there an abnormal lump?)

• Follow-up clinical tests (e.g. blood chemistry; urine chemical analysis; blood, urine, or sputum cultures to detect abnormal numbers or types of microbes; blood cell numbers and percentages by cell subpopulation types; biopsies of tissues and their interpretation by histopathologists: etc.)

• Internal examinations using “non-invasive” imaging (e.g. standard x-rays, CAT (Computerized Axial Tomography) scans, MRI (Magnetic Resonance Imaging) scans; PET (Positron Emission Tomography) “functional” imaging

• Occasional “molecular” tests (gene relocations, amplified gene copies, etc.) Occasionally tests on relatives of the patient to establish genetically determined diseases

• Comparison of individual results with “normal ranges” of “normal” individuals thought to not be diseased.

Some problems with conventional medicine

1. Waiting for a patient to feel symptoms means:

   a. Disease detection is not early (where the possibility of successful treatment is higher) and may be missed until it is too late to treat

   b. By the time symptoms are felt, tissue and/or organ destruction has already begin and may be irreversible

   c. Many diseases have similar symptoms making diagnoses based on symptoms at best a guessing game

2. Since trained people and modern drugs are expensive:

   a. there is a medical personnel triaging system in place which means that many diseases are “diagnosed” and treated by people with only modest levels of medical expertise.

   b. Many people are not treated at all (roughly 2/3 of the world has little or no access to modern medicine!)

3. Diagnostic technologies, if available, are still relatively primitive; or if expensive, are not readily available

4. Drugs and other treatments are either completely or only crudely targeted to the actual diseased cells leading to potentially extensive damage to normal bystander cells

1.4 How Conventional Medicine Works for Treatment of Disease

How Conventional Medicine Works for Treatment of Disease

• Stabilization of the patient so that the patient can repair himself/herself (e.g. intravenous hydration with saline, blood transfusions, simple medicines to lower dangerous fevers

• Surgical repair of injuries (“reconstructive surgery”) or removal or diseased tissues or organs

• Treatment with chemical drugs that are delivered locally (e.g. ointments to skins, injection of drugs into tissues or organs, etc.)

• Treatment with chemical drugs that are delivered systemically (e.g. chemotherapy, etc.)

• Treatment with targeted therapies (e.g. monoclonal antibodies targeted against diseased cells) – still very limited to a small number of diseases!

Why will nanomedicine happen?

The healthcare system is a "Perfect Storm"

- $ 1B to develop a new drug
- Fewer approved new drugs each year
- Every patient is currently a new test case for which we really have no idea how they will respond to a given drug (YOU are the next "guinea pig")

Who needs these new drug delivery tools?

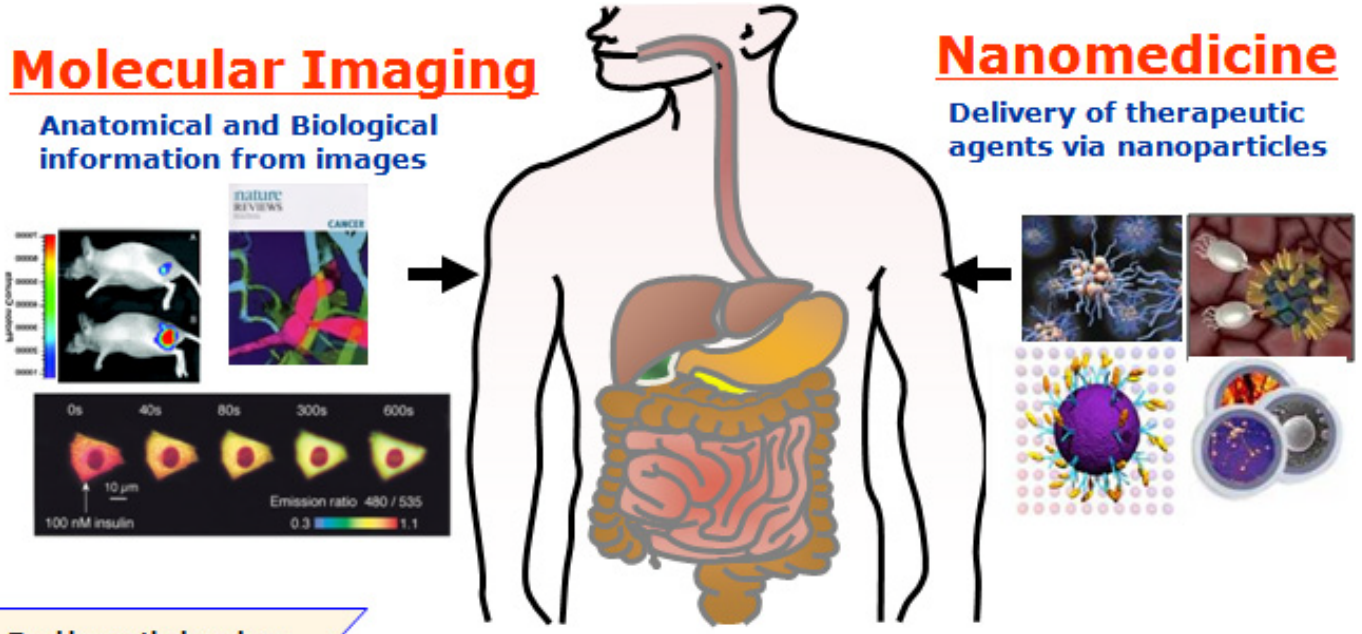
- Patients
- Drug companies
- Health care system

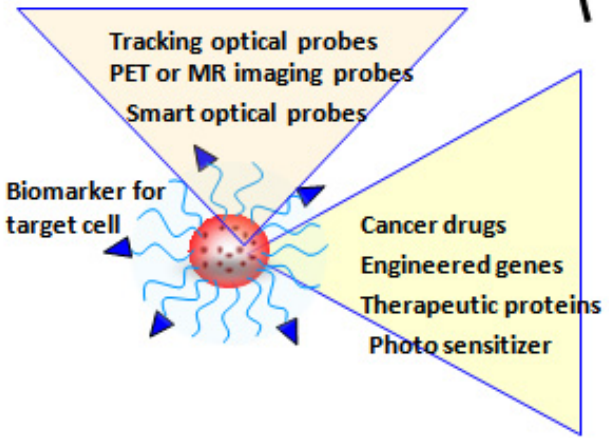
The problem and a solution, for the pharmaceutical industry

Great drugs but poor drug delivery systems to the wrong patients.

A solution: Put good existing drugs into highly targeted nanodelivery systems and administer only to the right patients

“Smart” Nanoparticles=drug + device





- Molecular based diagnosis/therapy
- Early diagnosis
- Personalized therapy
- Real-time monitoring of therapeutic effects
- Predictive and preventive medicine

Future: Regenerative Nanomedicine

- Medicine performed at the single cell level for advanced targeted drug therapy
- Possible repair, rather than just elimination, of diseased cells at the single cell level ("regenerative medicine") using nanomedicine
- Sufficiently early diagnosis and treatment of disease that the distinction between prevention and treatment is blurred!

Why does Nanomedicine Represent a Huge Promise for our Healthcare System?

Earlier diagnosis increases chances of survival. By the time some symptoms are evident to either the doctor or the patient, it may be already too late, in terms of irreversible damage to tissues or organs.

When this damage occurs, the costs of the treatments rise steeply and the probability of successful patient outcomes declines steeply.

Nanomedicine will diagnose and treat problems at the molecular level inside single-cells, prior to traditional symptoms and, more importantly, prior to irreversible tissue or organ damage – saving both costs and, more importantly, improving the chances for a successful patient outcome.

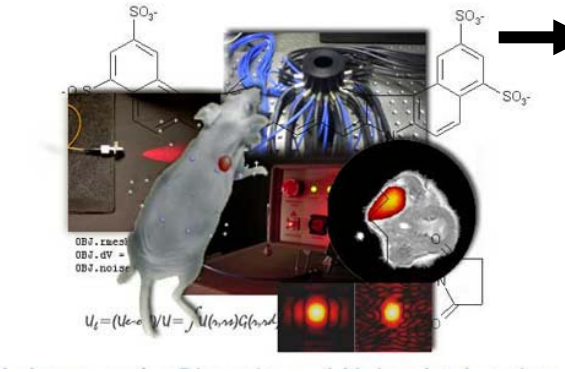
Some ways that nanotechnologies will directly impact on healthcare

- Greatly improved “directed therapies” for treating cancer using new nano- drug/gene delivery systems precisely targeted to tumor cells without side effects.
- Tiny implantable devices to monitor health.
- New point-of-care and home healthcare devices. Immediate diagnosis of specific pathogens permitting mono-, rather than broad-spectrum, therapy
- Tiny implantable devices with nanobiosensors to treat diseases (retinopathies, glaucoma, diabetes, cardiovascular, arthritis, Parkinson’s disease, Alzheimer’s disease,…) with fewer side-effects.

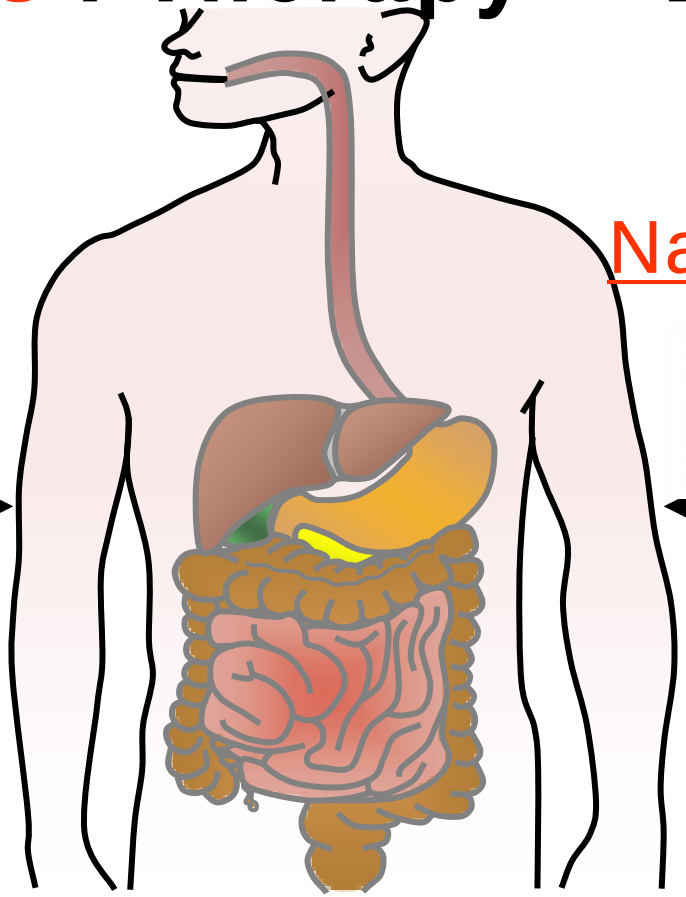
Future Medicine: Theragnosis

Theragnosis : Therapy + Diagnosis

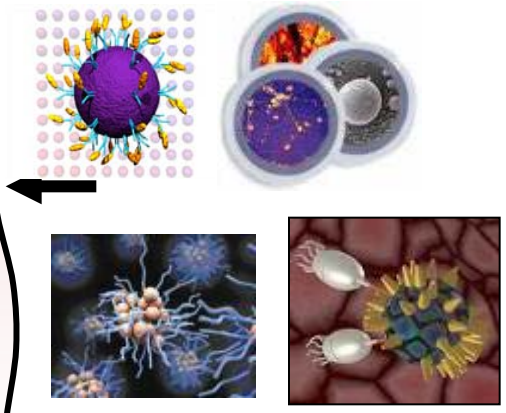
Molecular Imaging



Medical Information from imaging modality



Nanomedicine



Chemical drug
DNA & Protein
Imaging agents

1.5 Factors Limiting the Progress of Medicine

- Economics
- Politics
- Regulation

Limitations on rate of progression of medicine are driven by a variety of forces other than scientific or technological

Economics affect the rate at which new scientific methods or technology is introduced. Typically the new methods or technology must either be less expensive or save significant health care costs. In some countries, rate of progression of medicine is controlled by the government, in others by the health care industry

Politics can affect whether specific groups of people receive treatment at all or the amount of treatment (independent of medical condition). Ignorance or prejudice can drive treatment amounts and options (e.g. treatment of AIDS in some countries).

1.7 What is the Basis for Nanomedicine?

- Creation of nano-sized tools
- These nanotools permit single-cell medicine
- These “nanomedical systems” can be “smart” devices

A paradigm shift…

Nanomedicine Concept of Regenerative Medicine "Fixing cells one cell at-a-time"

- Conventional therapies try to cut out the bad cells (surgery), burn them out (radiation therapy), or poison the bad cells faster than the good cells (chemotherapy).
- Nanomedicine attempts to make smart decisions to either remove specific cells by induced apoptosis or repair them one cell-at-a-time. Single cell treatments will be based on molecular biosensor information that controls subsequent drug delivery at the appropriate level for that single cell.

Features of Nanomedicine

Beyond the obvious application of nanotechnology to medicine, the approach is fundamentally different:

- Nanomedicine uses "nano-tools" (e.g. smart nanoparticles) that are roughly 1000 times smaller than a cell (knives to microsurgery to nanosurgery …)
- Nanomedicine is the treatment or repair (regenerative medicine, not just killing of diseased cells) of tissues and organs, WITHIN individually targeted cells, cell-by-cell.
- Nanomedicine typically combines use of molecular biosensors to provide for feedback control of treatment and repair. Drug use is targeted and adjusted appropriately for individual cell treatment at the proper dose for each cell (single cell medicine).

Why does Nanomedicine Represent a Huge Promise for Health Care?

Earlier diagnosis increases chances of survival. By the time some symptoms are evident to either the doctor or the patient, it may be already too late.

- Conventional medicine is reactive to tissue-level problems that are happening at the symptomatic level. Nanomedicine will diagnose and treat problems at the molecular level inside single-cells, prior to traditional symptoms.
- Conventional medicine is not readily available to much of humanity because it is labor-intensive and that labor is sophisticated and expensive. Nanomedicine will be much more preventive, comparatively inexpensive because it will minimize use of expense human experts, and can be more readily mass produced and distributed.

1.8 Some ways that nanotechnologies will impact on healthcare

- Greatly improved “directed therapies” for treating cancer using new nano- drug/gene delivery systems
- Tiny implantable devices to monitor health.
- New point-of-care and home healthcare devices.
- Tiny implantable devices with nanobiosensors to treat chronic diseases (diabetes, cardiovascular, arthritis, Parkinson’s disease, Alzheimer’s disease,…) with fewer side-effects.

Additional Resources

Course website

Old Nanohub 2007 version

New 2011 NanoHUB version of course being filmed/recorded

http://www.nanohub.org/nanomedicine (2007 version)