NATIONAL CANCER INSTITUTE

NCI Alliance for Nanotechnology in Cancer

The National Academies

Critical National Needs in New Technologies: Opportunities for the Technology Innovation Program

Nanotechnology: Transformational Technologies for Cancer and Other Diseases

24 April 2008

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Deputy Director
National Cancer Institute

Catalyzing – Accelerating Progress Toward Molecular-Based Cancer Medicine

NCI Alliance for Nanotechnology in Cancer

- Why nanotechnology for cancer?
- Why Nano is Promising for Cancer
- The NCI Alliance for Nanotechnology in Cancer - Current Status
- *Examples of the Science*

Why Cancer? Mind-Numbing Statistics

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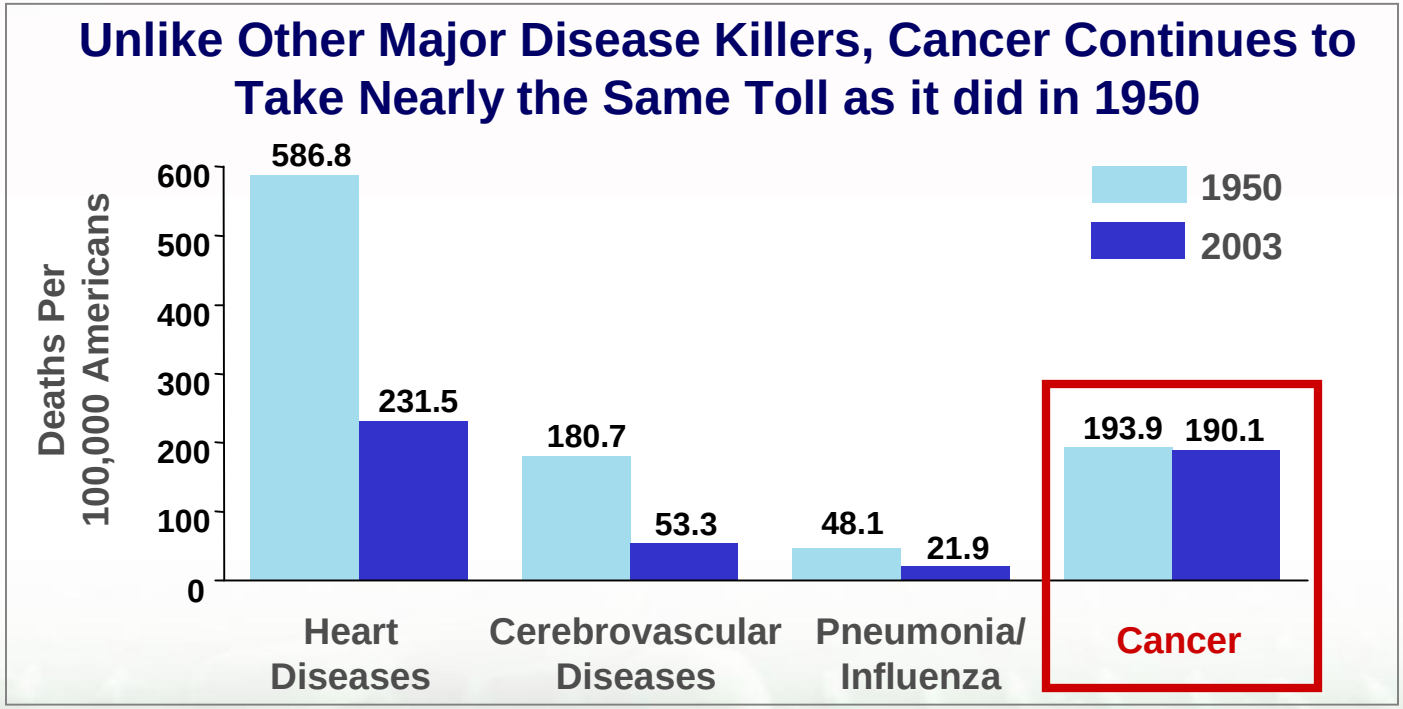
- 564,830 Americans died of cancer in 2005
- 1,399,790 Americans will be diagnosed with cancer this year
- $209.9 billion in 2005 for cancer healthcare costs
- Numbers of new cancer cases will approach 2 million by 2025 (Aging of the baby boomers)



Source for 2006 deaths and diagnoses: American Cancer Society (ACS) 2006 Cancer Facts & Figures; Atlanta, Georgia
Source for 2003 age-adjusted death rate: National Center for Health Statistics, U.S. Department of Health and Human Services, NCHS Public-use file for 2003 deaths.

Why Cancer: A Major Barrier - Cancer's Complexity

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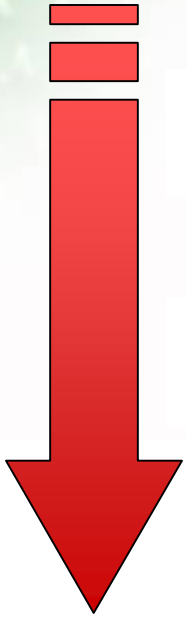
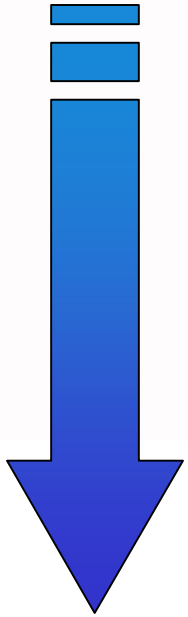


Genomics

Proteomics

Systems Biology



Increasing layers of complexity

Decreasing Technological & Methodological Capabilities / Reagents / Systems

Nanotechnology: New Ways to Interrogate the Complexity and and Specifically Intervene

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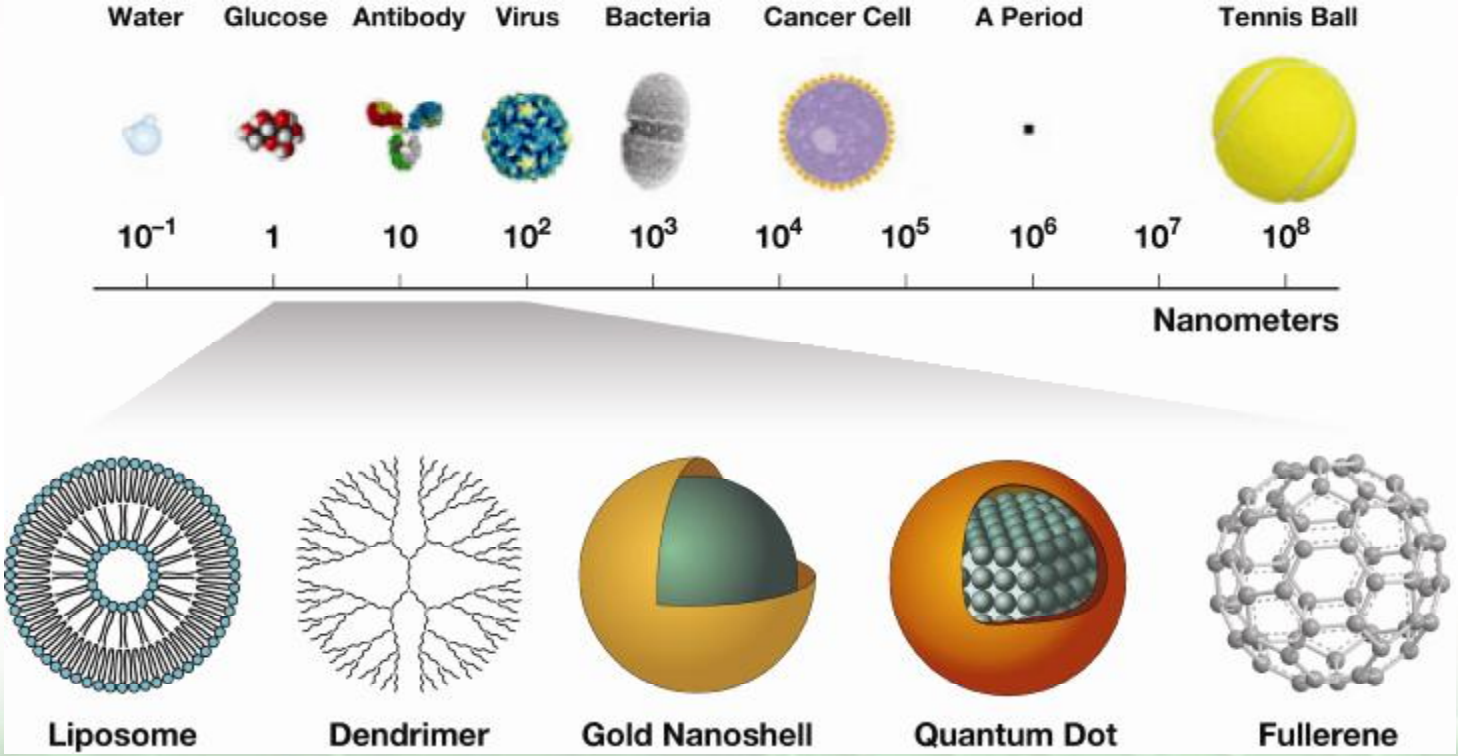
Varying dimensions and constructs lead to wide array of functional elements – physics at the nanoscale is complex – classic physics….quantum mechanics



Nanotechnology and the Future of Cancer

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Nanotechnology is a "disruptive technology" that promises to enable the transition of molecular-based science into the clinic – creating a new generation of diagnostics, therapeutics and preventives for cancer

Controlling matter in the range of 1-100 nanometers

§ **Early detection –**	**highly sensitive and specific sensors**
§ **In-vivo imaging –**	**new contrast agents, localization**
§ **Therapeutics –**	**local, on-particle delivery, targeted, monitoring, multi-plexing**
§ **Prevention -**	**detect early genomic/proteomic changes**

National Cancer Institute's Nanotechnology Initiative for Cancer

Technology and its Impact on the Disease

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- Devices to diagnose the disease
- Devices to treat the disease
- Devices to monitor the disease in post-treatment stage

- Tools and devices to understand the processes behind the development and spread of the disease
- Devices to reverse/alter the progress of the disease

NCI Alliance for Nanotechnology in Cancer – Funded in 2005

NCI Alliance for Nanotechnology in Cancer

- Multi-Year planning process, extramural meetings and workshops – dedicated NCI and expert nanotechnology leadership*
- Focus on multi-disciplinary teams, addressing key problems in oncology, accelerating progress of nano-products to the clinic

$144.3M initiative

Hallmarks of the Alliance

NCI Alliance for Nanotechnology in Cancer

- Requires academic and commercial partnerships for each supported Alliance project
- Commits major funding that leverages existing infrastructure
- Establishes training programs
- Coordinates with other Federal agencies to leverage NCI funds and creates synergies
- Pre-qualifies new materials and informs standards through the Nanotechnology Characterization Laboratory
- Reduces the risk of investment in new products
- Leverages effective input and outreach through patient advocacy communities

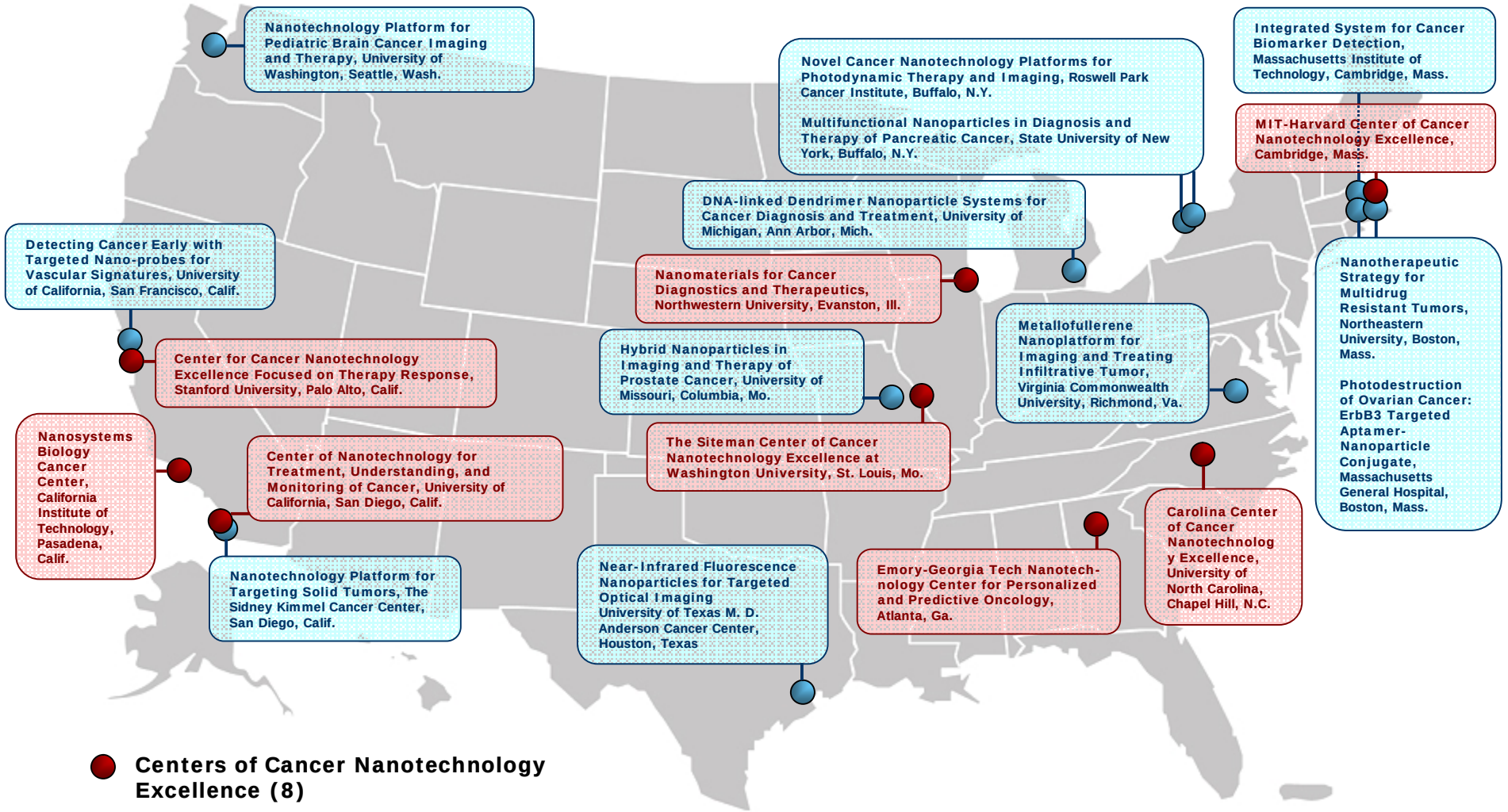
Major Programs of the Alliance

NCI Alliance for Nanotechnology in Cancer

1. **Centers of Cancer Nanotechnology Excellence**
2. **Nanotechnology Platforms for Cancer Research**
3. **Multidisciplinary Research Training and Team Development**
   - Fellowships in Cancer Nanotechnology Research
   - Interagency Collaborations
4. **Nanotechnology Characterization Laboratory**

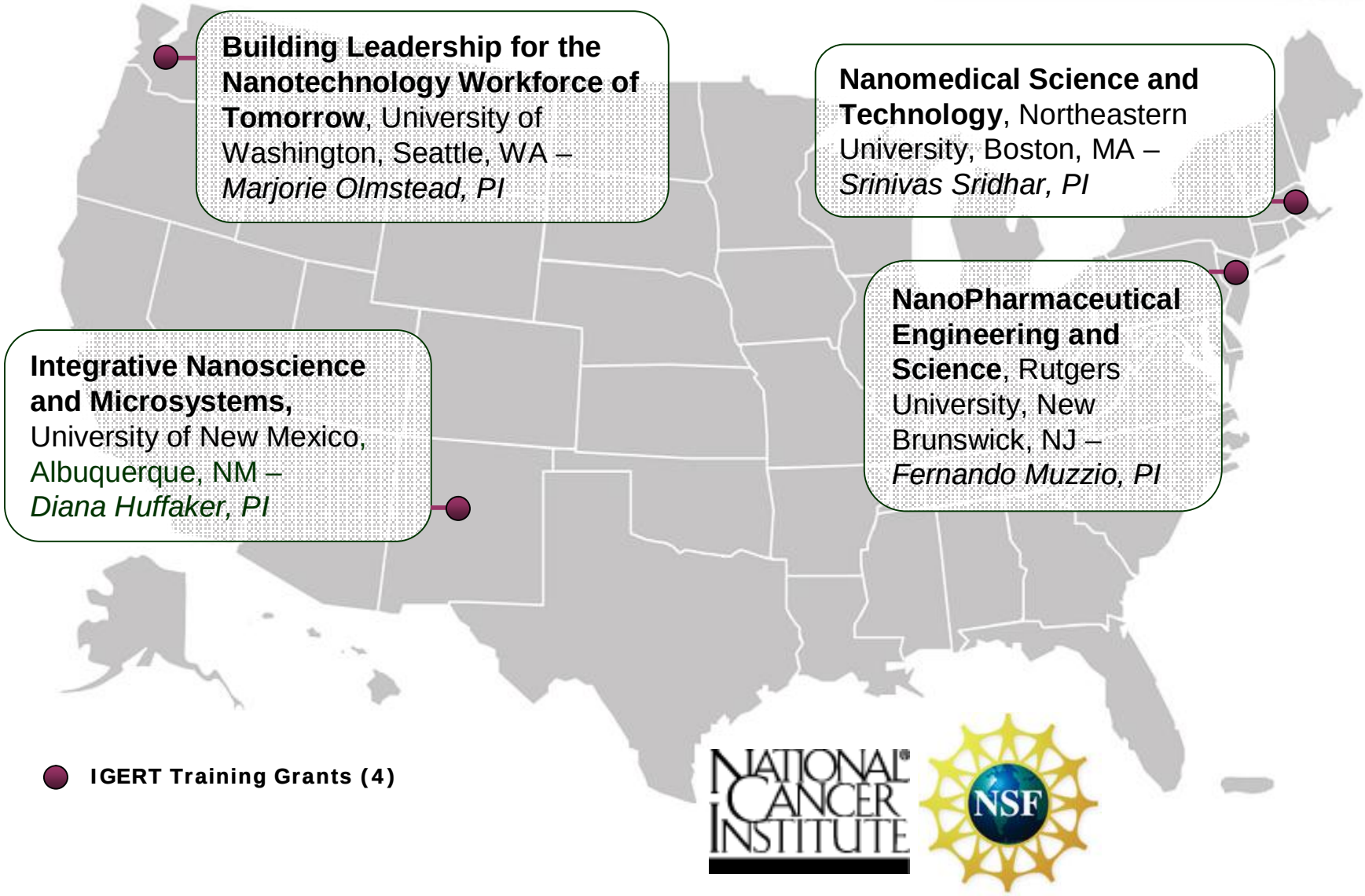
NCI's Alliance for Nanotechnology in Cancer

NCI Alliance for Nanotechnology



NCI-NSF Nanobiotechnology Collaboration

NCI Alliance for Nanotechnology in Cancer



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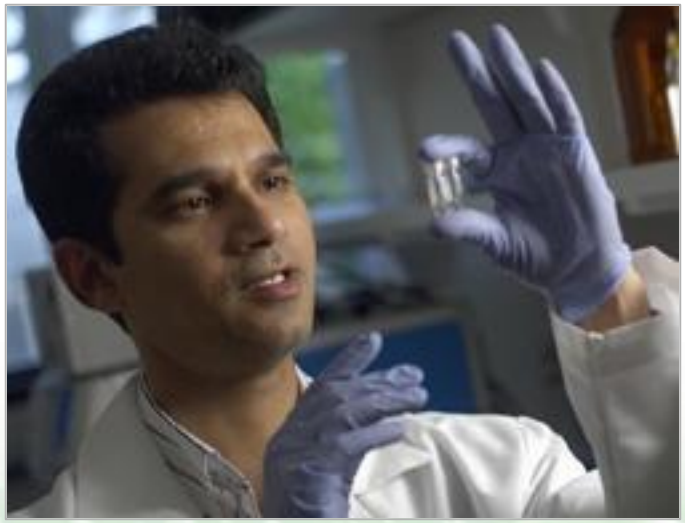
NSF

Nanotechnology Characterization Laboratory (NCL)

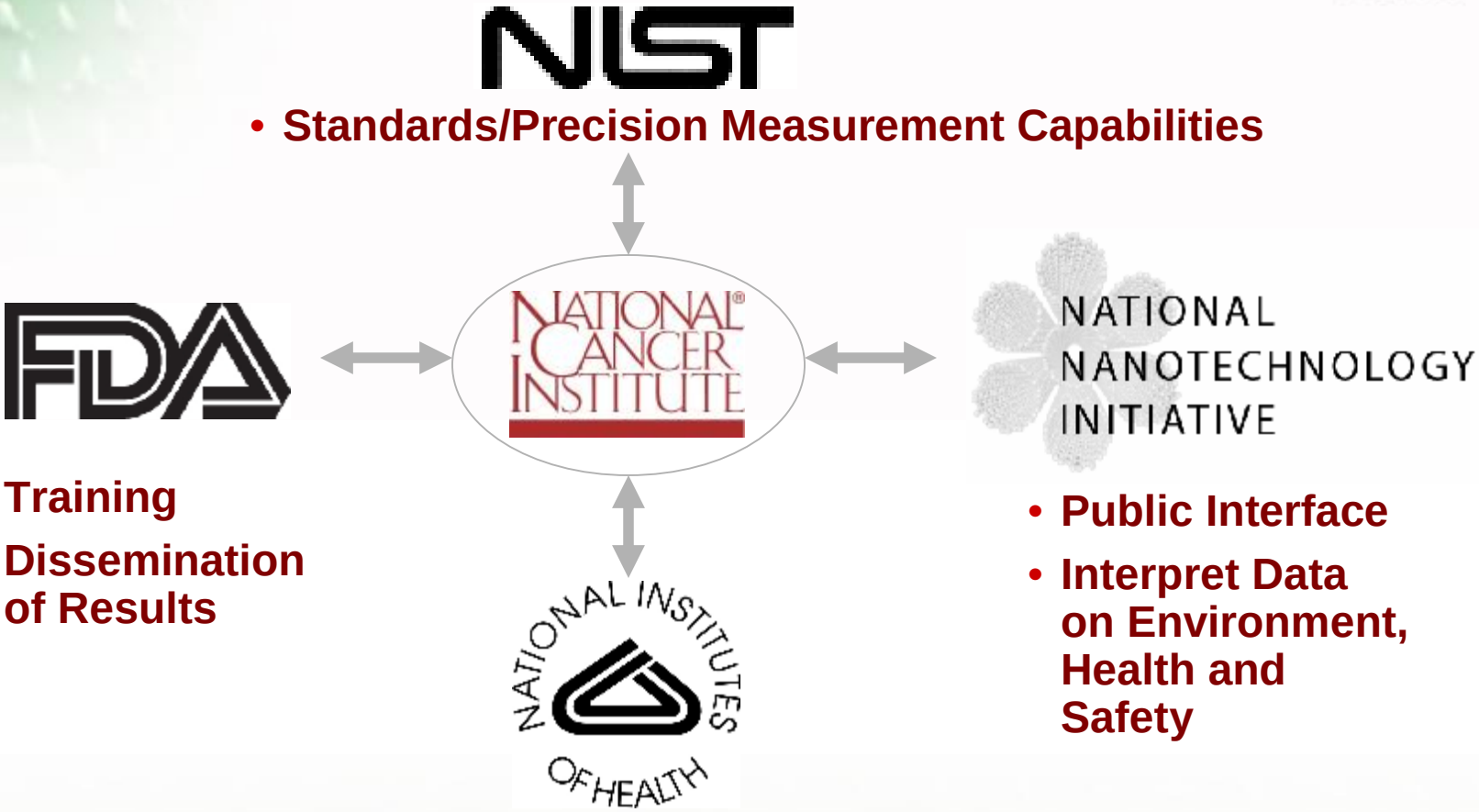
NCI Alliance for Nanotechnology in Cancer

- NCL Role:
  - Interface with CCNEs, individual investigators, NIST and FDA to develop standards and characterization data for nanoscale materials
  - Perform preclinical toxicology, pharmacology, and efficacy testing of nanoscale devices
  - Formulate and validate protocols for physical, *in vitro*, and ADME/tox characterization of nanoparticles



Alliance Involves Interagency Collaborations

NCI Alliance for Nanotechnology in Cancer



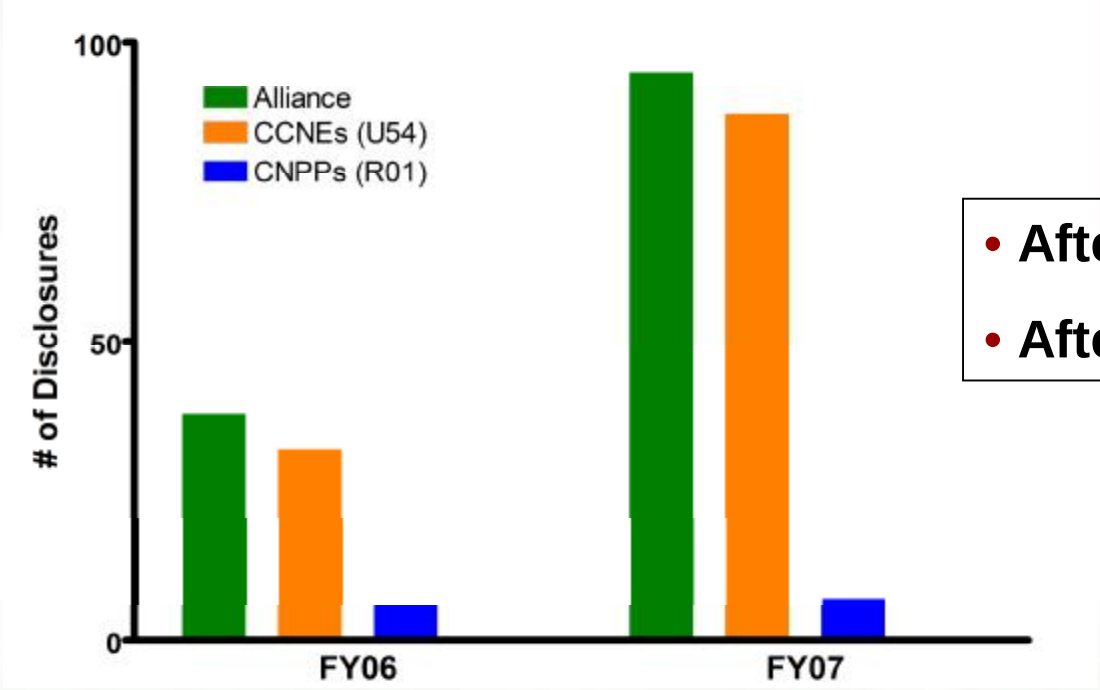
Two Years Later: Some Snapshots from the Alliance

Patent Applications, Technology Transfer, New Companies

NCI Alliance for Nanotechnology in Cancer

29 Companies Formed to date

By Nano-Alliance Members



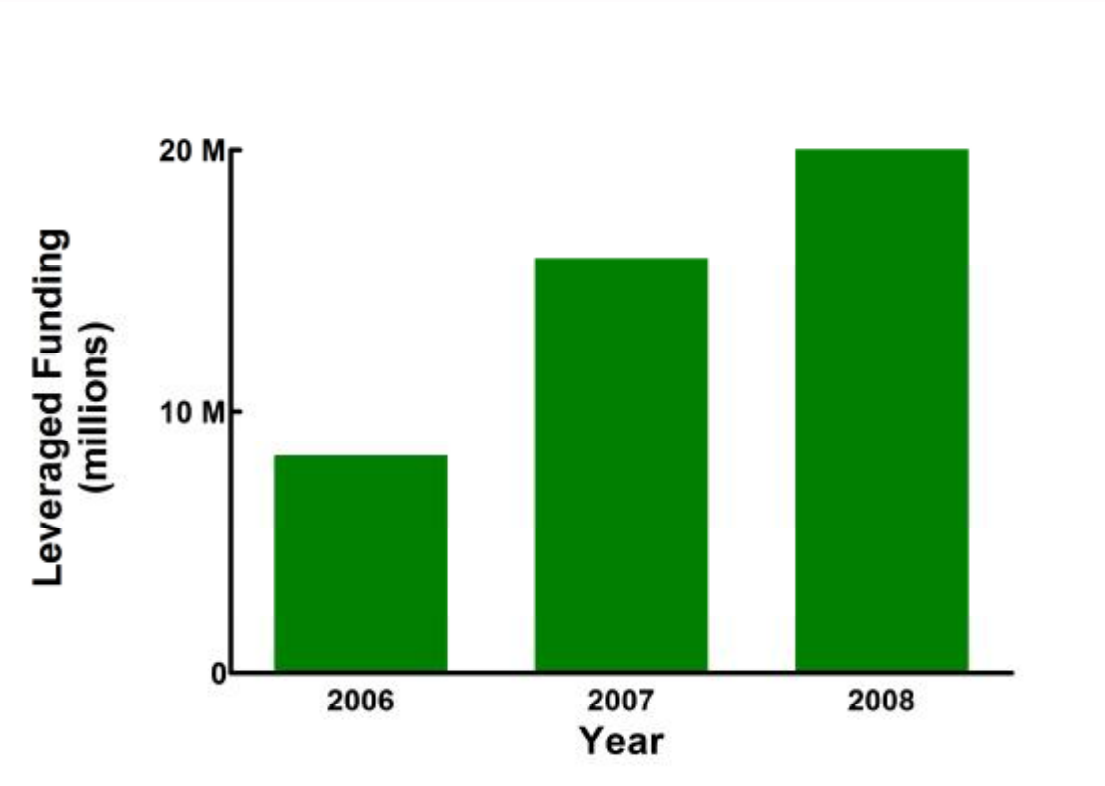
- **After 1st year – 38 disclosures**
- **After 2nd year – 133 disclosures**

Leveraged Funding

NCI Alliance for Nanotechnology in Cancer

- Over $80 million of new research funds (accumulative amount for period of next five years)
- Diversified portfolio from federal, state, and foundation sources

- $100 M donation to MIT for new cancer center
- $25-50 M from state of N. Carolina towards cancer research



Developing and Delivering A New Generation of Cancer Nanotherapies

Nano-therapeutics

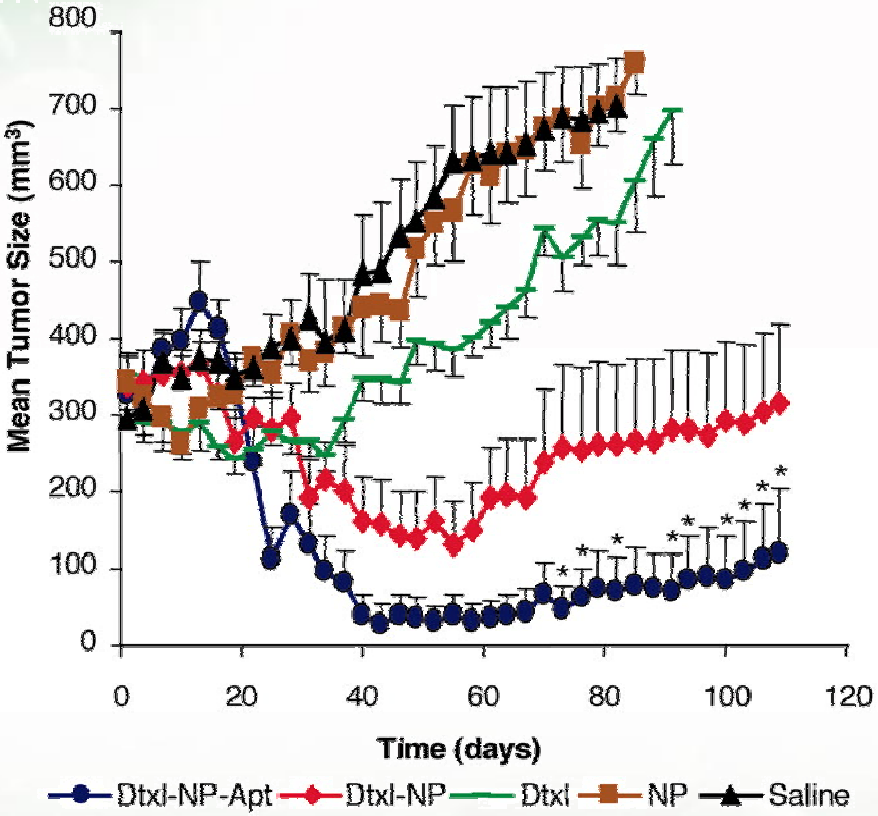
NCI Alliance for Nanotechnology in Cancer

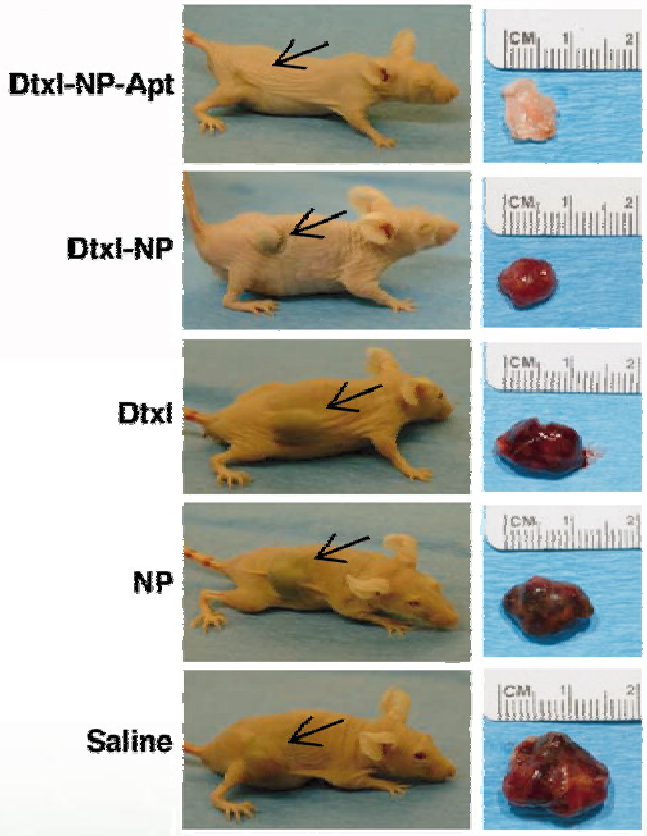
- Two drugs approved by FDA: 1) Abraxane – paclitaxel bound to albumin (Abraxis Bioscience) and 2) Doxil – liposome encapsulated doxorubicin
- Handful of clinical trials
- Common scheme for therapeutics – use existing drugs and adapt them to nano-based delivery platform
- Several companies (2-5) ready to file IND within next 12 months

Docetaxel-Encapsulated PLGA Nanoparticle-Aptamer Conjugates

NCI Alliance for Nanotechnology in Cancer

NP-Apt conjugates show greater efficacy in a xenograft mouse model than non-targeted nanoparticles





LNCaP s.c. xenograft nude mouse model of PCa; single intratumoral injection (day 0)

Farokhzad, Cheng, Langer et al.

Nanoparticle-based Therapies: Different Approaches

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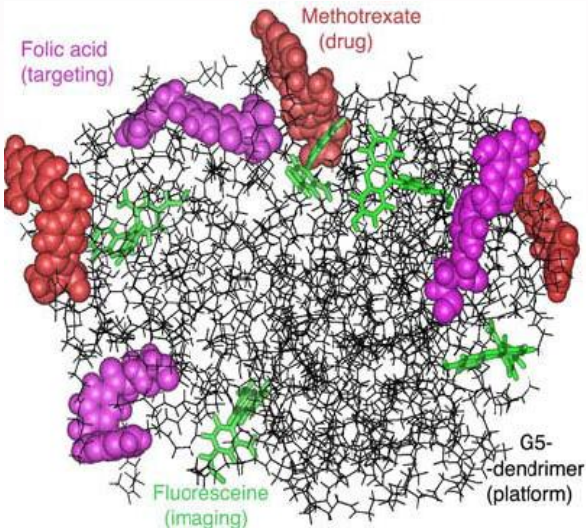
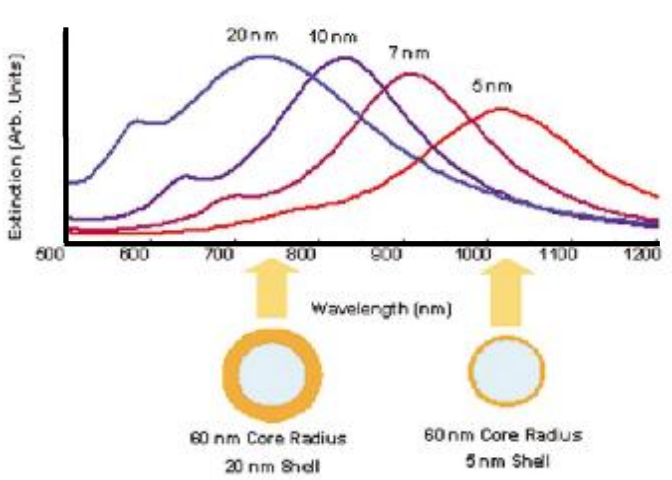
Dendrimers:
Targeted delivery of methotrexate



J. Baker, et al., Cancer Res. 65, 5317 (2005)

Nanoshells:
Photothermal therapy



N. Halas, J. West et al,
Ann Biomed Eng. 34, 15 (2006)

Company	Product(s)	Material	Indication	Status	Admin.
Abraxis Bioscience	**Abraxane**	Albumin-bound paclitaxel	NSC lung cancer, breast, others	**Approved**	IV
Advanced Magnetics	Combidex	Iron oxide nanoparticles	Tumor imaging	NDA filed	IV
Avidimer	Platform, ATI-001	Targeted dendrimers	Various cancer	Pre-clinical	IV
BIND	Platform technology	Targeted PLGA-PEG nanoparticles	Prostate cancer, others	Pre-clinical	IV
Calando	Targeted siRNA	Cyclodextrin polymers- siRNA	Cancer, others	Pre-clinical	IV
Carbon Nanotechnology	DF1	Dendritic fullerene	Chemoprotection	Pre-clinical	IV
Cytimmune	**Aurimune**	TNFα-bound colloidal gold	Solid tumors	**Phase I**	IV
Cytimmune	Auritol	Taxol and TNFα-bound colloidal gold	Solid tumors	Pre-clinical	IV
Dendritic Nanotechnologies	Dendrimer-Magnevist	PAMAM dendrimer	MRI imaging agent	Pre-clinical	IV
ImaRx Therapeutics	MRX-951	Self-assembling block copolymer	Cancer	Pre-clinical	IV
Insert Therapeutics	**Cyclosert-camptothecin**	Cyclodextrin nanoparticles	Metastatic solid tumors	**Phase I**	IV
Introgen	**INGN-401**	Liposome	Metastatic lung cancer	**Phase I**	IV
Kereos	Platform technology	Perfluorocarbon polymers	Cancer and cardiovascular	Pre-clinical	IV
Liquidia Technologies	Platform technology	PRINT™ nanoparticles	Cancer, others	Pre-clinical	IV
Nanospectra Biosciences	**AuroLase**	Gold nanoshell	Head and neck cancer	**Clinical trial - start**	IV
OrthoBiotech	**Doxil**	PEGylated liposome	Metastatic ovarian cancer	**Approved**	IV
Triton Biosystems	TNT-Anti-Ep-CAM	Polymer-coated iron oxide	Solid tumors	Pre-clinical	IV

Diagnostics and Imaging: Examples from the NCI Nanotechnology Alliance

Nanotechnology: Opportunities to Increase Sensitivity – New Molecular Diagnostics/New Generation of Imaging

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Biomolecule Detection Technology

Concentration	Molecule/Drop	Detection/ Targets/Disease
10^{-3}- Millimolar	Quadrillions	Colorimetric/Enzymatic Chemistry Blood Sugar (Diabetes)
10^{-6}- Micromolar	Trillions	
10^{-9}- Nanomolar	Billions	ELISA & Chemiluminescence Troponin, CK-MB, BNP, bHCG
10^{-12}- Picomolar	Millions	
10^{-15}- Femtomolar	Thousands	Bio-barcode Technology Cancer: Prostate, Ovarian, Breast Alzheimer's Disease, Mad Cow Pulmonary Disease, Cardiovascular Disease
10^{-18}- Attomolar	Tens	
10^{-21}- Zeptomolar	<1	

Problem: Sensitivity to Detect Early Changes in Cancer – (BioBarCode (BBC) Assay Detection)

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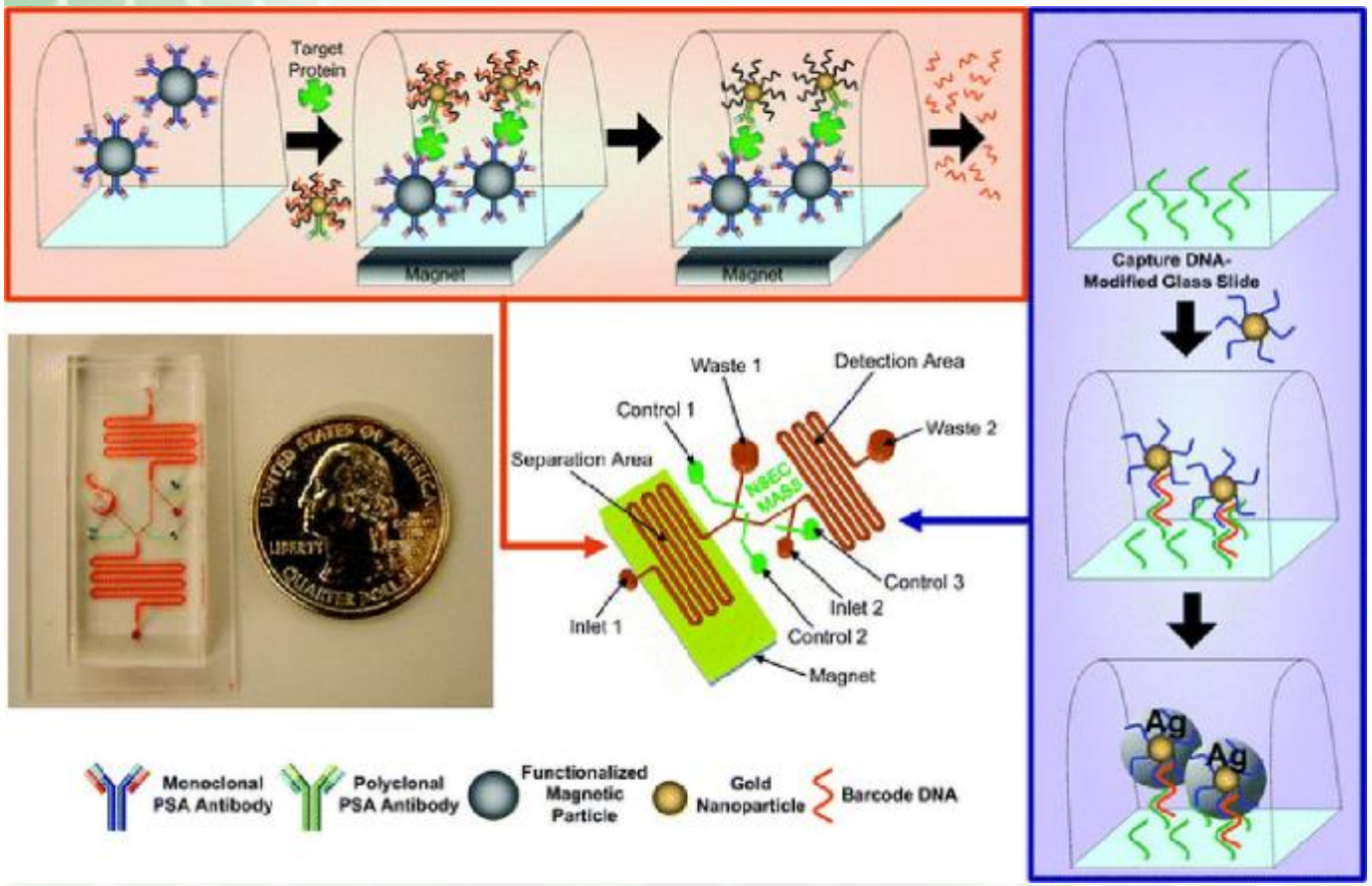

'Nano' Added Value

- Use nanoparticles (NP) as tags to target specific protein ***AND attach 10^3 - 10^6 DNA strands***
- The 10^3 - 10^6 DNA strands provide *built-in* signal amplification to each NP. ***(Amplification w/o PCR)***
- ***Ultrahigh sensitivity***
- The approach should be applicable targets with with known Abs.

Protein Detection Using Sensitive Silicon Nanowire Technology

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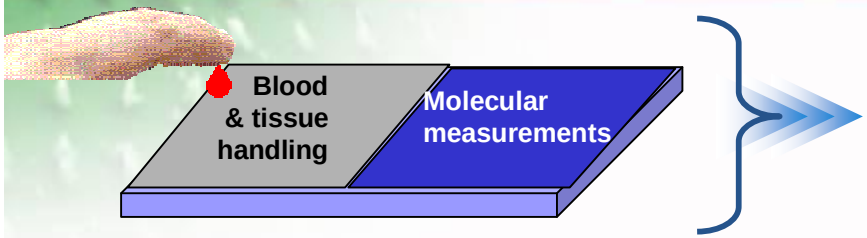

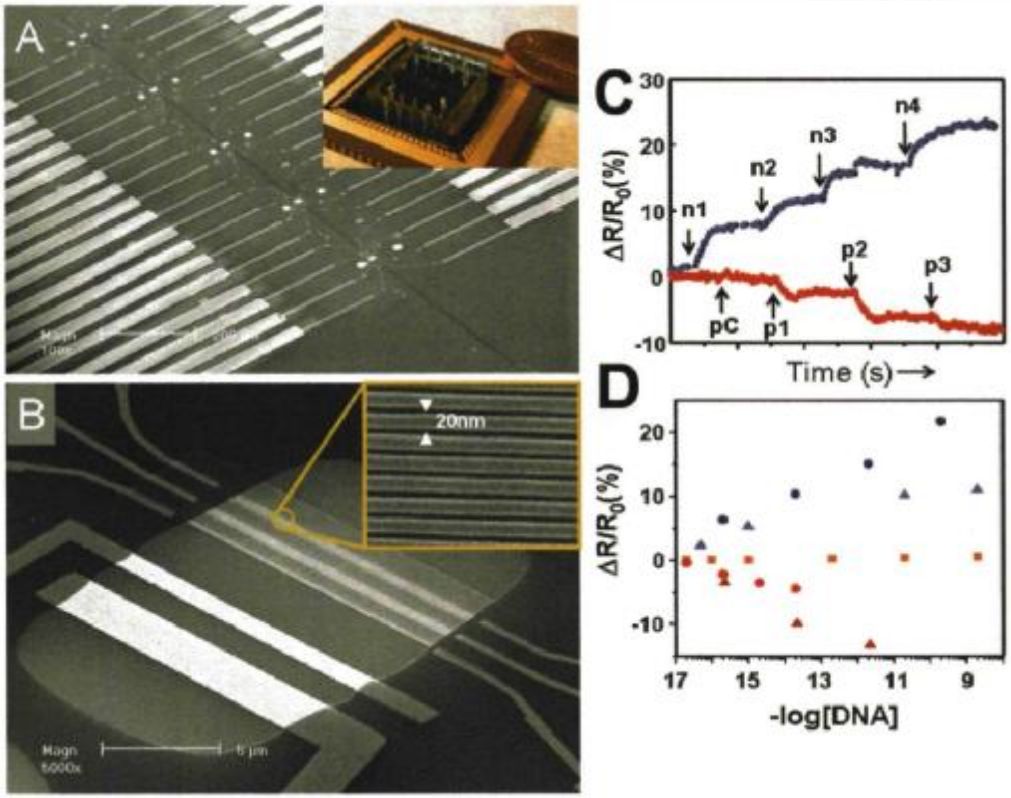

- **Systems biology approach**
  - Personalize detection, treatment, and monitoring of cancer
- **Silicon nanowires chips**
  - **~100 attoM** sensitivity and **10^6** dynamic range
  - Up to **3200** simultaneous measurements can be made
  - Tested in serum-like environments

Silicon nanowires

§ Detect target analytes through changes in nanowire's DC conductivity due to target binding to a surface-bound capture probe

James Heath, *Caltech*

Novel Quantum Dots That Do Not Require External Illumination

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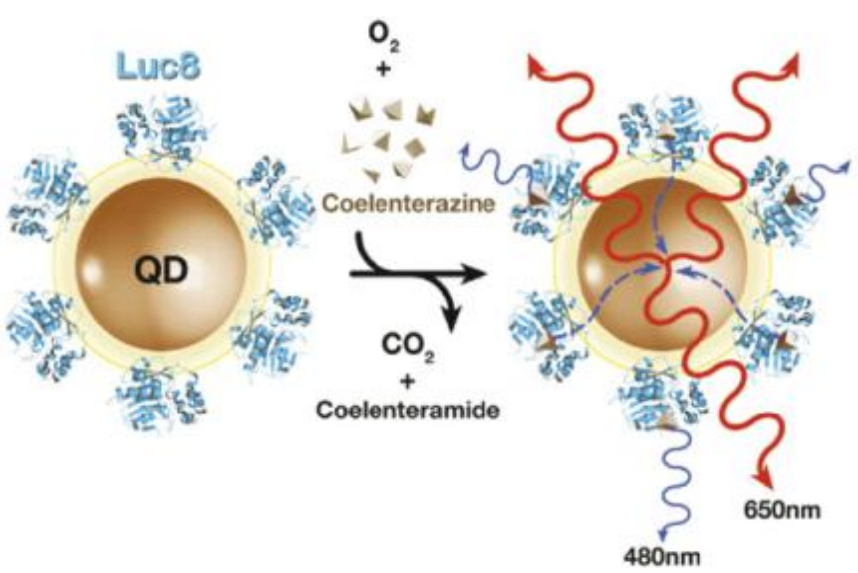
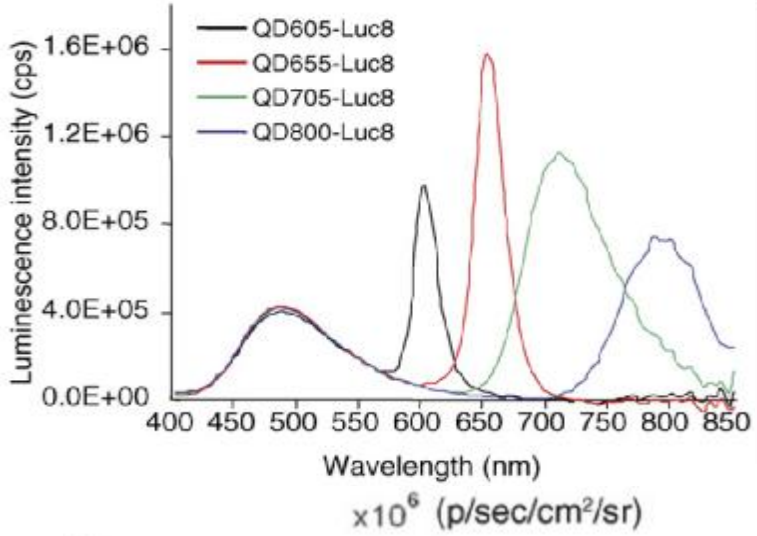
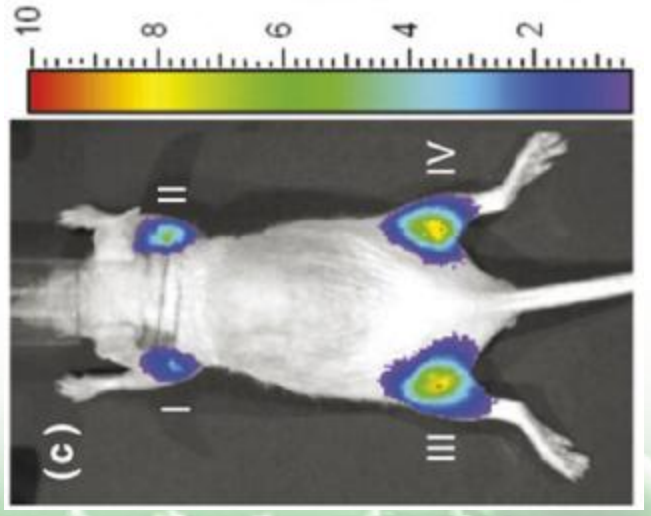






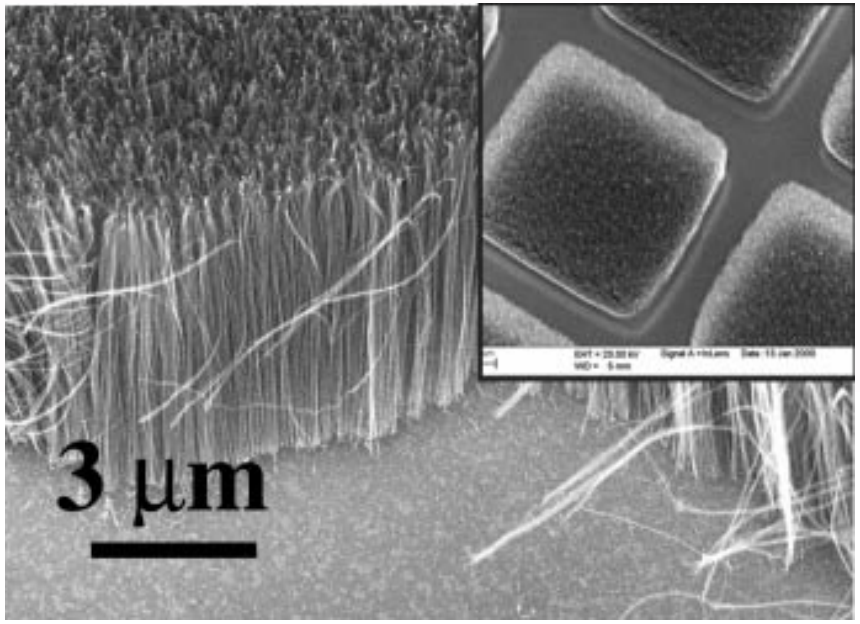
- Quantum dots conjugated with fluorescent proteins bioluminesce in response to an enzyme-catalyzed reaction
- Bioluminescence resonance energy transfer (BRET) is shown for the first time with quantum dots
- Blood does not interfere with quantum dot signal

So, Gambhir, Rao et al., Self-illuminating quantum dot conjugates for in vivo imaging,Nat. Biotechnol. 24, 339 (2006)

Problem – Imaging Single Cells: X-rays From Carbon Nanotubes Irradiate Individual Cells

NCI Alliance for Nanotechnology in Cancer

- **Exciting an individual carbon nanotube causes it to release high-energy electrons only from its tip, producing a high-energy electron beam with a diameter of 10 microns, small enough to irradiate specific locations in single cells.**
- **As many as 10,000 of these microbeam electrodes can be combined to produce an electron source capable of irradiating single cells or arrays of cells with a finely tuned dose of electrons.**
- **Radiation therapy is an important component of modern cancer therapy, but is a blunt weapon at best. Carbon nanotube-generated electron beams should give it scalpel-like precision.**



S. Chang, et. al., *Radiation Protection Dosimetry, 2007*
Image courtesy of O. Zhou, University of North Carolina at Chapel Hill

Nanotechnology: Innovative Solutions for Complex Cancer Problems

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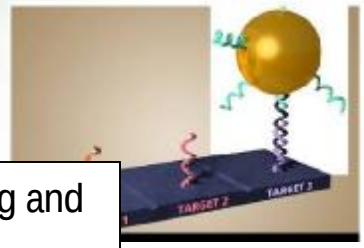
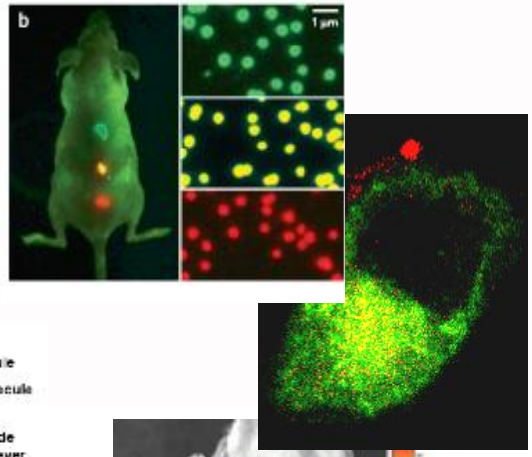
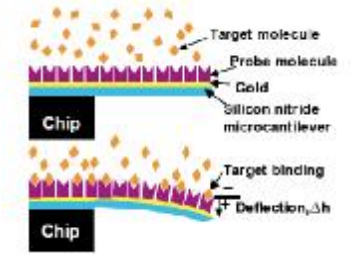
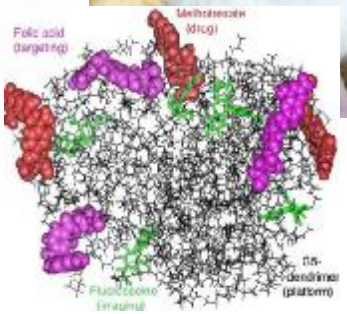
Focus Areas:

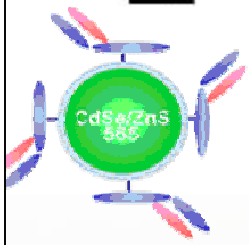
- Molecular imaging and early detection
- In vivo imaging
- Reporters of efficacy
- Multifunctional therapeutics
- Prevention and control
- Research enablers

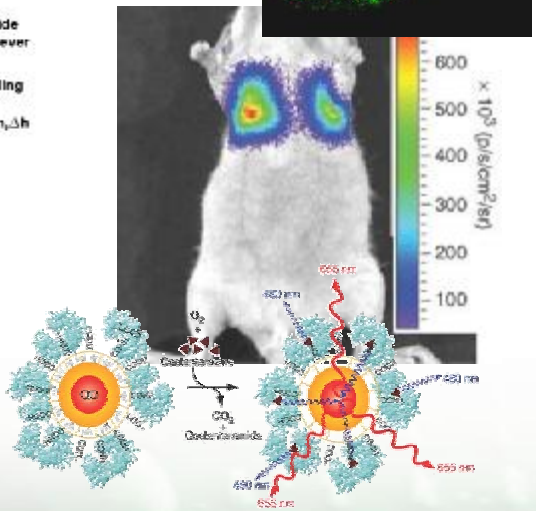


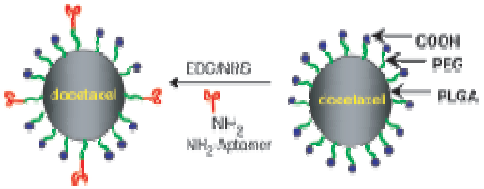












Early detection

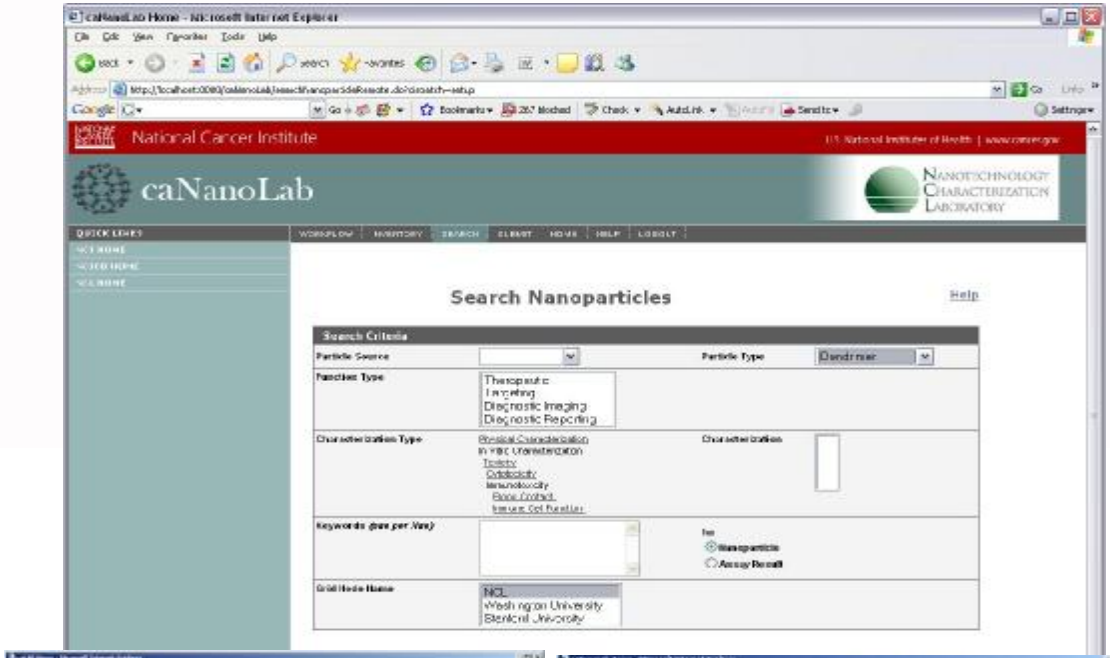
Imaging

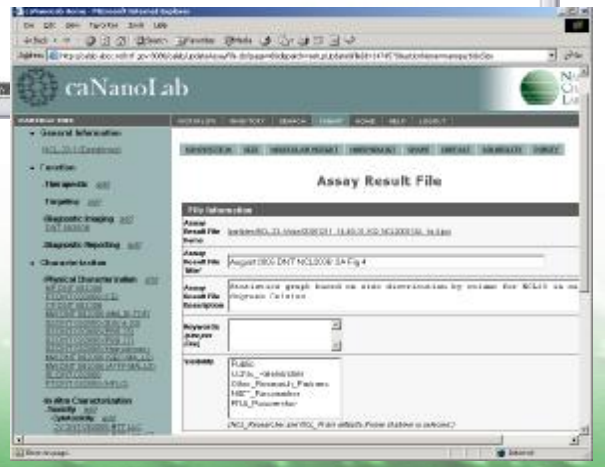
Therapy

Common Data Storage: caNanoLab Database

NCI Alliance for Nanotechnology in Cancer

- Standards Develop.
  - Terminology
  - Ontologies
- Searchable database
  - Particle data
  - In vitro data
  - In vivo data
- Role-based security
  - NCL view
  - Alliance view
  - Public view
- Interface with caBIG





Nano-Challenges

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- Convergence of physical and biological (specifically molecular oncology) – broadening scope in an already complex field
- Education – engagement of oncologists
- Limitations of trained scientists and new training models

- Defining properties at the meso-scale
- Building from the ground up – understanding performance
- Sensors – communication from the nano to macro environments
- Clinical trials models

- Regulatory hurdles
- Public perception (nano-bots to invisibility) vs. real promise for medicine

http://nano.cancer.gov

NCI Alliance for Nanotechnology in Cancer

- Timely reports of scientific advances
- Accessible, searchable updates on advances and scientific bibliography
- Teaming site for potential collaborations
- Multimedia communications
- Sign-up for email alerts

A Noble Vision

NCI Alliance for Nanotechnology in Cancer

"A grand challenge is the ability to detect cancer earlier — ***and the answer almost certainly will be nanotechnology*.**"

"In addition to detecting cancer, nano-based techniques will enable physicians to determine whether a particular treatment is working."

Dr. Richard Smalley, Nobel Laureate

September 13, 2004