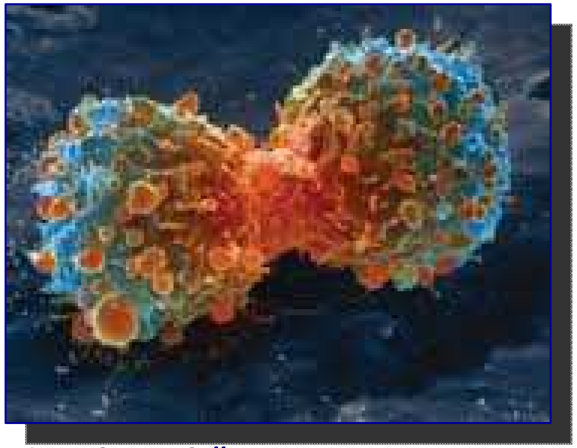
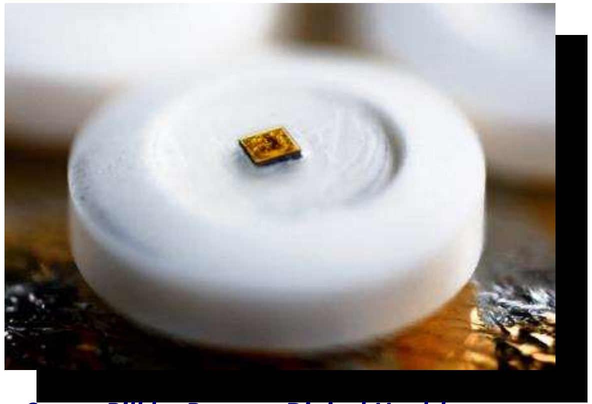
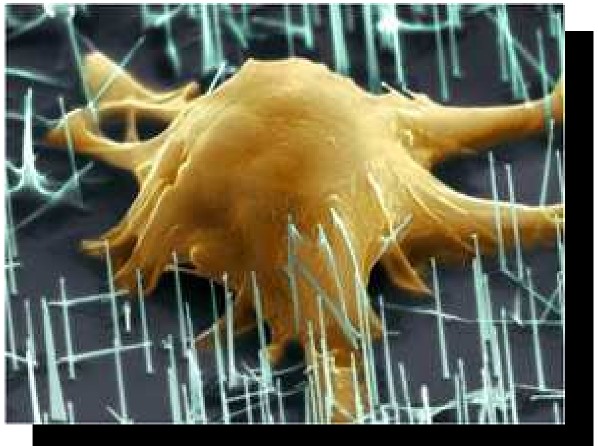


Lung Cancer Cell



Smart Pill by Proteus Digital Health



Stem Cell Secured Using Nanowires

Innovation, Nanotechnology and Cancer Care

IV International Conference on Integrative Oncology Therapy - Rome, Italy - 16 Nov. 2012

Michael S. Tomczyk

Managing Director - Mack Center for Technological Innovation – Wharton School
Author – NanoInnovation: What Every Manager Needs to Know (Wiley-VCH, 2012)

www.michaeltomczyk.com – tomczyk@wharton.upenn.edu

Some personal observations & insights…

"What distinguishes us is not our power or ability, but the *choices* *we make*."

Professor Dumbledore
Harry Potter and the Chamber of Secrets

The Mack Center for Technological Innovation

The Mack Center at The Wharton School (University of Pennsylvania) is the world's leading academic center studying best practices and strategies for managing innovation.

We function as a high level corporate learning network.

Our partners include Air Liquide, Federal Express, Hertz, Lockheed Martin, Merck, NASA, etc.

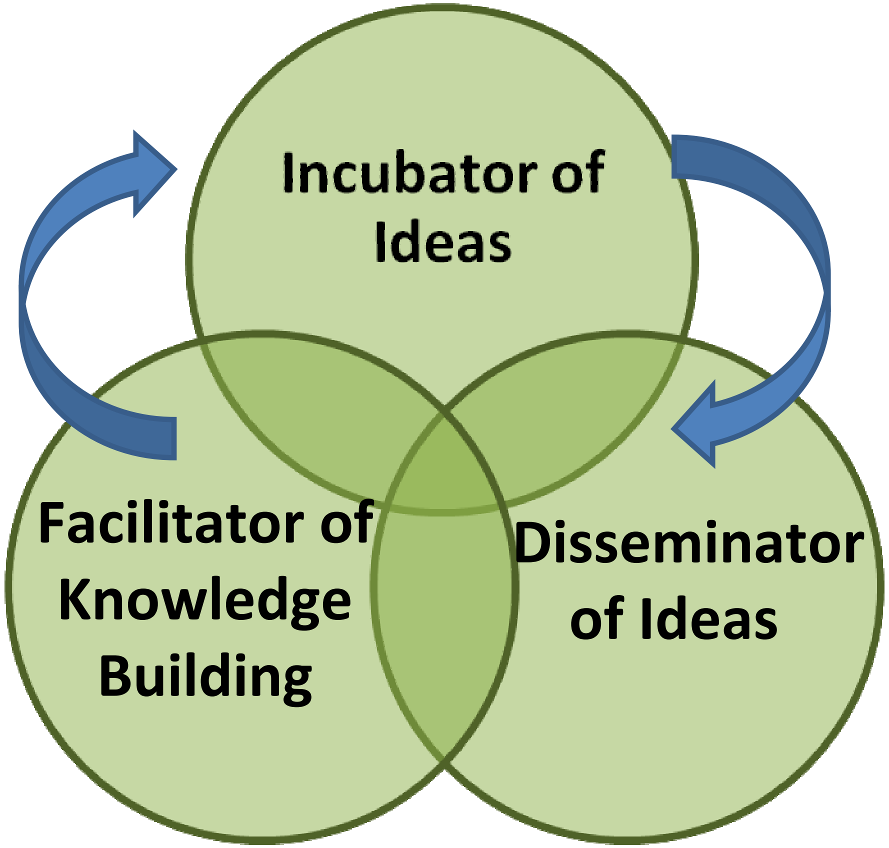
Website - http://mackcenter.wharton.upenn.edu

The Mack Center is the Hub of a Global Innovation Ecosystem

We educate Wharton MBAs and Executive Education Students

Our faculty designs and hosts 3-4 conferences each year

Our motto is: KNOWLEDGE FOR INNOVATION



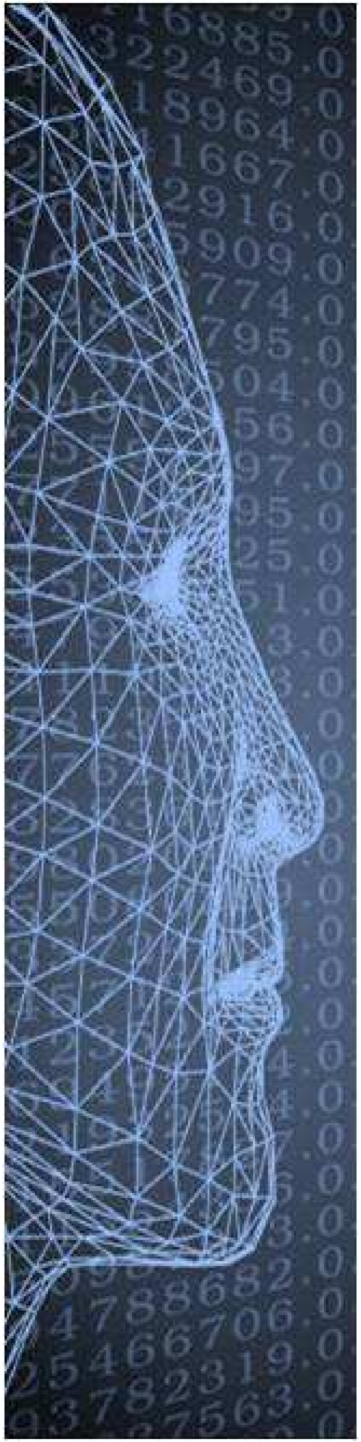
Fund 25 - 30 faculty research projects per year

Books, working papers, podcasts, videos, website, conference reports

Conferences & Workshops: Dec. 13 – Leveraging Big Data for Innovation - Feb. 22 – The Future of Medical Miracles

Research Priorities & Areas of Focus

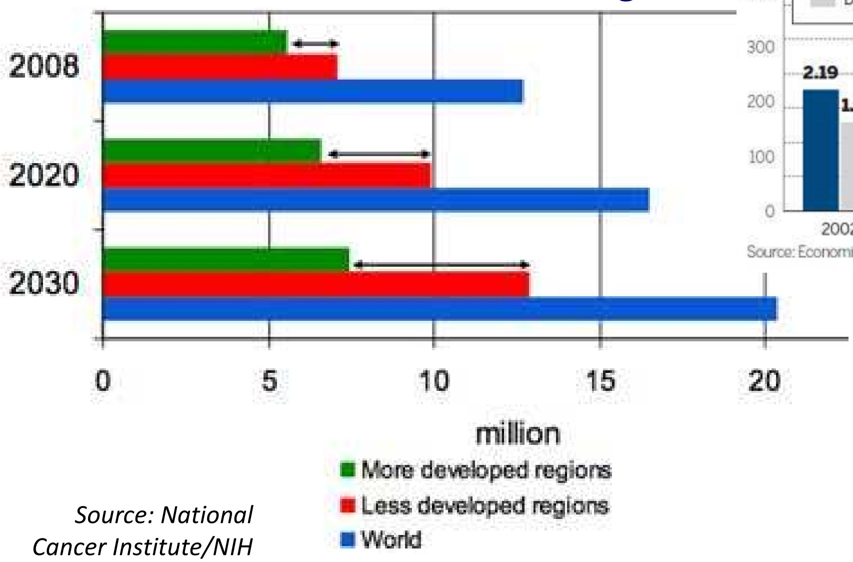
Understanding Emerging Technologies and Markets	Organizing for Innovation	Strategies for Innovating	Capturing Economic Value from Innovations
• How do emerging technology-based industries or markets differ from established industries? • How do they emerge and evolve? Does this vary by technology and economic system? • What explains patterns of competitive entry, shakeout and survival in these industries? • When, why and how do new entrants prevail over established companies?	• How do best practice firms act on opportunities and threats sooner than rivals? • What new forms of organization are enabled by advances in technology? • How do firms use innovation networks and webs of alliances to draw on innovation resources beyond their boundaries? • What capabilities are needed to manage and motivate partners? • What metrics are needed to identify weak links in its innovation process, allocate innovation resources and hold managers accountable?	• When should firms pursue an embryonic technology on their own, acquire or partner with other firms or actively watch and wait? • What strategies and tools can help assess and contain risk in adjacencies and white spaces? • How do winning firms bring their innovations to market ahead of their rivals? • How can firms improve their peripheral vision and prepare for new opportunities?	• How do firms make better choices for long run innovation projects amidst uncertainty? • What is the right balance of risk and return in innovation portfolios? • How should resources be allocated and projects be prioritized and selected? • How do firms preserve and exploit the value of the intellectual property they have created? • How can firms protect returns on their investments when they participate in alliances, global networks and innovation ecologies?



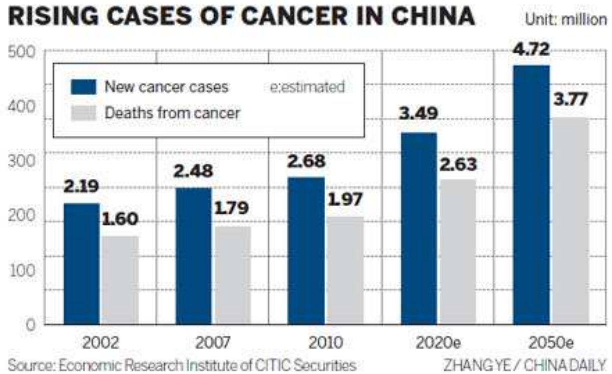
The Medical World is Changing

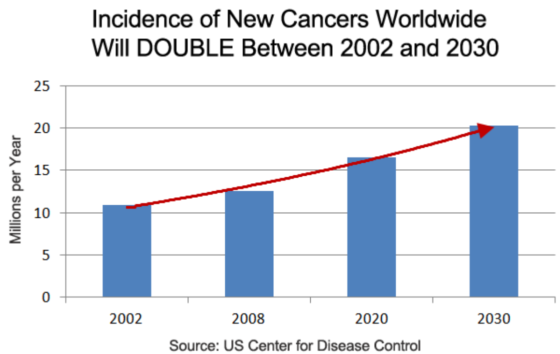
Cancer is the second leading cause of death in the U.S. and causes 20% of all deaths in the European region. The global incidence of cancer is projected to double from 2002 to 2030 – however, cancer <u>mortality</u> is declining in the EU and the U.S. Cancer is becoming a more manageable disease. Many other “fatal” diseases are becoming survivable and chronic.

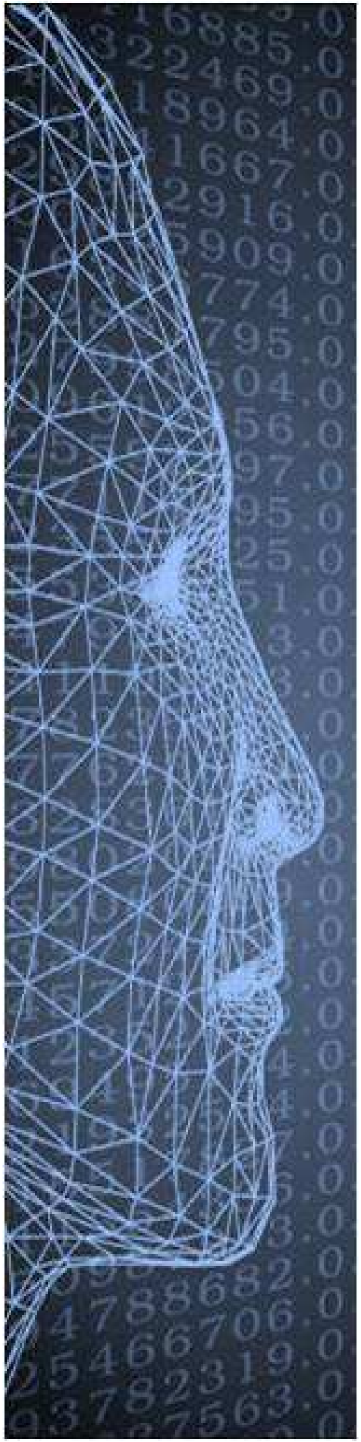
Global cancer incidence rising



Source: National Cancer Institute/NIH



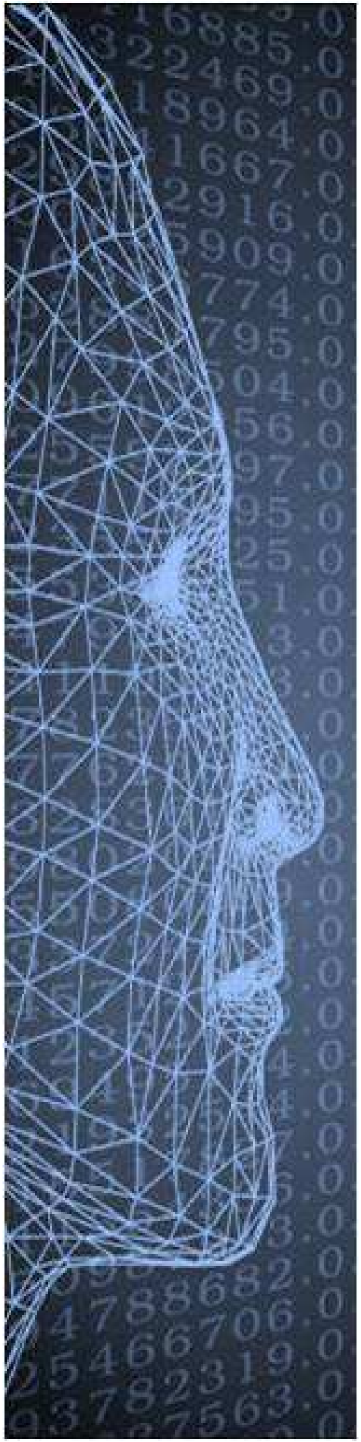




The Medical World is Changing

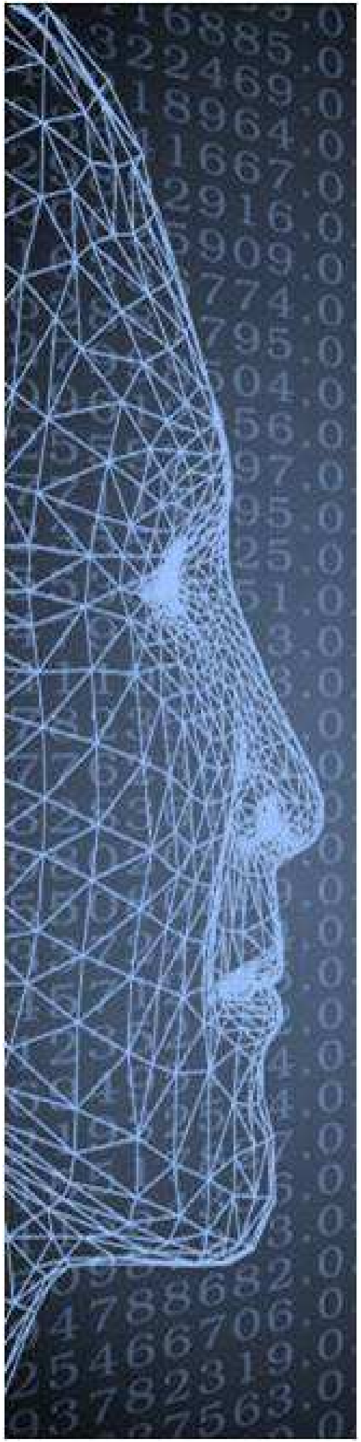
- **The world is straining to recover from a global economic crisis**
- **Healthcare is increasingly expensive**
  (16% of GDP in the U.S., 10-11% of GDP in Europe – expected to grow 50% by 2025)
- **Fewer blockbuster drugs are being developed and at much higher cost**
- **Populations are aging in the U.S., Europe, China and Japan…straining care systems**

Radical Solutions are Needed



There is also Good News…

- **Today we can diagnose virtually ANY disease.**
- **We know how viruses and other diseases attack cells – the first broad spectrum antiviral medicines are being developed**
- **Gene Therapy is finally beginning to succeed**
- **Nanotechnology (nanosizing) is making cancer drugs soluble and bio-available**
- **Major advances in stem cell therapy are enabling regeneration of tissue and organs**



How can we change the future?

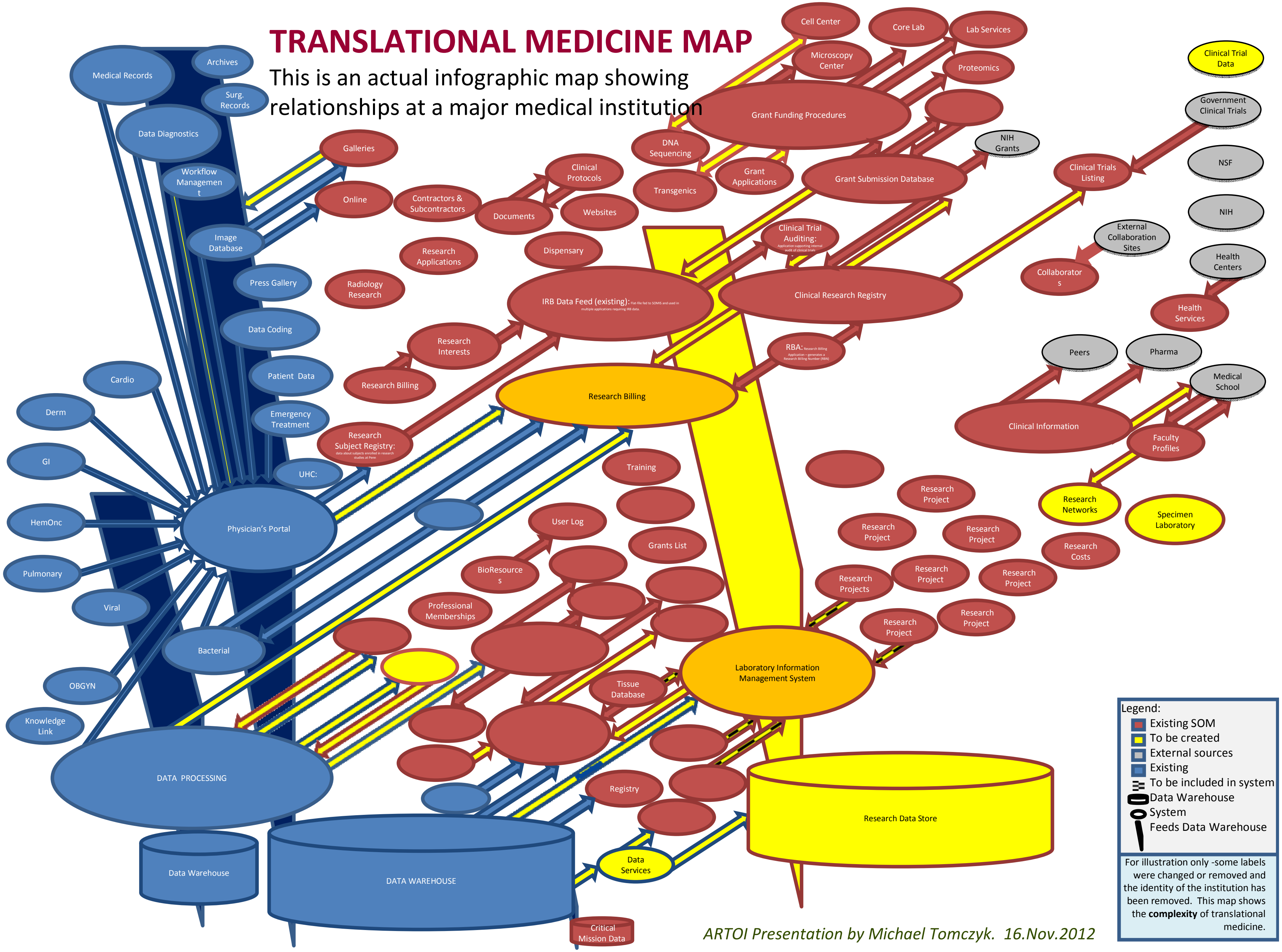
Keep Promoting Medical Innovation and Translational Medicine

INNOVATION is the <u>implementation</u> of a discovery, idea or invention (to create value)

TRANSLATIONAL MEDICINE is the speedy translation of medical solutions from research labs to patient beds – expediting funding, testing, approval, commercialization, etc.

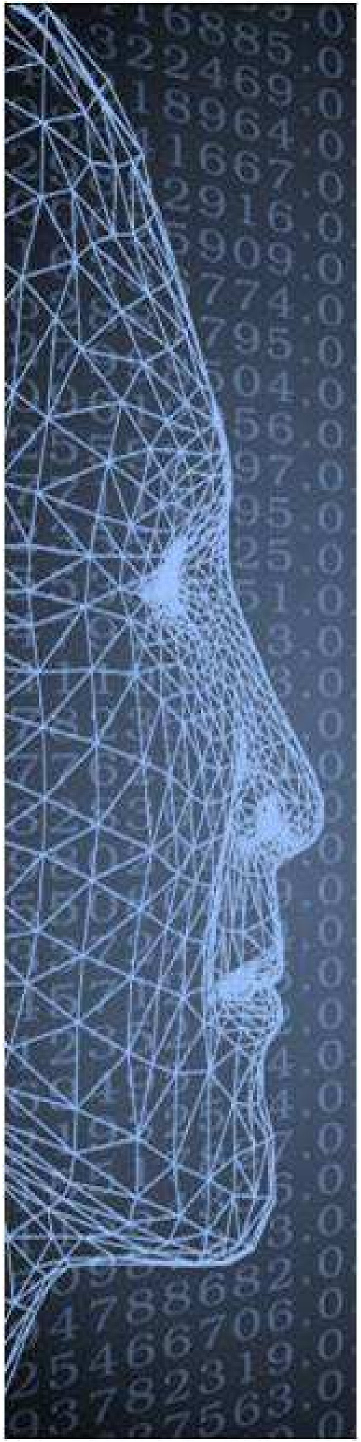
TRANSLATIONAL MEDICINE MAP

This is an actual infographic map showing relationships at a major medical institution



For illustration only -some labels were changed or removed and the identity of the institution has been removed. This map shows the **complexity** of translational medicine.

ARTOI Presentation by Michael Tomczyk. 16.Nov.2012



Be an Innovation Champion

- **ANYONE can be an innovation champion.**
- **Some of the most ingenious and “radical” innovations today are developed by physicians, surgeons, medical research faculty and students.**
- **Use your peripheral vision to scan the horizon for emerging technologies – “early signals” of things to come.**
- **Look for ways to translate innovations from lab to clinic.**

A Personal Innovation Story

In 1980, I had a university degree in literature, an M.B.A., and some consulting experience. I developed a keen interest in personal computing and persuaded the founder of Commodore (Jack Tramiel) to hire me as Assistant to the President.

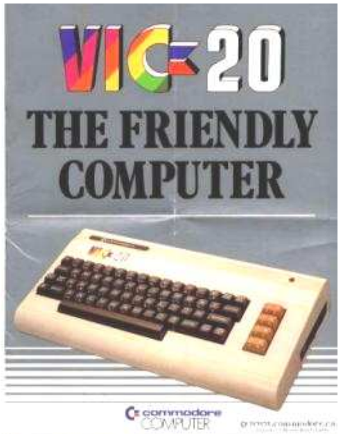
He said he wanted to make computers "for the masses, not the classes" and challenged us to develop a small color home computer.

I gave him a 30 page memo on the new computer and he put me in charge of guiding the development of the VIC-20.

Today I am listed in Wikipedia as a computer pioneer.

My point is that <u>anyone can be an innovation champion and pioneer</u>!

Jack Tramiel and Michael Tomczyk



The VIC 20 was the first microcomputer to sell one million units.

Showing Actor William Shatner how to use a computer

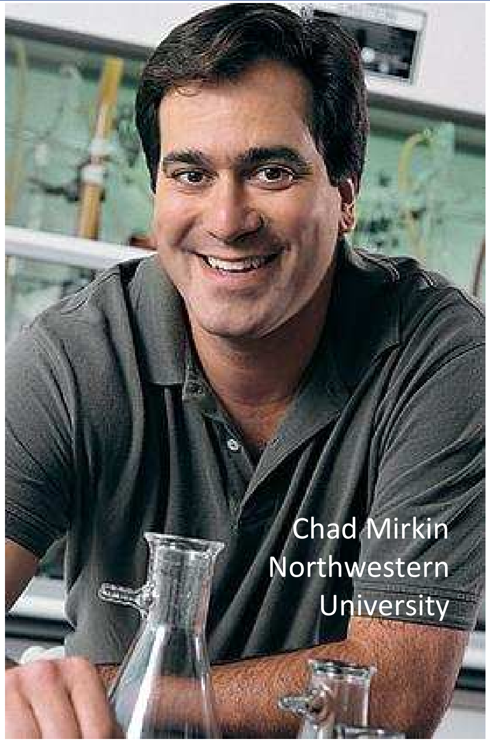
Innovators - Making a Difference

Invisibility Cloaks

Metamaterials are used to bend light for invisibility & optical lenses.

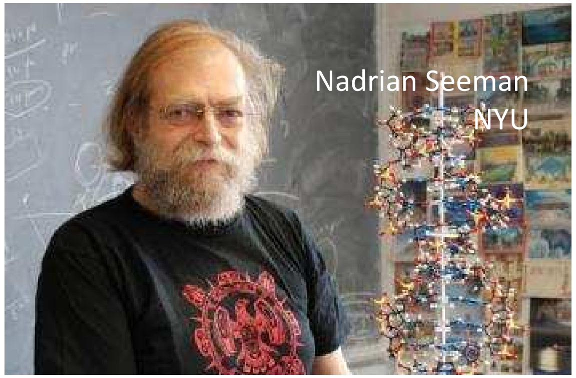
Bioluminescence

Cambridge University iGEM student winners used Biobricks to create biological lights.



Molecular Diagnostics

With more than 500 patents & apps – Chad Mirkin is the world's most cited chemist. His innovations include: Nanoink™ Verigene™ , Aurasense™



DNA Nanotechnology

Ned Seeman pioneered the use of DNA to create geometric structures used for drug delivery, nanobots, and more.

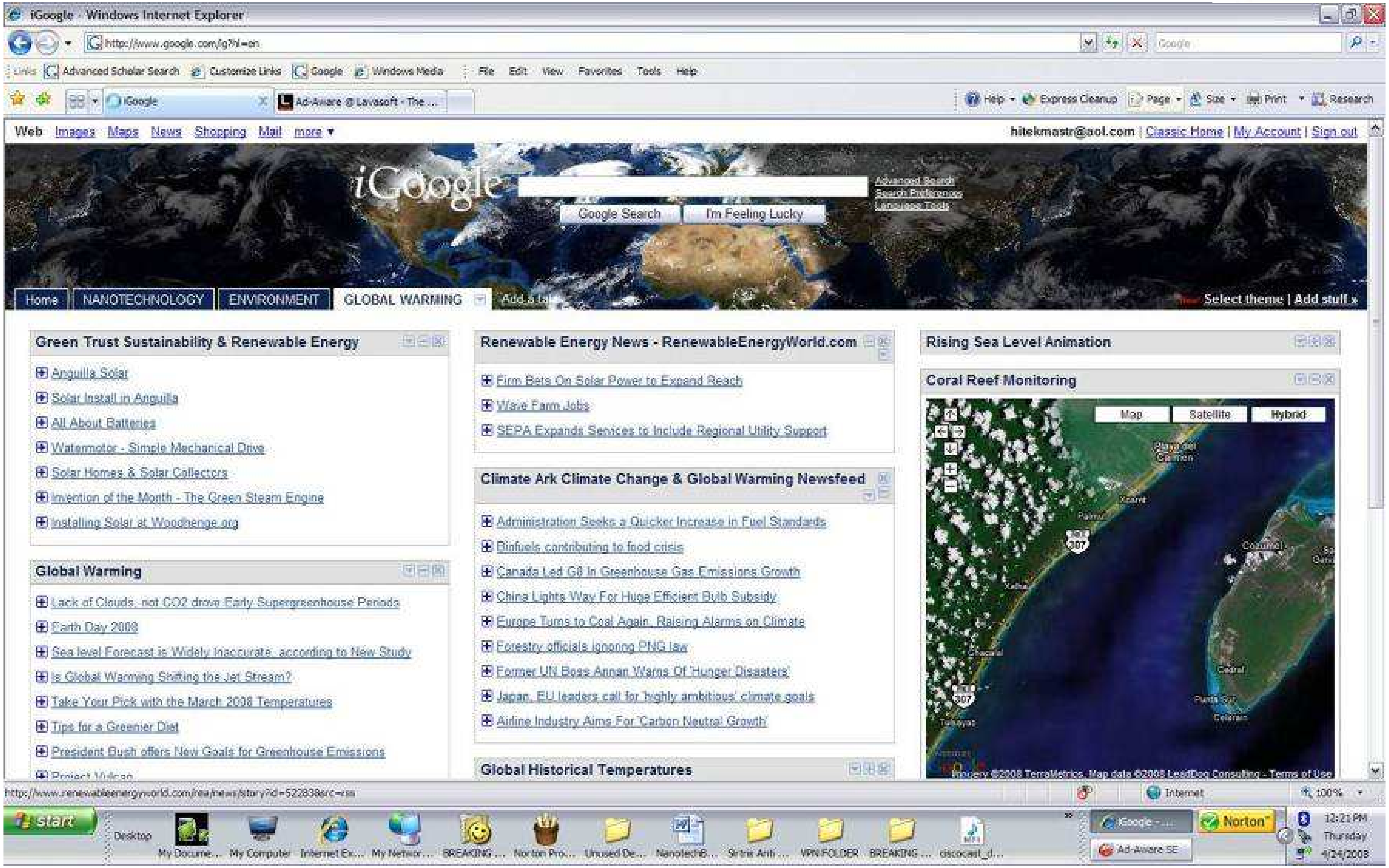
Neri Oxman – M.I.T

Carpal Skin

Nano-engineered "skin" works like a glove to relieve pain for carpal tunnel patients. Dr. Neri Oxman at M.I.T. got the idea when she injured her own wrist.

Keep Scanning the Future!

I scan more than 35,000 technology headlines each year, using my web portal.
I set RSS feeds to access a constantly updated stream of news and information.



Medicine requires Ambidexterity

Medicine

EXPLOIT

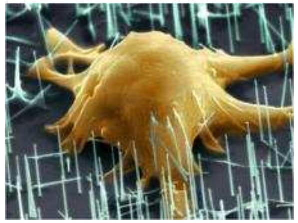
Existing Opportunities

TRADITIONAL MEDICINE

- **BROAD SPECTRUM ANTIVIRALS**
- **GENE THERAPY**
- **NANOMEDICINE**
- **ORGAN REGENERATION**
- **STEM CELLS**
- **DEVICES/IMPLANTS**
- **NEW DIAGNOSTICS**

EXPLORE

Emerging Opportunities



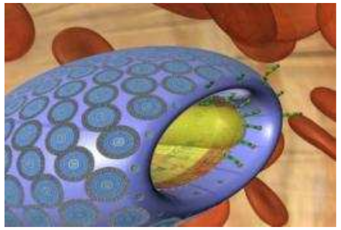
NOVEL THERAPIES

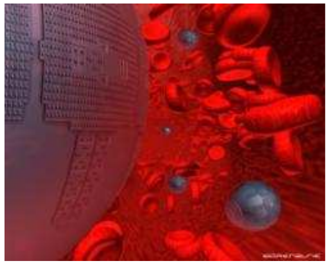
Medical practitioners are forced to become "ambidextrous" – relying on existing traditional solutions while exploring radical new innovations that are still emerging

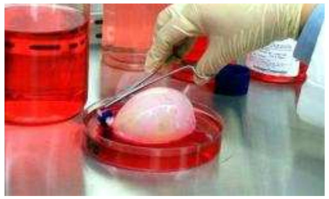
Gaining Traction is TOUGH

NOVEL THERAPIES MUST COMPETE IN AN
A MULTIDEXTROUS MARKETPLACE

DRUGS	E	E	Antivirals
SURGERY	X	X	Gene Therapy
CHEMOTHERAPY	P	P	Nanomedicine
RADIATION	L	L	Organ Regeneration
ACUPUNCTURE	O	O	Stem Cells
	I	R	
	T	E	

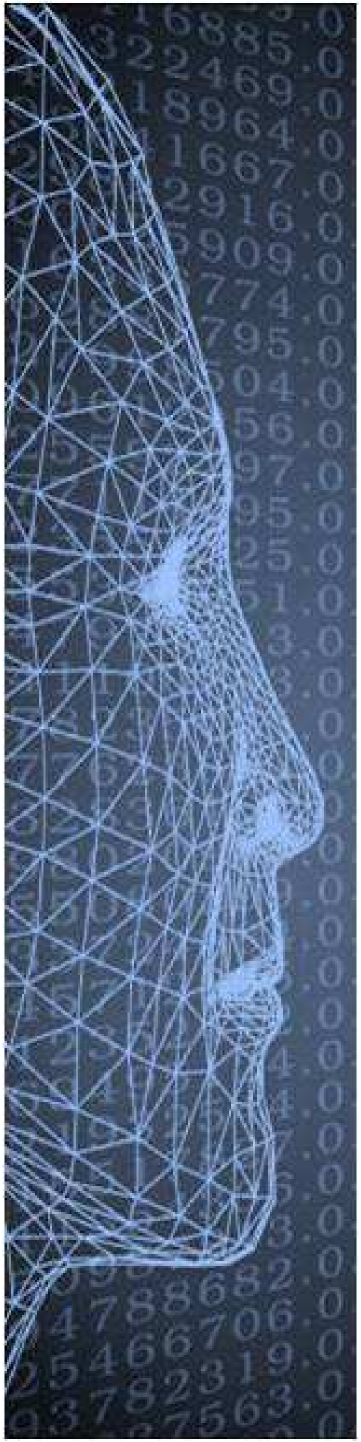






Most novel therapies involve “radical” innovations

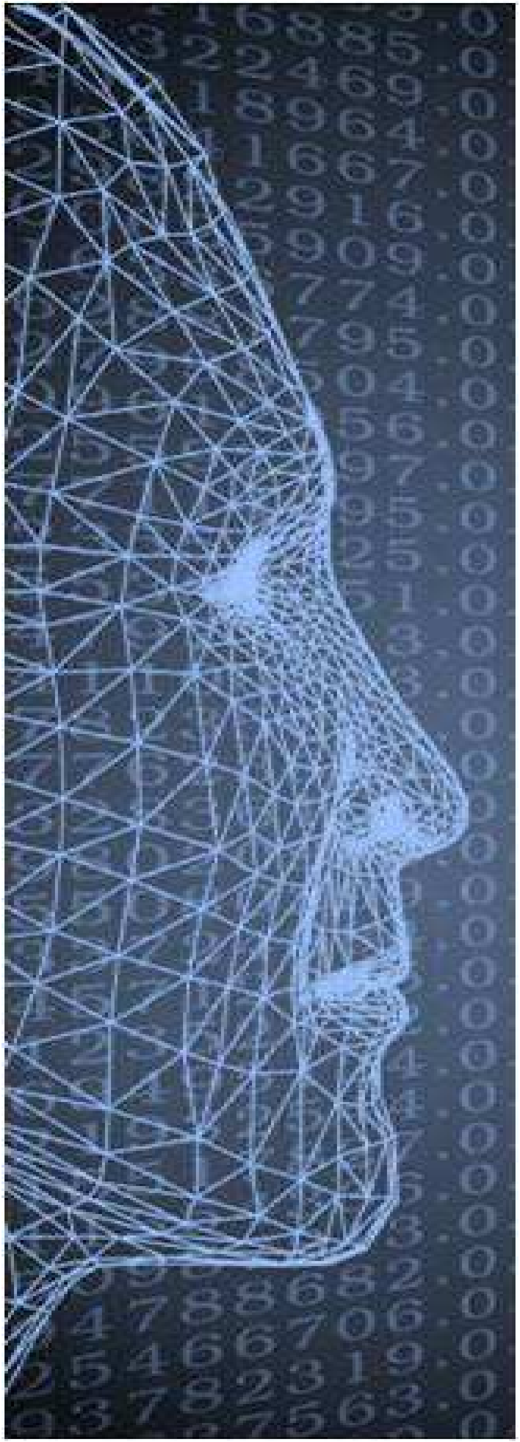
A radical Innovation is an innovation that <u>changes behaviors and consumption patterns</u> – *there are many innovations looming on the near horizon with the potential to transform medical practice.*



The simplest framework for identifying and developing radical innovations was developed at Procter and Gamble in the late 1990s:

What's Needed? ⟷ **What's Possible?**

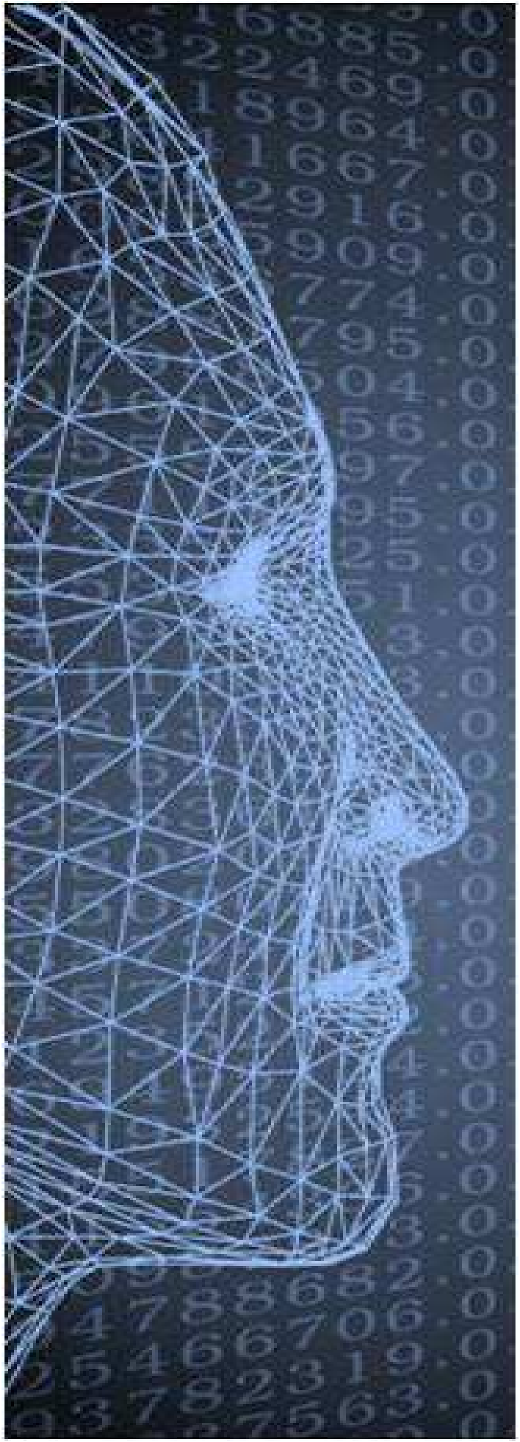
Market Scanning
Knowledge-building
Knowledge-sharing
Ideation & Invention
Luck!



WHAT'S NEEDED?

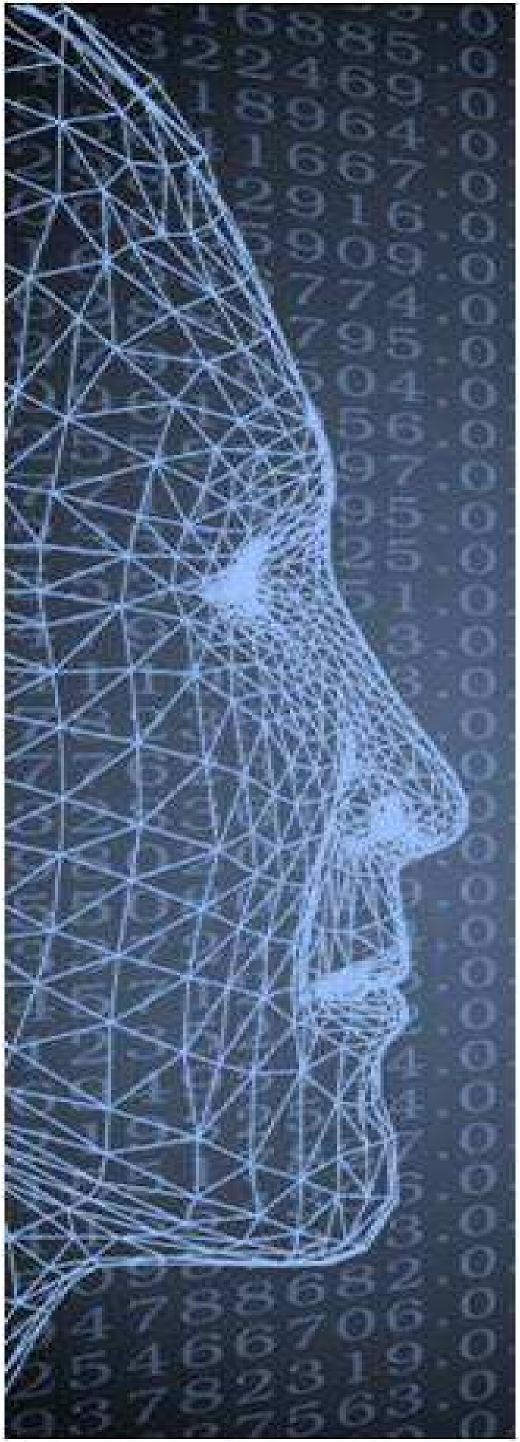
We need new medical solutions that are innovative and economical, and ways to improve existing methods…

- **New Medical Therapies**
- **Cheaper, Mobile Diagnostics**
- **Better Bio-Imaging**
- **Individual Cell Therapies**
- **Gene Therapies That Work**
- **Broad Spectrum Antivirals**
- **Transplant Organs/Tissues**



It’s not easy!

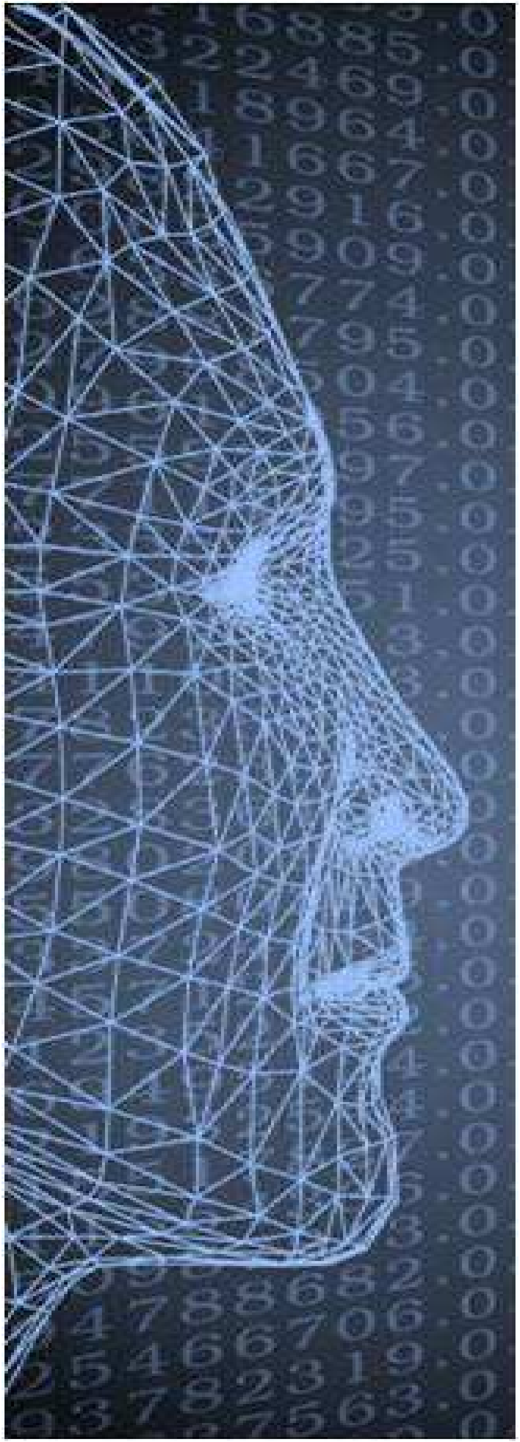
- **There are more than 200 forms of cancer**
- **Everyone develops pre-cancerous cells** *(although less than half the population develops cancer)*
- **Less than 10% of cancers are hereditary but there are many ways that genes play a role in causing or inhibiting cancer** – *what can we learn from gene therapy that will help fight cancer?*
- **Approximately 16% of cancers are caused by viral or bacterial infections —** *fighting viruses can help prevent many forms of cancer*
- **Viruses use dozens of strategies to attack cells and reproduce** – *what is needed to create a broad spectrum antiviral treatment?*
- **It’s extremely difficult to directly observe biological processes, including disease events –** *how can we improve nanoscale imaging?*



WHAT'S POSSIBLE?

A few examples of radical innovations that have the potential to transform medicine and healthcare…

- **Temperature can be a Therapy**
- **Bio-Nano-Innovation**
- **Better Nanoscale Imaging**
- **Gene Therapy that Works!**
- **Broad Spectrum Antivirals**
- **Organ/Tissue Regeneration**



WHAT'S POSSIBLE?

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- **Gene Therapy that Works!**
- **Broad Spectrum Antivirals**
- **Organ/Tissue Regeneration**

HEAT AND COLD

Some innovations are surprisingly simple. Oncologists are using HEAT in combination with chemotherapy to destroy tumors and also use COLD to cool patients during surgery and recovery.

Dr. Carlo Pastore is an oncologist and pioneer in the use of hyperthermia to treat cancer.

Dr. Lance Becker at the University of Pennsylvania is a pioneer in "Resuscitation Science" who has used therapeutic hyperthermia and hypothermia (cooling) to treat patients.

BIONANOTECHNOLOGY

Most disease-related biological structures and processes have nanoscale elements *(100 nanometers or less).*

Listed here are a few promising areas benefiting from "bionano-innovation."

Overcoming the body's immune response is the greatest challenge.

Nano-Diagnostics

- ***Biochips - Genetic Tests – Biosensors***
- ***Using nanoparticles to image tumors***

Targeted Drug Delivery

- ***Nanosized Drugs- Nanocarriers***
- ***Miniature Devices/Implants***

Novel Disease Therapies

- ***Near Infrared Radiation*** *(nanoparticles)*
- ***Broad Spectrum Antivirals***

Regenerative Medicine

- ***Stem Cells & Scaffolds***
- ***Regeneration of Tissues & Organs***

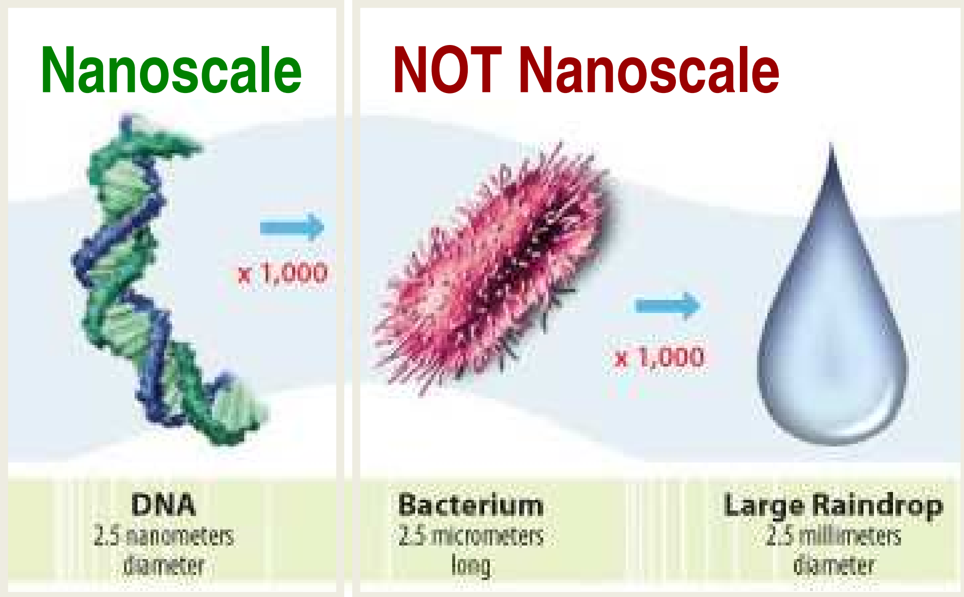
Gene Therapy

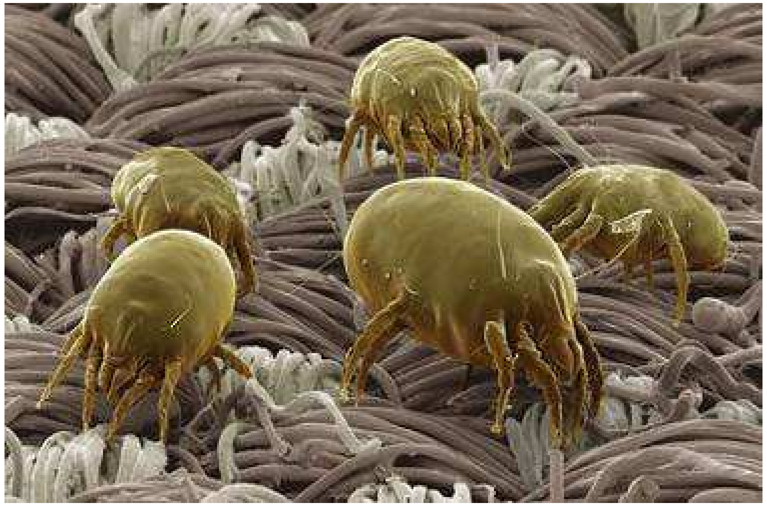
- ***Adeno Associated Virus Vectors***

Nano-enabled Bionics & Devices

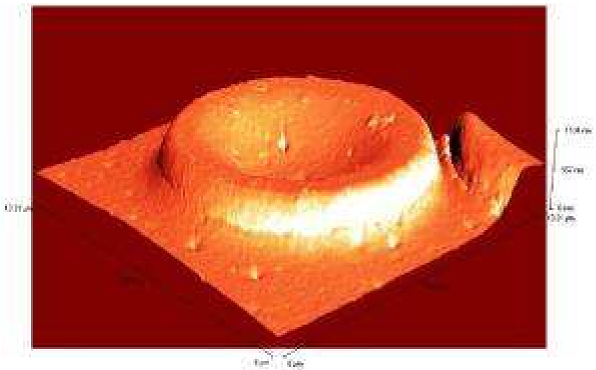
- ***Electronic Skin - Intelligent Biomaterials***
- ***Digestible Computers***
- ***Artificial Blood Cells/Tissue/Organs***

Quick! Name something Nanoscale! (<100nm)

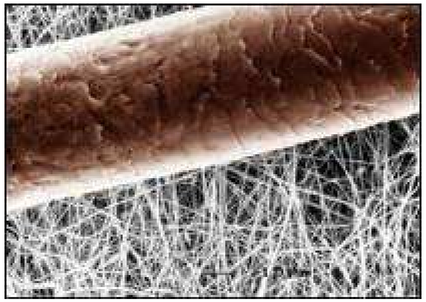




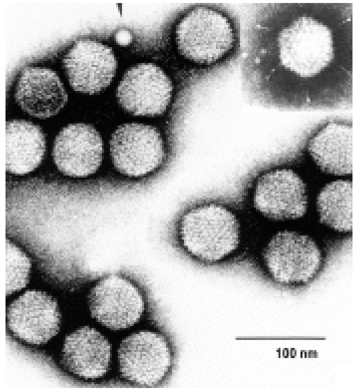
Dust mites on a bedsheet (200nm)
Source: TIME, May 2, 2008



Red Blood Cell-6.5nm
Source: Sverre Myhra, Yale Univ.



Nanofibers (1 to 10nm) compared to a human hair (10 to 50nm) *(EPA)*

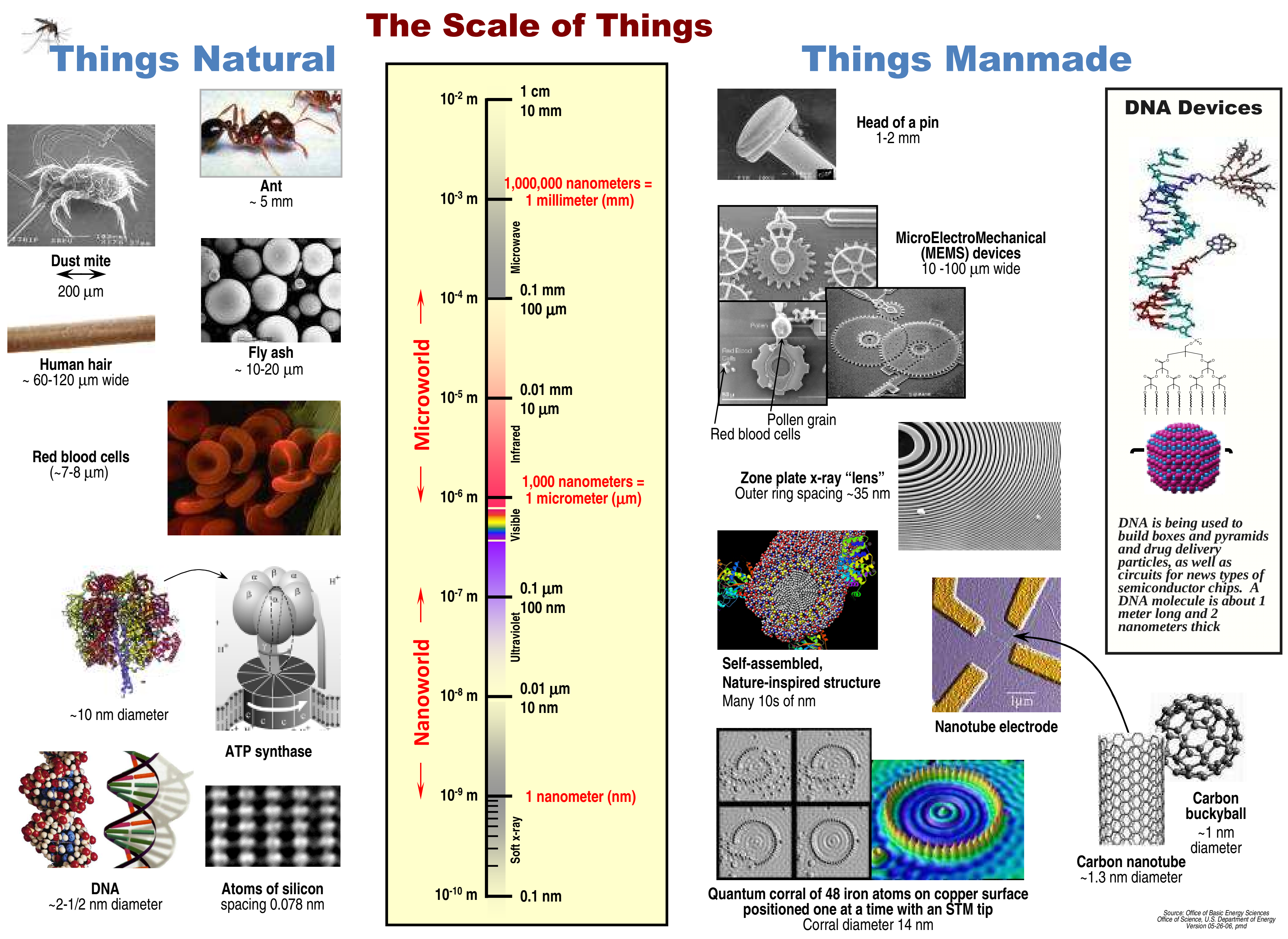


Adenovirus (NIH)

The page of a book is 100,000 nanometers thick.

A human hair is 10,000 nm.

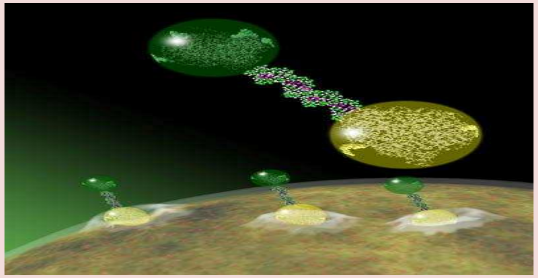
The head of a pin is 1 million nm.



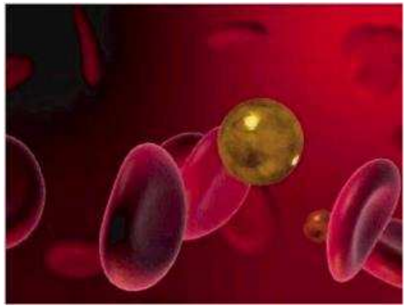
The Scale of Things
Things Natural
Dust mite
200 µm
Ant
~ 5 mm
Human hair
~ 60-120 µm wide
Fly ash
~ 10-20 µm
Red blood cells
(~7-8 µm)
~10 nm diameter
ATP synthase
DNA
~2-1/2 nm diameter
Atoms of silicon
spacing 0.078 nm
10^-2 m
1 cm
10 mm
10^-3 m
1,000,000 nanometers =
1 millimeter (mm)
Microwave
10^-4 m
0.1 mm
100 µm
10^-5 m
0.01 mm
10 µm
Infrared
10^-6 m
1,000 nanometers =
1 micrometer (µm)
Visible
Microworld
10^-7 m
0.1 µm
100 nm
Ultraviolet
10^-8 m
0.01 µm
10 nm
Nanoworld
10^-9 m
1 nanometer (nm)
Soft x-ray
10^-10 m
0.1 nm
Things Manmade
Head of a pin
1-2 mm
MicroElectroMechanical
(MEMS) devices
10 -100 µm wide
Pollen grain
Red blood cells
Zone plate x-ray "lens"
Outer ring spacing ~35 nm
Self-assembled,
Nature-inspired structure
Many 10s of nm
Nanotube electrode
Quantum corral of 48 iron atoms on copper surface
positioned one at a time with an STM tip
Corral diameter 14 nm
Carbon nanotube
~1.3 nm diameter
Carbon
buckyball
~1 nm
diameter
DNA Devices
DNA is being used to build boxes and pyramids and drug delivery particles, as well as circuits for news types of semiconductor chips. A DNA molecule is about 1 meter long and 2 nanometers thick
Source: Office of Basic Energy Sciences
Office of Science, U.S. Department of Energy
Version 05-26-06, pmd

BIO-NANO-INNOVATION

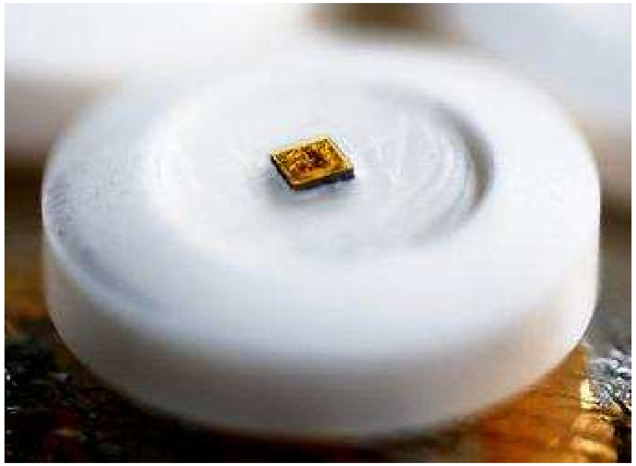
Cancer Research Goals



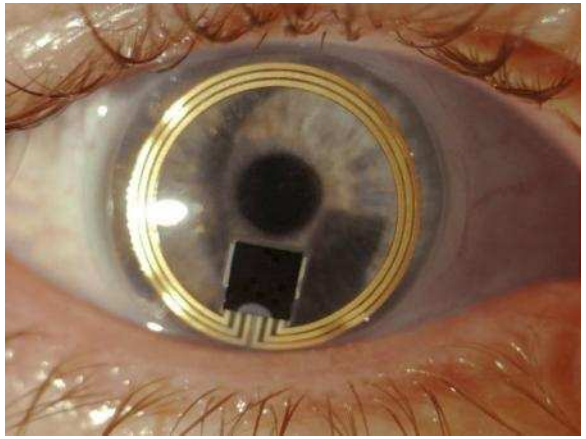
1) Detect and treat free/ dispersed cancer cells
2) Kill cancer cells without injuring healthy cells
3) Target and treat individual cancer cells
4) Develop cancer vaccines
5) Understand and use cancer genetics



Gold nanoparticles accumulate in tumors, where they can be heated with Near Infrared Radiation that kills the tumors without heating the surrounding healthy cells – this needs to be perfected to treat organs deeper inside the body.



Proteus Digital Health is marketing a digestible computer chip embedded in a pill, connected wirelessly to a wristband that sends data over the Internet to a caregiver or lab.



Bionic solutions combine nanomaterials with computer chips in many applications.

NANOSIZING DRUGS

Cancer fighting compounds are being nano-sized to make them more soluble and bio-available – most of this research is promising but still experimental:

- **Cancer Binding Drugs: Cancer binding drugs are improving the concentration of cancer-fighting drugs such as Docetaxel (Taxotere).** *(“BIND-014 “ clinical trials – Robert Langer, M.I.T.)*
- **Cancer Fighting “Seeds”: A nanosized compound found in tea leaves (EGCg) is combined with radioactive gold nano- particles to treat prostrate tumors.** *(U .of Maryland, animal studies)*
- **Curcumin: Cumin (turmeric) fights cancer but the molecule needs to be nanosized to make it bioavailable/deliverable.**

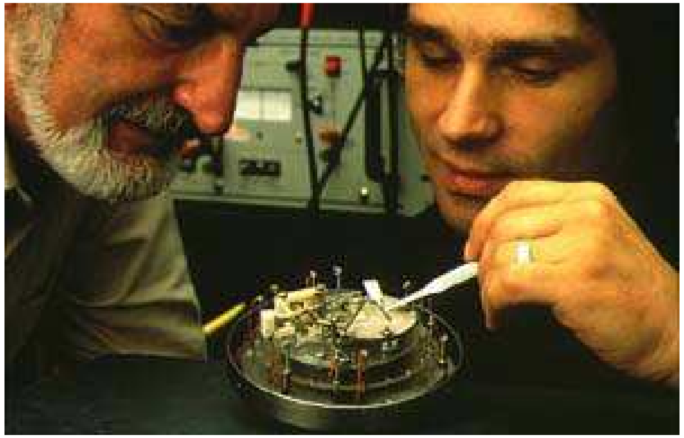
  (“Advances in nanotechnology-based delivery systems for curcumin”; Nanomedicine, July 2012, Vol. 7, No. 7, pgs. 1085-1100)
- **Gold Nanoparticles: Gold nanoparticles migrate to tumors - Near Infrared Radiation heats the gold to kill the cancer.**
- **Nanophotomedicine: Light sensitive nanoparticles are being used to treat neuro-endocrine tumors.**

BETTER BIO-IMAGING

The nanotechnology revolution began with the development of the scanning tunneling microscope.

It is appropriate that the scanning probe microscope was developed in Switzerland, home of precision instruments and timepieces.

Today, modern “nanoscopes” use nanoscale lenses made of metamaterials to focus and optically view nanostructures that are smaller than visible lightwaves.

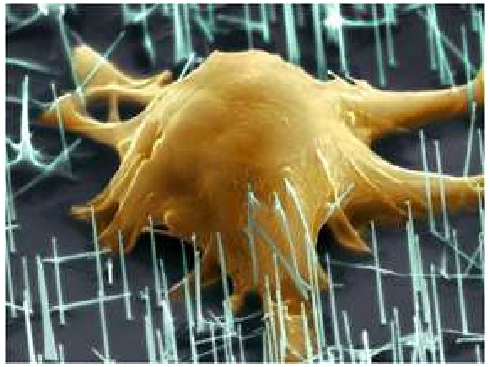


The 1986 Nobel Prize in Physics was awarded to Gerd Binnig and Heinrich Rohrer at IBM Zürich for the scanning tunneling microscope which allowed scientists to image and manipulate what was previously based mostly on theory.

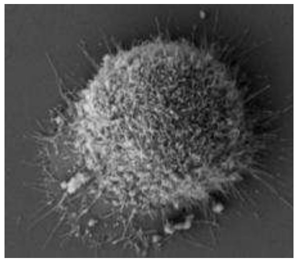
(Note: Ernst Ruska was the co-recipient for his design of the electron microscope)

Bio-Nano IMAGING

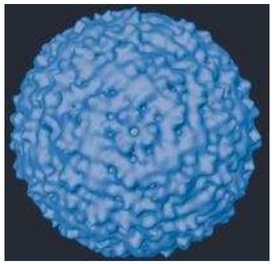
These are some of the remarkable images that are unlocking the secrets to disease



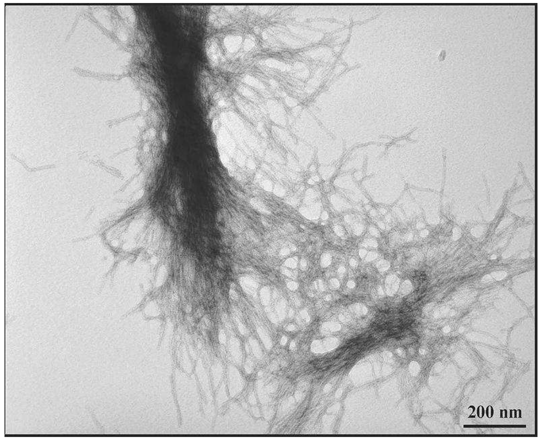
Mouse embryonic stem cell cultured on nanowires
(image courtesy Peidong Yang, UC-Berkeley)



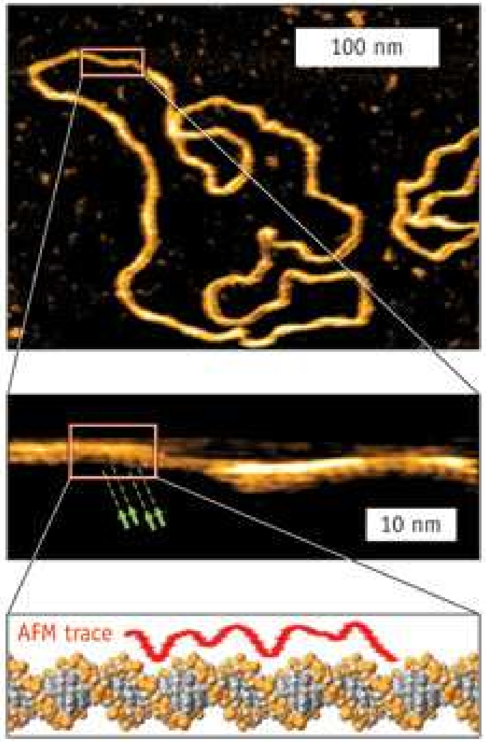
Cancer stem cell
(Univ. of Bergen, Norway)



West Nile Virus
(Duke University)



A special instrument called "BIO-Sans" was used to create a time series showing formation of the renegade Huntingtin Protein that destroys neurons in the brain. These studies are revealing the early stage growth pathways that cause Huntington's Disease.
(Oak Ridge National Laboratory & University of Tennessee - USA).

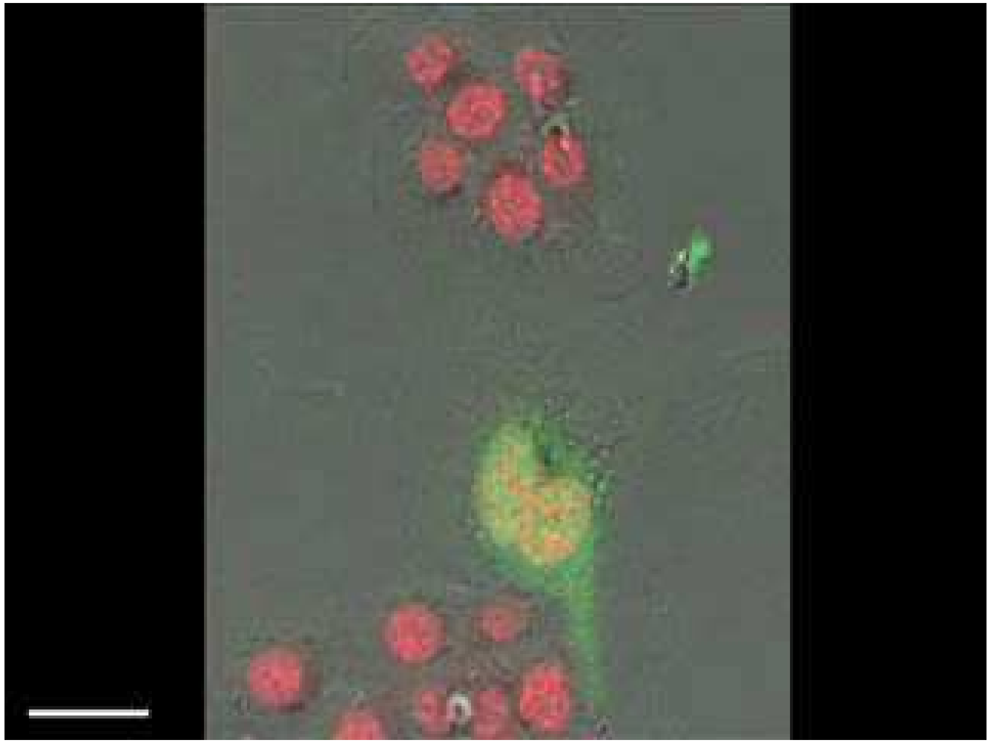


This is the most detailed image captured of the DNA helix, showing the spaces in the DNA "ladder" and confirming also that DNA spirals "right" or "left".
Image courtesy of Carl Leung,

Nano VIDEO IMAGING

This video shows a head and neck cancer cell (the green cell) killing a neighbouring normal cell (the transparent cells with red nucleus) after a close cell-to-cell contact .

Nanoscale videos are difficult to produce because nanoscale structures are often transparent, moving, changing shape and may be smaller than visible light waves. ***Better bio-imaging systems are needed.***



Video Source: The Gade Institute, University of Bergen, Norway

What's Needed?

AFFORDABLE NANOSCALE MICROSCOPES FOR SCHOOLS

The U.S. and EU (FP7) need to develop scanning probe microscopes that any school can afford.

This system should fit on a desktop, use modular probes/tips, and come with educational samples and software.

NanoProfessor™ by NanoInk, provides a nano imaging and fabrication system with teaching and learning modules for school systems.

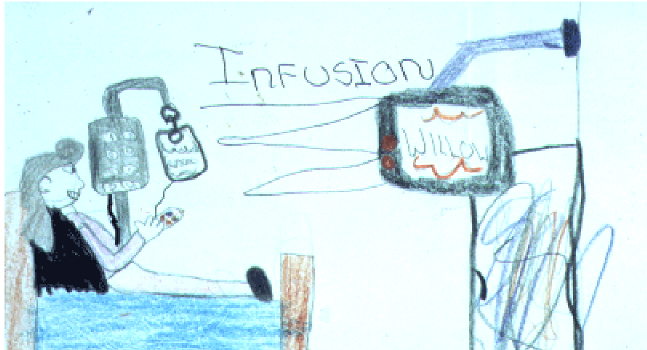
GENE THERAPY

In 1996 I co-authored a white paper for a workshop on "The Obstacles of Gene Therapy" which was summarized in Nature Biotechnology. Unfortunately, ALL of the threats and risks came true.

- **The Human Genome Project gave us a map, not a guide book**
- **Gateway technologies (gene switches, vectors) did not succeed**
- **Immune responses were stronger than expected**
- **Patients died (or contracted cancer) in the U.S. and Europe**
- **Many genes thought to be "junk" or evolutionary dead-ends actually have hidden functions, work with other genes, or turn on and off.**

GENE THERAPY

After 20 years and billions of dollars in research, gene therapy is finally succeeding.

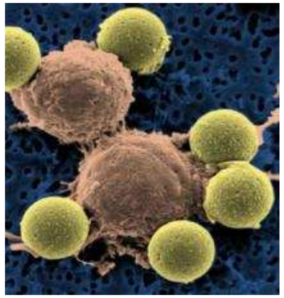


Drawing by 9 year old ADA patient showing her gene therapy infusion. Source: National Museum of American History.

- **1979 – p53 tumor suppressor protein (TP53 gene) discovered**
- **1990 – First gene therapy corrects ADA**
- **1999 – Jesse Gelsinger dies in a gene therapy clinical trial.**
- **2000 – Working Draft of Human Genome Map – completed in 2003**
- **2002 – Two babies in France develop leukemia after G.T.**
- **2003 – First gene therapy approved in China** - *recombinant Ad-p53 gene therapy (Gendicine™)for head & neck squamous cell carcinoma*
- **2008-2011 – G.T. reverses LCA blindness** *(Jean Bennett, U. of Pennsylvania)*
- **2011 – G.T. successfully treats 6 Hemophilia B patients**
- **2011 – G.T. cures 3 Leukemia patients who cut back or stopped their regimen of blood clotting factors** *(Carl June, U. of Pennsylvania)*
- **2012 – First G.T. in EU approved (for a rare single gene disease) –** *Glybera treats lipoprotein lipase deficiency*

GENE THERAPY

Immune system T-cells (center) bind to beads which cause the cells to divide – Source: Dr. Carl June, Univ. of Pennsylvania



- **Gene Therapy has evolved from "untargeted" to "targeted" applications – for safety & efficacy**
- **The newest gene therapies use Lentiviral and Adeno Associated Virus (AAV) vectors.** *The AAV vector was developed at the University of Pennsylvania in the laboratory of Dr. James Wilson, and is available to academic, government and corporate users.*
- **Complications include: 1) flooding the kidney with dead cancer cells after treatment; and 2) leukemia treatments kill virtually all B-cells.**
- **Other promising applications include cystic fibrosis, Parkinson's Disease, neurodegenerative diseases, hemophilia A, and more.**

BROAD SPECTRUM ANTIVIRALS

Most anti-viral drugs interrupt the life cycle of a specific type of virus – new research is is focusing on broad spectrum solutions

Todd Rider, who heads the research at M.I.T., believes this approach could treat up to 90% of all viruses.

DRACO (Double-stranded RNA (dsRNA) Activated Caspase Oligomerizer) is a broad spectrum antiviral that targets and kills infected cells when the virus creates double stranded RNA

REGENERATING ORGANS

10 years ago, Dr. Anthony Atala "grew" a kidney that he implanted into a patient who survives today.

Dr. Anthony Atala's research team at Wake Forest University used inkjet printers to spray stem cells on scaffolds. Today he uses 3D printers and decellurized organs.

Dr. Atala's goal is to grow organs instead of transplanting them from donors. His lab has successfully engineered more than 30 tissues and whole organs. He believes that soon we will "print" human tissue on demand.

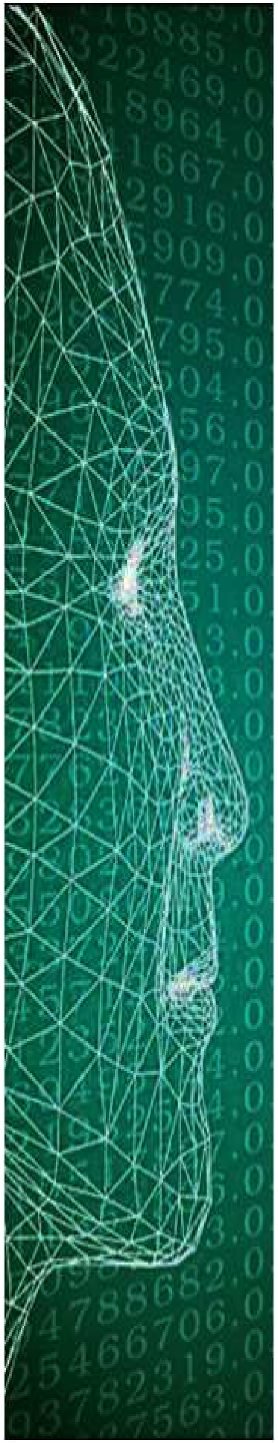
BIONIC EXOSKELETONS

Science Fiction inspires many innovations

Mickey Rourke wore an exoskeleton in IRON MAN 2

Ekso Bionics' exoskeleton is a wearable robot that allows Amanda Boxtel to walk – she was paralyzed in a skiing accident nearly 20 yrs. ago. Current battery life is 2 hours. Production units began shipping in 2012.

Lockheed Martin's HULC Exoskeleton (originally developed by Ekso Bionics)



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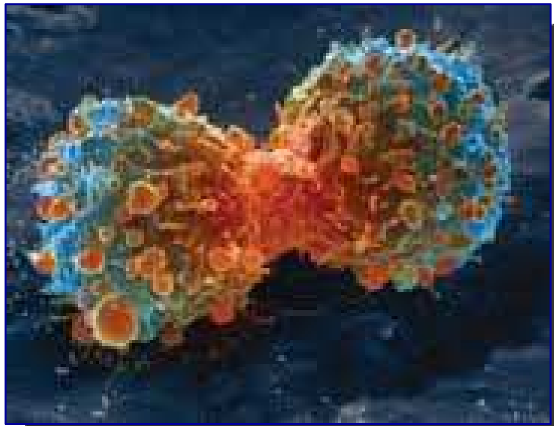
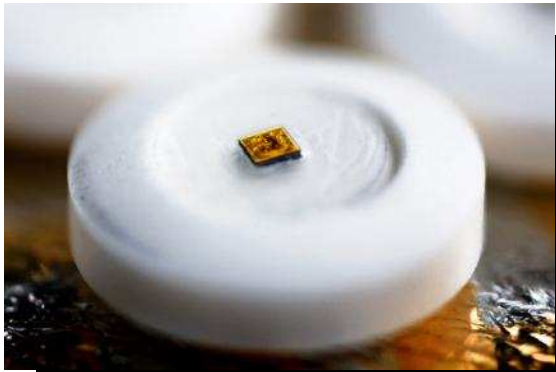
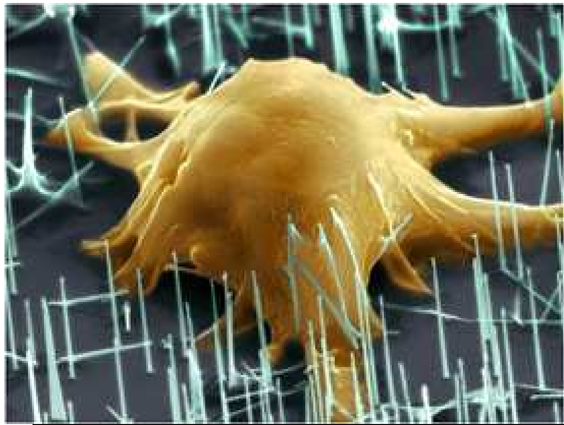


Lung Cancer Cell



Smart Pill by Proteus Digital Health



Stem Cell Secured Using Nanowires

Innovation, Nanotechnology and Cancer Care

IV International Conference on Integrative Oncology Therapy - Rome, Italy - 16 Nov. 2012

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