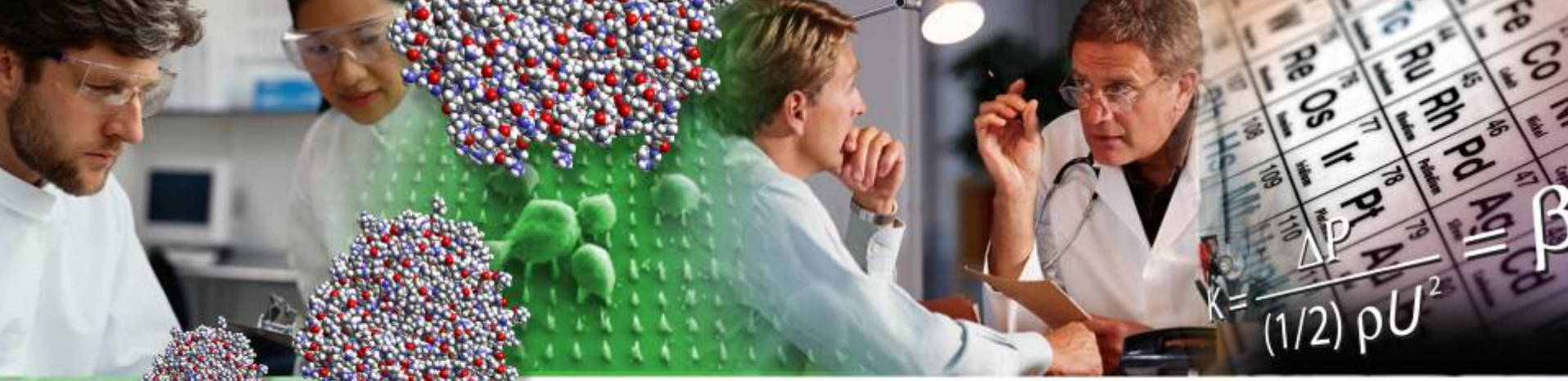


Galvanizing the New Generation of Nano-Based Products for Cancer

ASTM Workshop – May 19, 2005

Characterization of Nanomaterials for Medical and Health Applications

Gregory Downing

Director, Office of Technology and Industrial Relations

National Cancer Institute

The Potential of Nanotech in Cancer

NCI Alliance for Nanotechnology in Cancer

Nanotechnology is a disruptive technology with major potential to drive a new generation of cancer diagnostics and therapeutic products that address major markets.

But, realization of this potential requires systems-level changes and new product development approaches...

Systems-level Changes are Now Getting Underway

NCI Alliance for Nanotechnology in Cancer

- NCI is realigning the way we do technology development
  - Multi-disciplinary teams
  - Built-in collaborations with the private sector
  - Transparency of opportunities
- NCI is establishing the needed infrastructure
  - caBIG for bioinformatics
  - Nanotechnology Characterization Laboratory for standards
  - Centers of Cancer Nanotechnology Excellence for integration

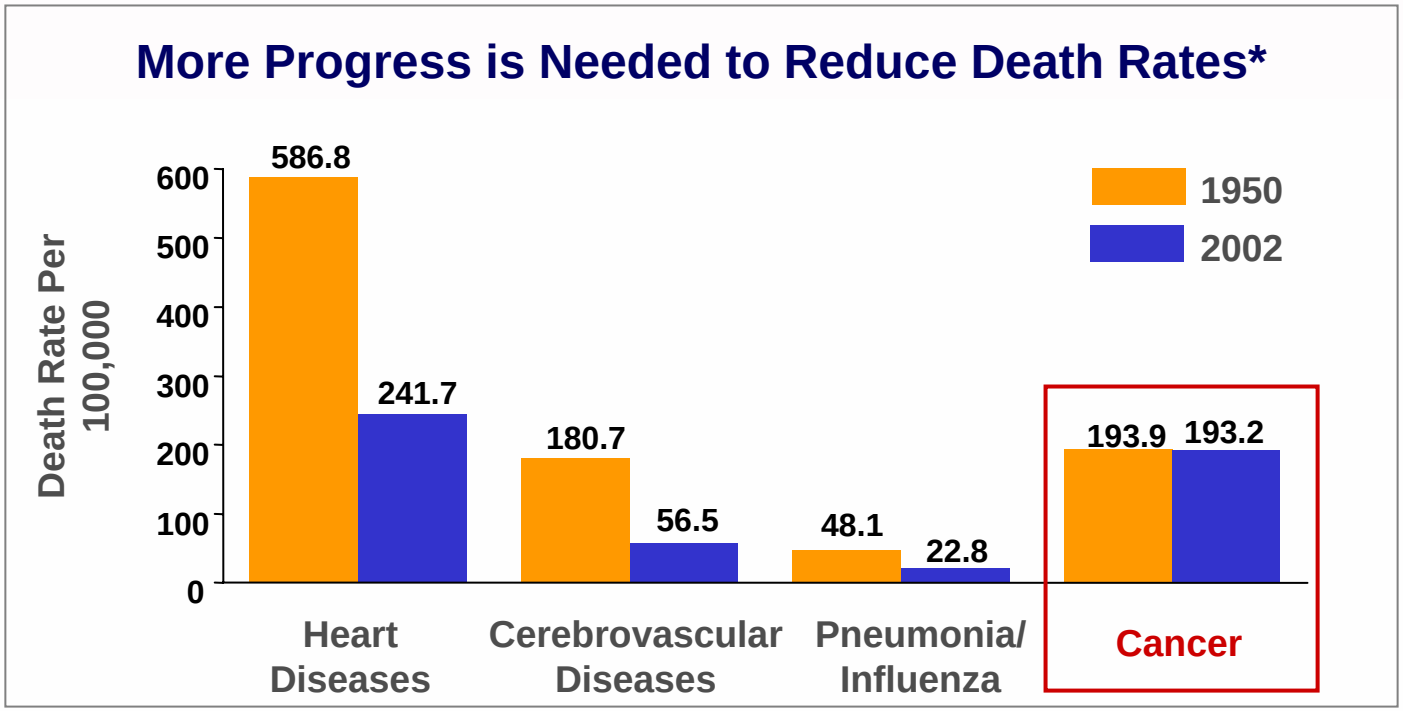
NCI wants your input to bridge the gap from
Research ➡ VC funding ➡ Product Commercialization

Why It's Important

NCI Alliance for Nanotechnology in Cancer

The human and economic burden of cancer on our society continues to grow…

- Cancer now the #1 killer
  - 570,300 Americans will die of cancer this year
  - 1,372,900 Americans this year will hear the words "you have cancer…"



* Age-adjusted to 2000 US standard population. Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised. 2002 Mortality Data–NVSR-Death Final Data 2002–Volume 53, No. 5. Cost data from American Cancer Society Cancer Facts & Figures 2005.

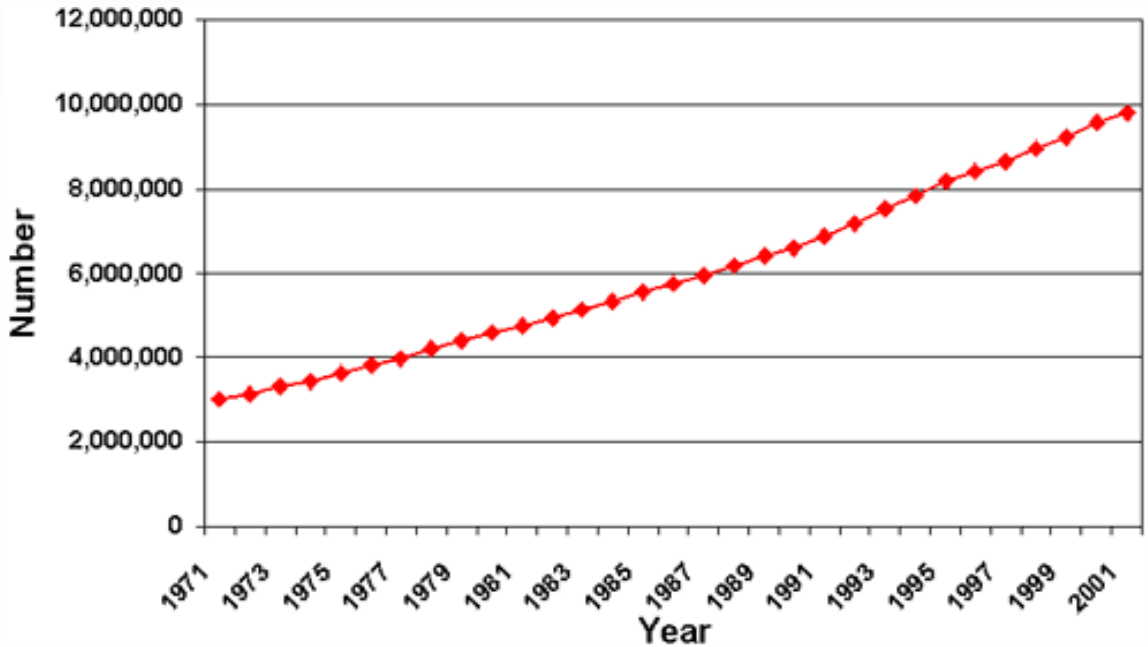
Why It's Important (cont'd)

NCI Alliance for Nanotechnology in Cancer

The human and economic burden of cancer on our society continues to grow…

- 9.6 million cancer survivors in the United States today
- Healthcare costs attributable to cancer at $189 billion/year

The number of people living with a diagnosis of cancer has increased dramatically



Data Source : November 2003 Submission: Populations from January 2001 were based on the average of the July 2000 and July 2001 population estimates from the US Bureau of Census. Complete prevalence is estimated using the completeness index method (Capocaccia et. al. 1997, Merrill et. al. 2000). US Estimated Prevalence counts were estimated by applying US populations to SEER 9 Limited Duration Prevalence proportions.

Why It's the Right Time: Technology and Product Development

NCI Alliance for Nanotechnology in Cancer

- The science is exploding
  - Major advances in genomics, proteomics, and computation and materials sciences
  - Tidal wave of data on molecular underpinnings of disease and increased understanding of cancer mechanisms
- The nano-based biomedical product candidate is expanding*
  - 61 nanotech-based drugs and delivery systems
  - 91 devices or diagnostic tests
- The private sector is getting into the game**
  - $1.7 billion invested in nanotech in 2004
  - Steady stream of IP (88,546 U.S. patents from 1976 to 2002)
  - 109 nanotech startups have secured VC funding since 1998

* Source: 2005 Nanomedicine, Device & Diagnostic Report, National Health Information, LLC.

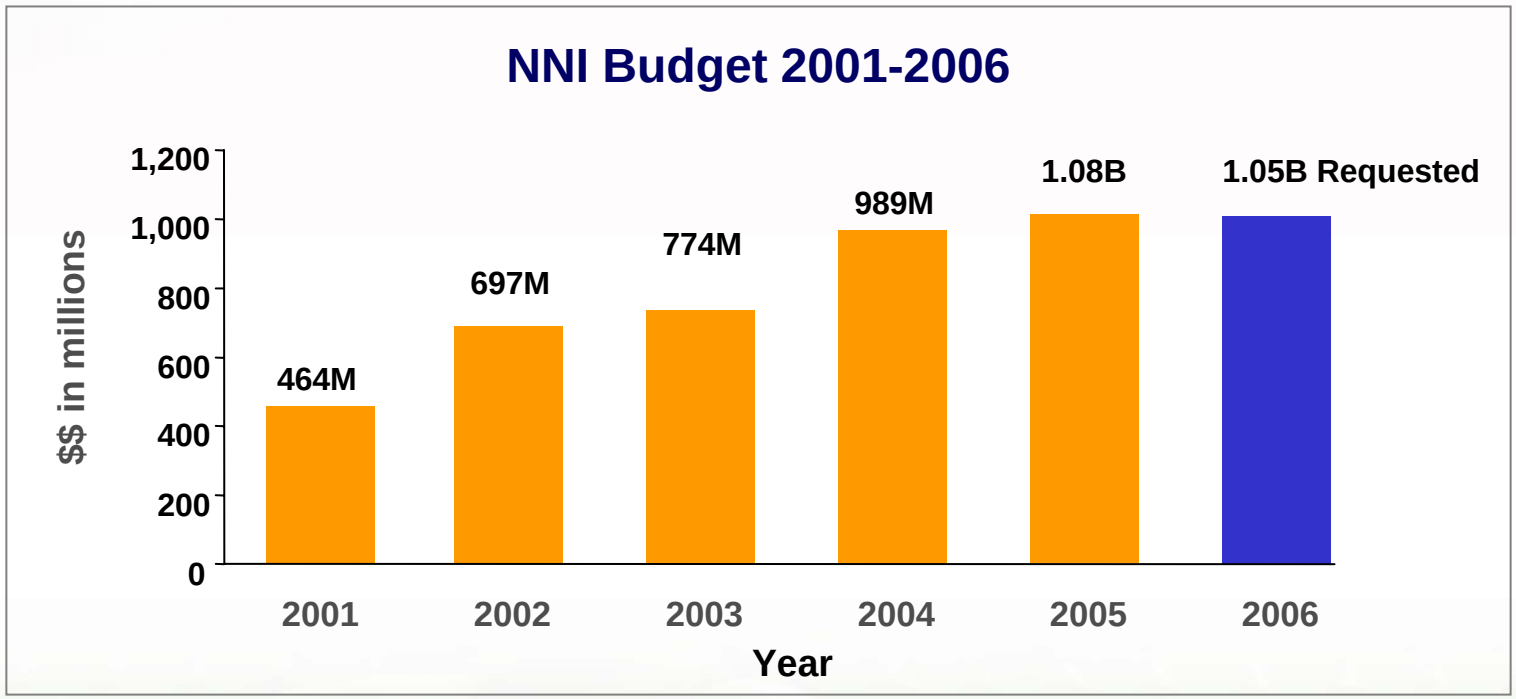
** Source: The Nanotech Report 2004, Lux Research.

Why It's the Right Time: Federal Funding

NCI Alliance for Nanotechnology in Cancer

Government investment is huge

- National Nanotechnology Initiative: 2006 request for $1.05 billion



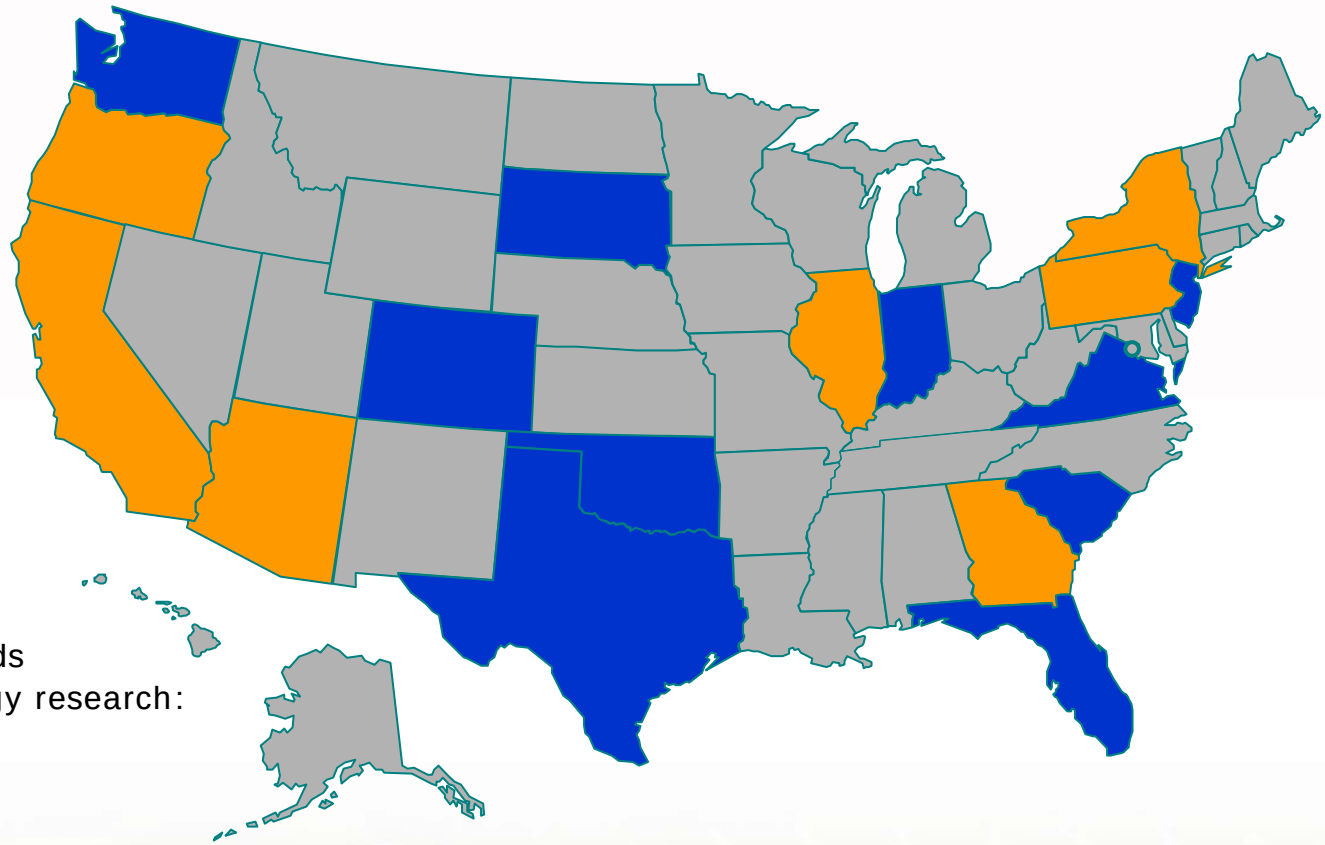
Source: National Nanotechnology Initiative (NNI).

Why It's the Right Time: State and Regional Commitment

NCI Alliance for Nanotechnology in Cancer

Up to $20 million
state, regional and matching funds committed:
CO, FL, IN, NJ, OK, SC, SD, TX, VA, WA

Over $20 million
state, regional and matching funds committed:
AZ, CA, GA, IL, NY, OR, PA



Total state and regional funds committed to nanotechnology research:

$864 million

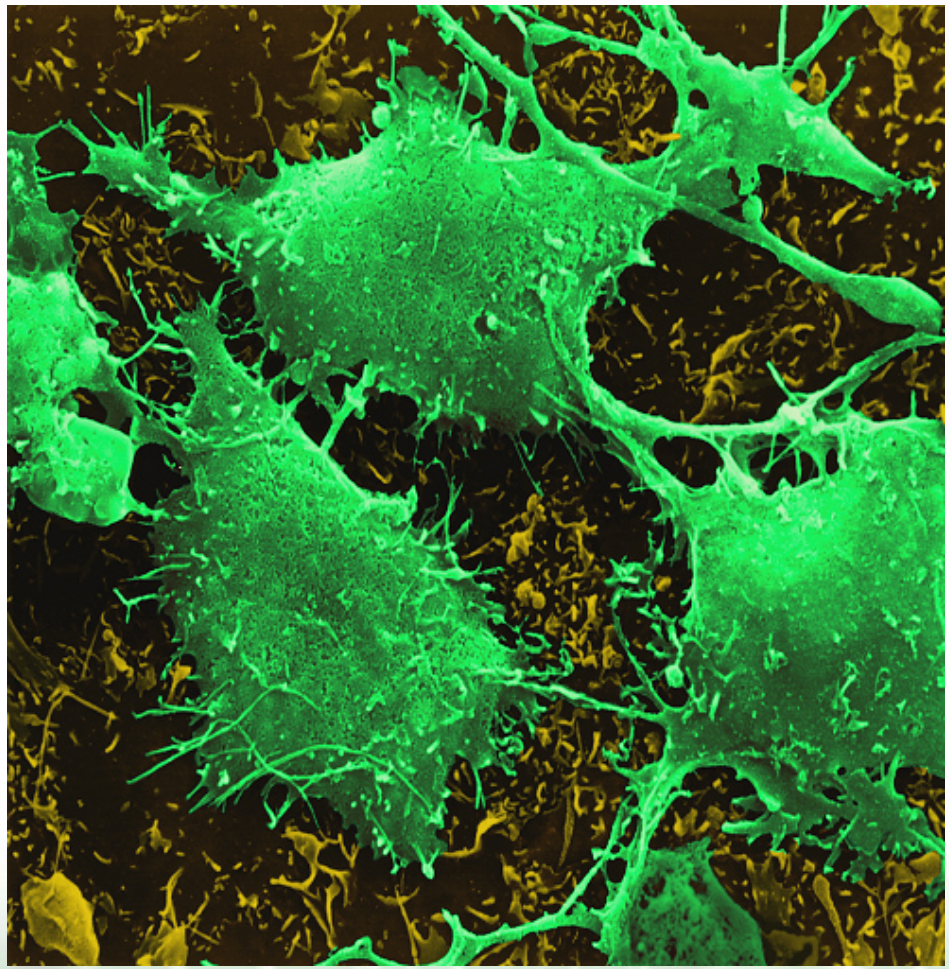
Source: *"Regional, State and Local Initiatives in Nanotechnology,"* Report of the NNI Workshop, 2003.

Scientific, Clinical and Commercial Potential of Nanotechnology in Cancer

Cancer is a "Disease Process"

NCI Alliance for Nanotechnology in Cancer

- Proliferation
- Micro-Invasion
- Immune Evasion
- Cellular Recruitment
- Dissemination
- Targeting
- Penetration
- Colonization
- De-Differentiation



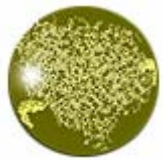
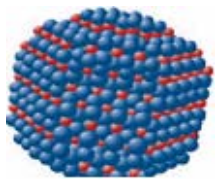
Why Nanotechnology Can Enable Fundamental Biomedical Breakthroughs

NCI Alliance for Nanotechnology in Cancer

- Novel multifunctional nanostructures may be placed in micro-sensors or pills
- Sensitivity may approach single molecule detection for cancer markers or toxic substances
- Multifunctional nanostructured drugs can target very basic intracellular processes at the subcellular level
  - Redox reaction
  - Protein folding
  - Signal transduction cascades
  - Cell death pathways

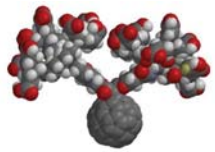
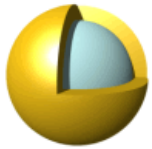
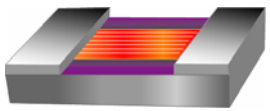
Nanotech "Toolbox" for Cancer Products

NCI Alliance for Nanotechnology in Cancer

Modality	*Potential Applications*
Cantilevers 	• High-throughput screening • Disease protein biomarker detection • DNA mutation detection (SNPs) • Gene expression detection
Carbon Nanotubes 	• DNA mutation detection • Disease protein biomarker detection
Dendrimers 	• Target sequestration • Controlled release drug delivery • Image contrast agents
Nanocrystals 	• Improved formulation for poorly soluble drugs

Nanotech "Toolbox" for Cancer Products

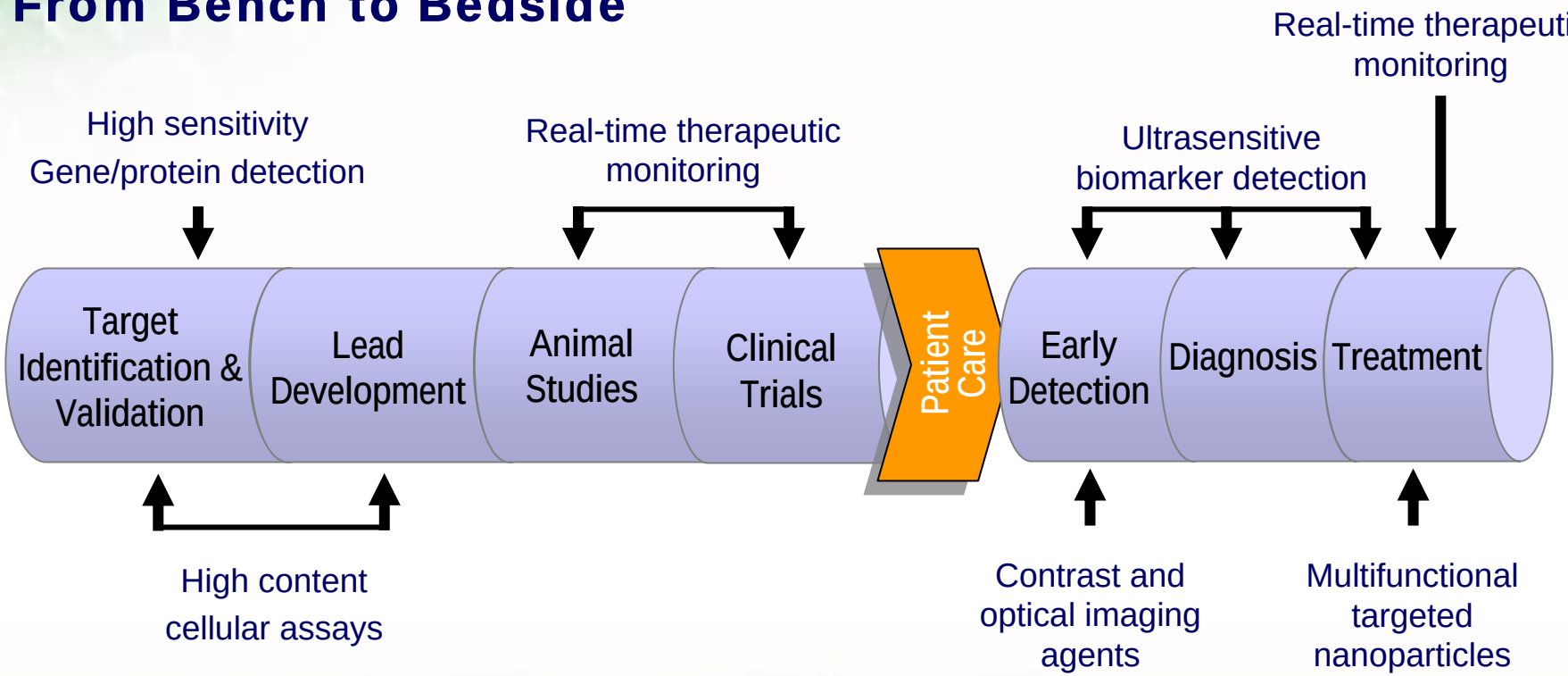
NCI Alliance for Nanotechnology in Cancer

Modality	*Potential Applications*
Nanoparticles 	• Multifunctional therapeutics • Targeted drug delivery, permeation enhancers • MRI and ultrasound image contrast agents • Reporters of apoptosis, angiogenesis, etc.
Nanoshells 	• Deep tissue tumor cell thermal ablation • Tumor-specific imaging
Nanowires 	• High-throughput screening • Disease protein biomarker detection • DNA mutation detection (SNPs) • Gene expression detection
Quantum Dots 	• Optical detection of genes and proteins in animal models and cell assays • Tumor and lymph node visualization

Nanotech Has Multiple Applications

NCI Alliance for Nanotechnology in Cancer

From Bench to Bedside

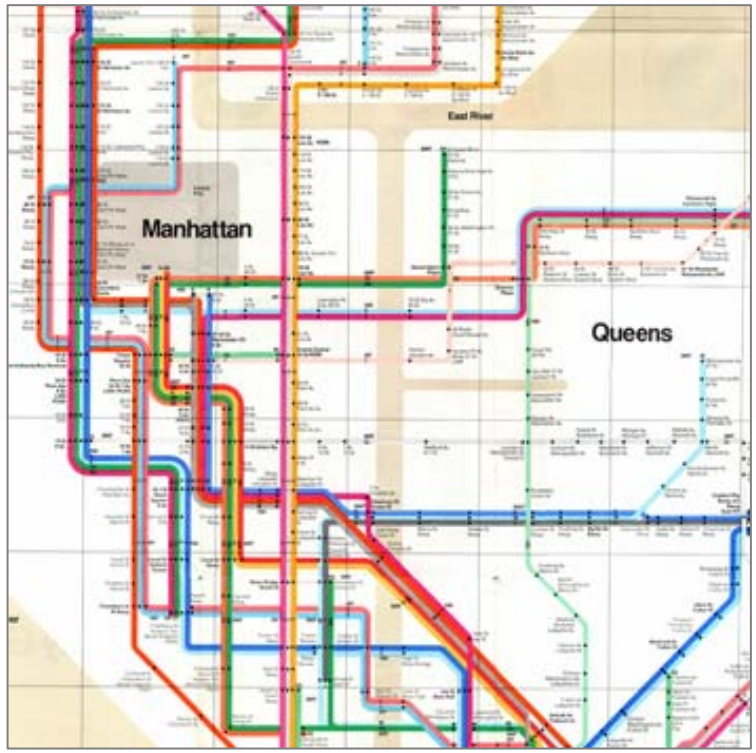


Nanotech in Drug Discovery

NCI Alliance for Nanotechnology in Cancer

- Current problems:
  - Cancer is a highly complex disease
  - Redundancy in biological systems leads to resistance to therapies that are based on a single biological target

- How nanotech helps:
  - Nanoparticles have biosensing ability to hit multiple targets
  - Nanoparticles offer multifunctional capability
  - Nanotechnology-based drugs may block collateral damage due to radiation therapy and chemotherapy



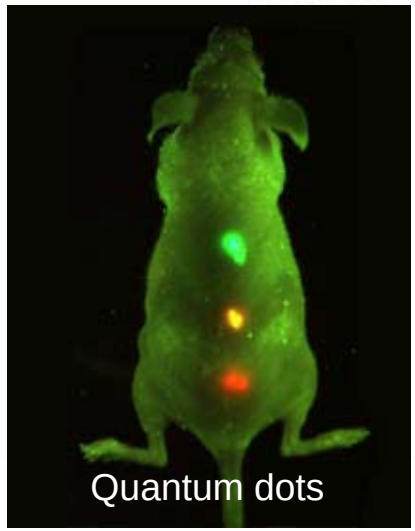
Similar to the NYC subway, a biological system has many pathways to a single target

Nanotech for *In Vivo* Detection of Cancer

NCI Alliance for Nanotechnology in Cancer

- Current problems:
  - Disease is detected too late to arrest metastasis
  - No non-invasive method to know if drug is working for months
  - Difficult to assess risk of environmental factors

- How Nanotech helps:
  - Quantum dots expand capabilities of transgenic mouse mouse models for drug discovery
  - Paramagnetic nanoparticles enable MRI imaging of cancer cells at pre-symptomatic stage
  - Nanoshells enable real-time assessment of drug action
  - Nano reporting systems enable mutagen detection



Quantum dots

Source: JAMA, Vol. 292, No.16, p.1944-1945, 2004.

Nanotech in Targeted Therapies

NCI Alliance for Nanotechnology in Cancer

- Current Problems:
  - Toxic agents kill healthy as well as diseased cells
  - Difficult for therapeutic to reach deep inside tumor
  - Difficult to sustain therapeutic levels of drug
  - Tumor cells develop multi-drug resistance

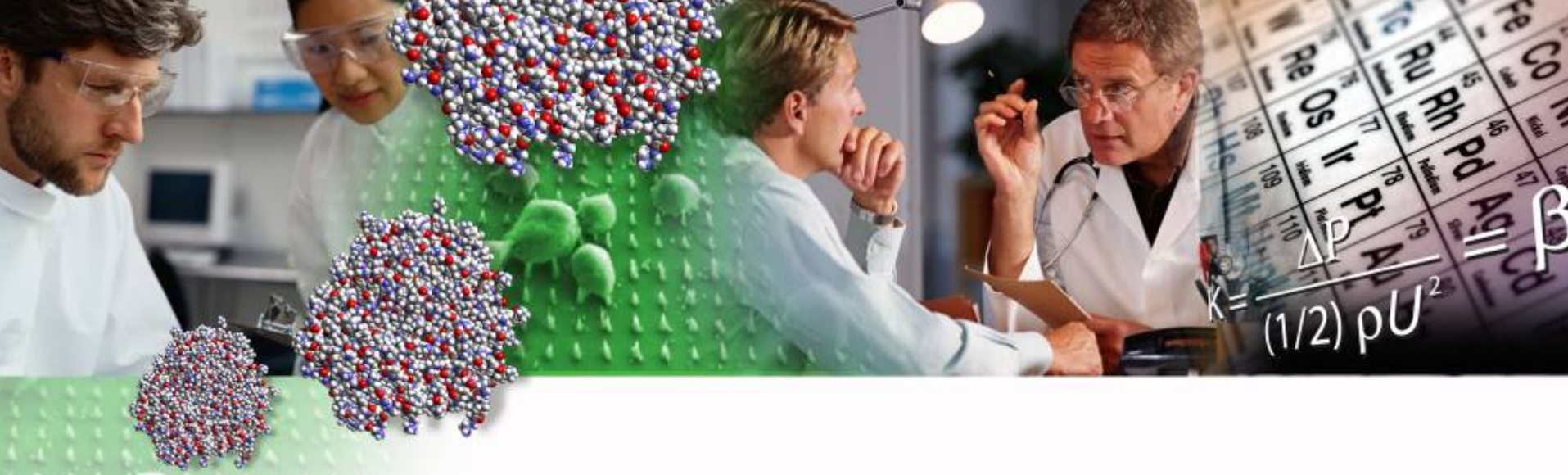
- How Nanotech helps:
  - Dendrimers, nanocrystals, nanotubes and nanoshells offer ability for more controlled delivery and sustained therapy for chronic treatments
  - Multifunctional nanoparticles can combine targeting agents with therapeutic payload and/or reporter of efficacy
  - Targeted multifunctional nanoparticles may be assembled *in vivo* from drug-like subunits
  - Radio frequency-triggered nanoparticles can enable localized “heat-killing” or “light-killing”

Nanotech in the Clinical Setting

NCI Alliance for Nanotechnology in Cancer

- Practical Problems in Current Oncology Practice:
  - Diagnostic and therapeutic procedures are conducted and provided in separate steps and facilities
  - Patient's genotypic data unavailable and/or unconnected to his/her clinical data
  - Diagnosis can take days
  - No pre-knowledge of which drug will be optimum for each patient leads to long periods of unnecessary side effects
  - Need to identify right patients for right drugs (i.e., Gleevec® , Herceptin®)

- How Nanotech helps:
  - "Lab on a chip" potentially deployable at point of service
  - Multifunctional nanoparticles enable "real time" assessment of drugs, permitting optimization for each patient



National Cancer Institute as Catalyst

NCI Investment to Date Has Brought Multiple Returns

NCI Alliance for Nanotechnology in Cancer

- NCI investment over the last 6 years (1998-2004):
  - $50M in Unconventional Innovations Program (UIP) alone
  - FY04 portfolio of development and applications ~ $42M
- Results:
  - 3 nanoparticle-based products being staged for clinical trials
  - Nanotech Platforms developed: biosensors, nanoparticles
- "Leveraging" Effect*
  - Research support in cancer centers reaches $1.5B annually, more than 10 times the amount of actual support from the NCI awards

*Source: "Advancing Translational Cancer Research: A Vision of the Cancer Center and SPORE Programs of the Future," Report of the P30/P50 Ad Hoc Working Group, February 2003.

NCI-Funded Cancer Nanotech Research to Date

NCI Alliance for Nanotechnology in Cancer

- NCI Cancer Centers (62)

NCI Has Launched the Next Phase of Its Commitment

NCI Alliance for Nanotechnology in Cancer

NCI Alliance for Nanotechnology in Cancer

- $144.3M initiative
- Designed to “ignite” nano-product development and commercialization
- Encompasses public and private sectors
- Launched September 2004

Alliance Strategies

NCI Alliance for Nanotechnology in Cancer

Major Programs of the Alliance:

1. **Centers of Cancer Nanotechnology Excellence**
2. **Multidisciplinary Research Teams**
   - Training
   - Interagency Collaborations
3. **Nanotechnology Platforms for Cancer Research**
4. **Nanotechnology Characterization Laboratory**

There Are Barriers to Rapid Commercialization

NCI Alliance for Nanotechnology in Cancer

- Culture clash
  - Life sciences and materials sciences typically unconnected
  - Device and biopharmaceutical developers work in different "worlds"
- Business models
  - Classic pharmaceutical, biotech or diagnostic models may need to be modified
- Lack of widespread expertise in nanotechnology
  - Increases risk of large capital investments
- Public Acceptance
  - Disruptive technologies can provoke fear and resistance

How the Alliance Overcomes Barriers

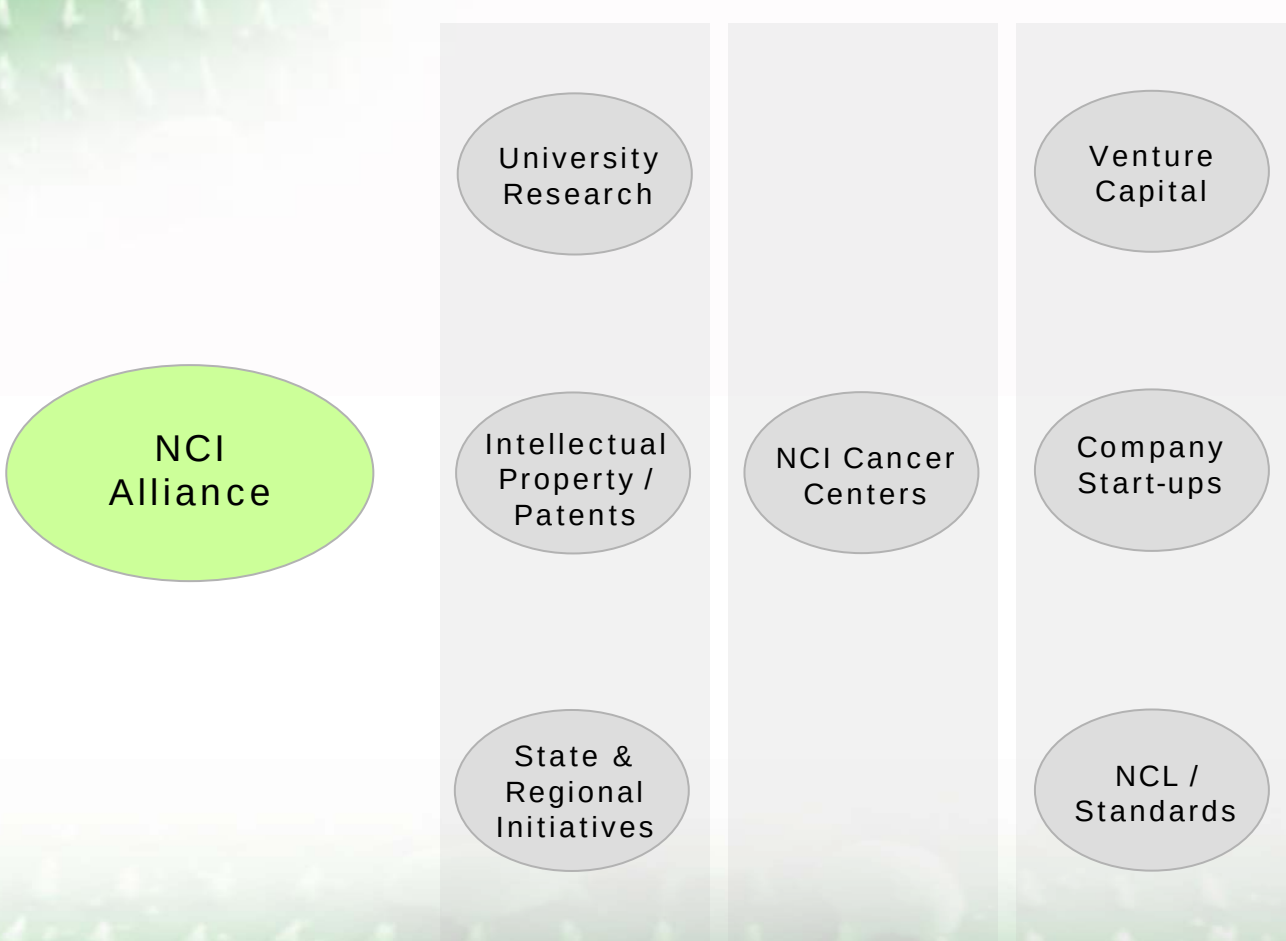
NCI Alliance for Nanotechnology in Cancer

- Requires academic and commercial partnerships for each supported Alliance project
- Establishes training programs
- Commits major funding that leverages existing infrastructure
- 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

The Opportunities

NCI Alliance Serves as a Catalyst

NCI Alliance for Nanotechnology in Cancer



NCI Alliance Serves as a Catalyst

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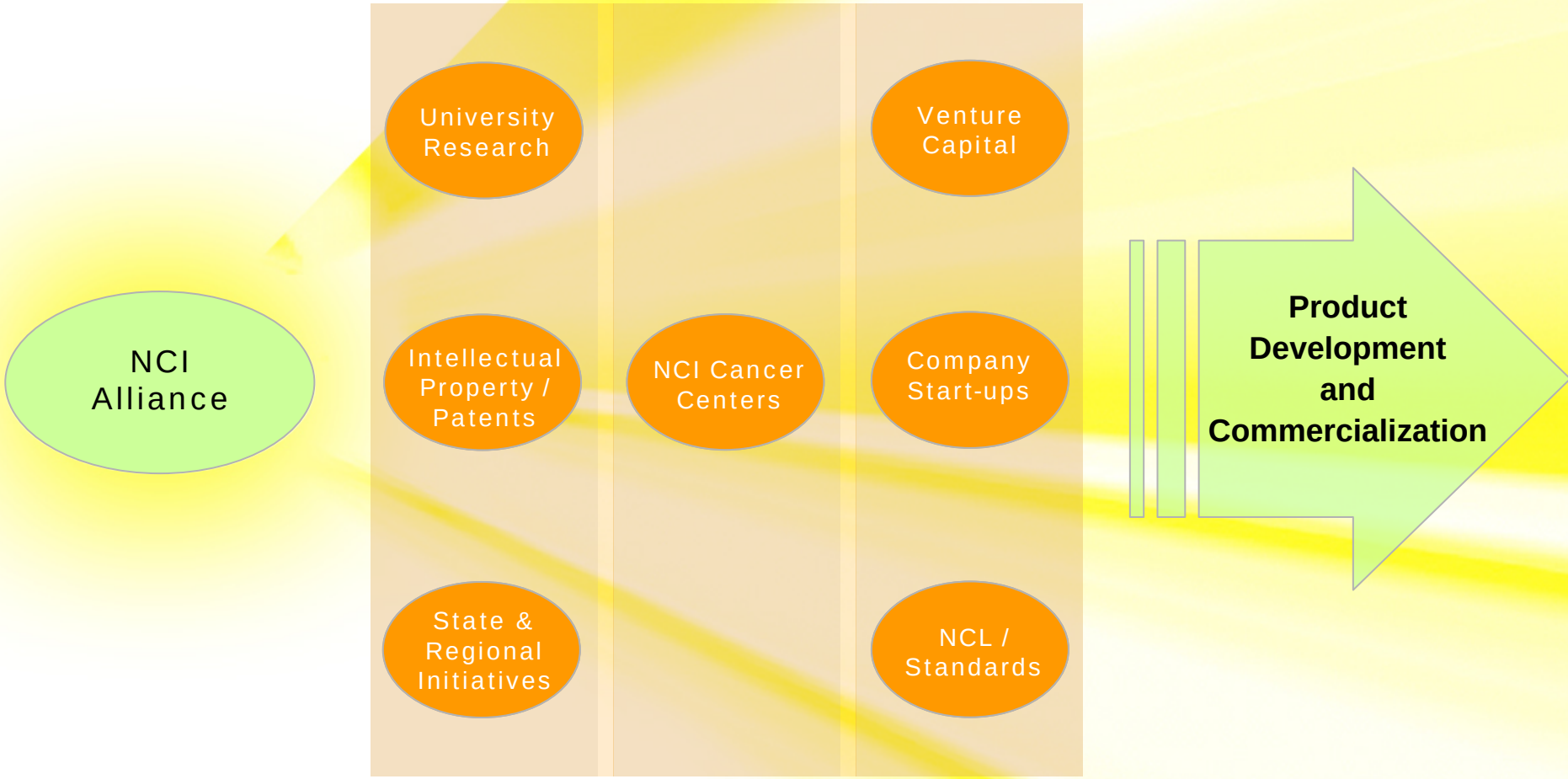
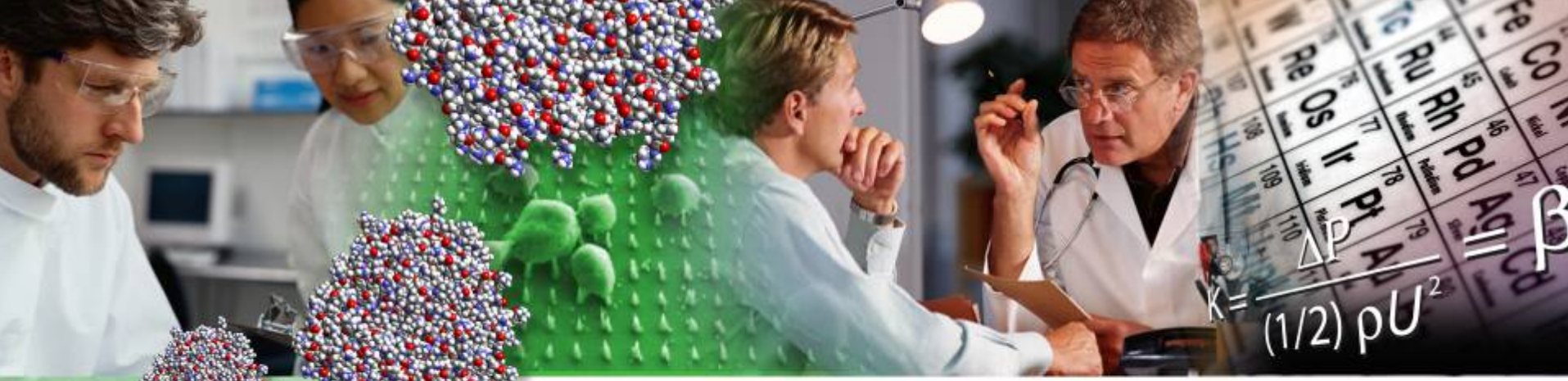


The Call to Action!

NCI Alliance for Nanotechnology in Cancer

- Leverage private investment:
  - In broad-based nanotech platforms
  - In nano-bio start-ups
- Enter into academic/government/commercial collaborations
- Think outside the box (and outside the healthcare industry) for new business models
- Development of research infrastructure:
  - common research resources,
  - bioinformatics grid computing,
  - public data sets, and
  - enhanced capabilities to develop products, test them, and bring them to the clinic



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