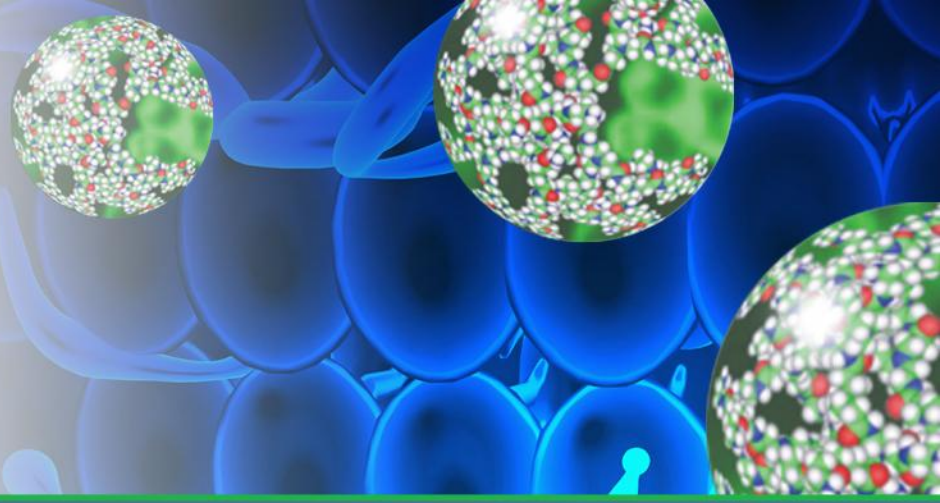
National Cancer Institute

NCI Alliance for Nanotechnology in Cancer



Cancer Nanotechnology – Opportunities and Challenges – View from the NCI Alliance for Nanotechnology in Cancer

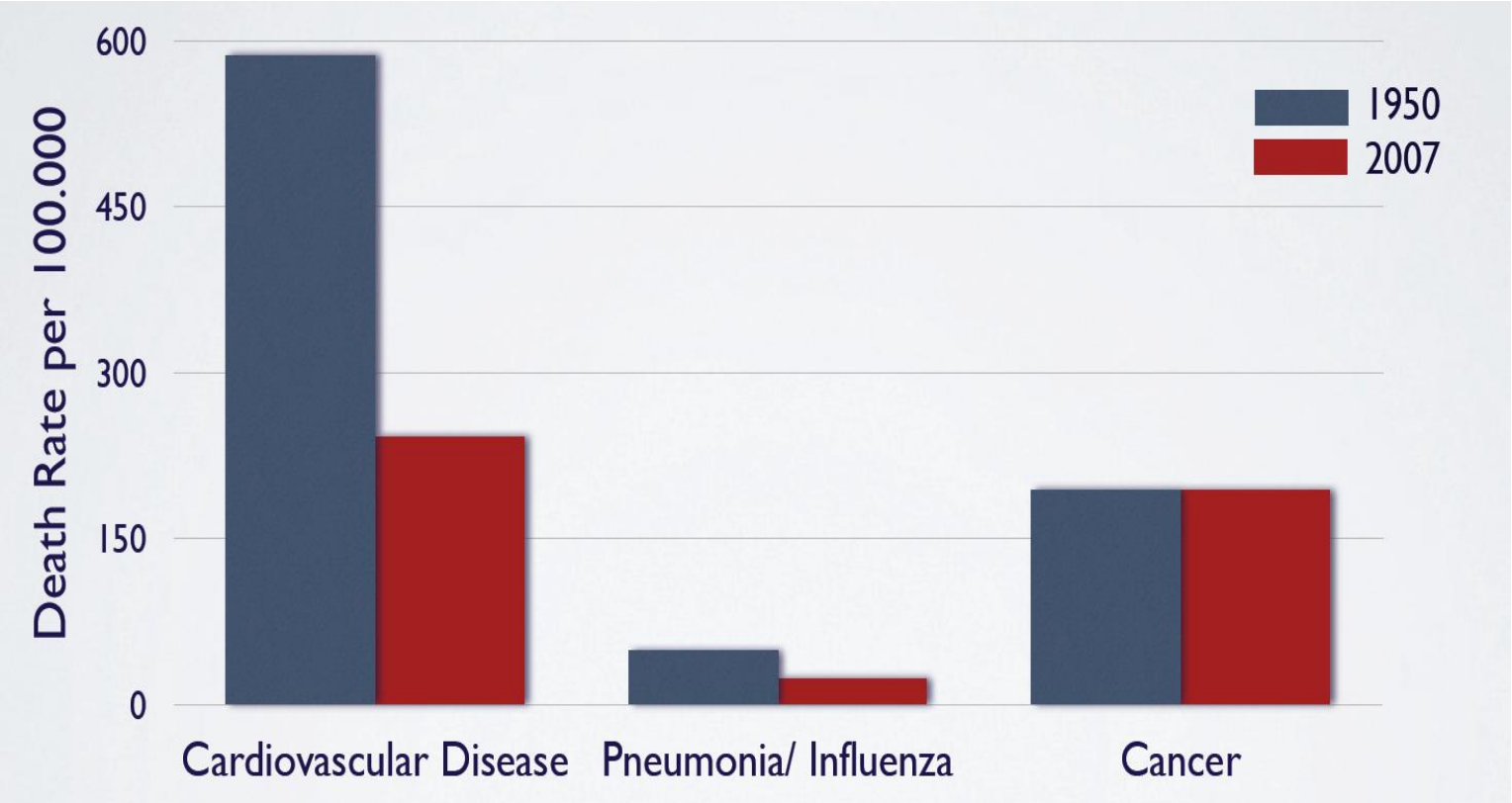
Nanobusiness Alliance Meeting
September 26, Boston, MA

Piotr Grodzinski, Ph.D.
Office of Cancer Nanotechnology Research, NCI

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

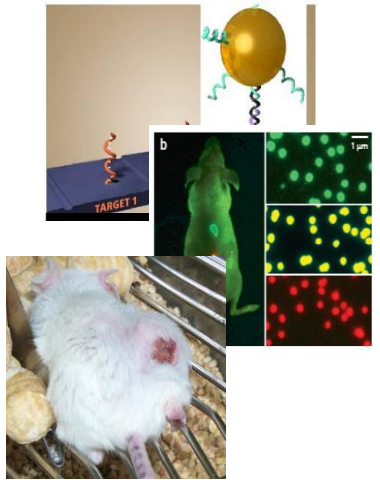
Burden of Cancer

- 556,900 American will die of cancer this year
- 1,372,900 Americans will be diagnosed with cancer this year

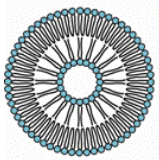


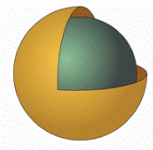
Cancer Nanotechnology: The Opportunity

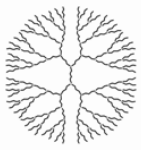
- Combine power of innovation in nano-materials and cancer biology to develop new solutions in cancer
- Detect Disease *Before* Health Has Deteriorated
  - Sensors
  - Imaging
- Deliver Therapeutics
  - Local delivery
  - Improved efficacy
  - Post-therapy monitoring

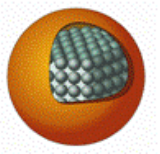


- Develop Research Tools to Enhance Understanding of the Disease

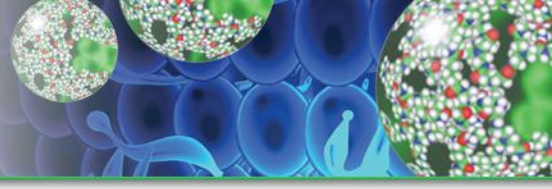

Liposome


Gold nanoshell


Dendrimer


Quantum Dot

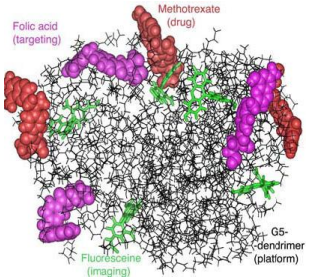
Early Diagnosis and Post-therapy Monitoring



- In-vitro assays
  - High sensitivity
  - Development of modular diagnostics based on bodily fluids, such as blood, serum, cerebrospinal, urine, stools, or saliva
  - Techniques to monitor and capture circulating tumor cells from blood
  - Multiplexing – capability to monitor several signatures at the same time
  - Multifunctional capabilities – one platform capable of detecting nucleic acids and proteins
- Imaging
  - Improved spatial and temporal resolution
  - Capability to probe tumor microenvironment – information on tumor mass and its biochemical signatures
  - Theranostic constructs allow for tumor recognition and subsequent treatment – image-guided therapy
  - Intra-operative techniques to monitor margins of surgically removed tissue in real-time

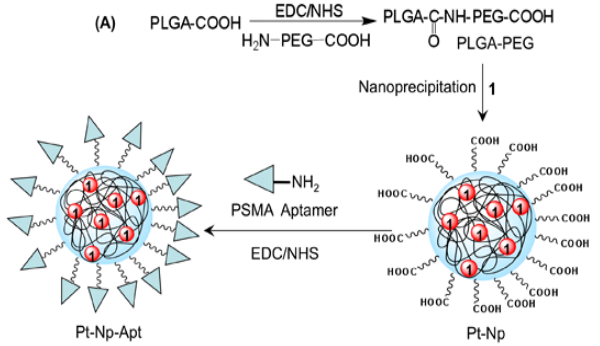
Nano-therapy Strategies

Delivery of chemotherapeutics



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

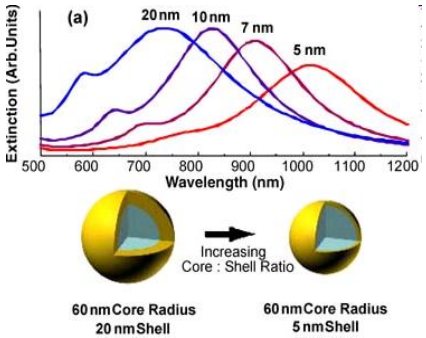
Pro-drug Strategies



Dhar, Langer et al. PNAS (2008) 105: 17356

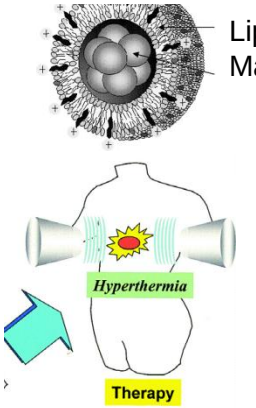
Hyperthermia

Photothermal



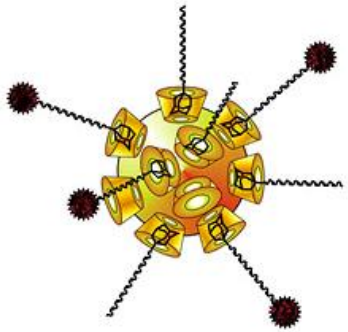
N. Halas, J. West et al, Ann Biomed Eng. (2006) 34: 15

RF heated



A. Ito et al., J. of Bioscience and Bioeng. (2005 100: 1)

Genetic therapy



M. Davis et al. Nature (2010) 464: 1067

NCI Alliance for Nanotechnology in Cancer (ANC) - Program Objectives

The ANC program was designed to develop research capabilities for multi-disciplinary team research, with the goal of advancing prevention, diagnostic and/or treatment efforts.

research discovery

pre-clinical

clinical

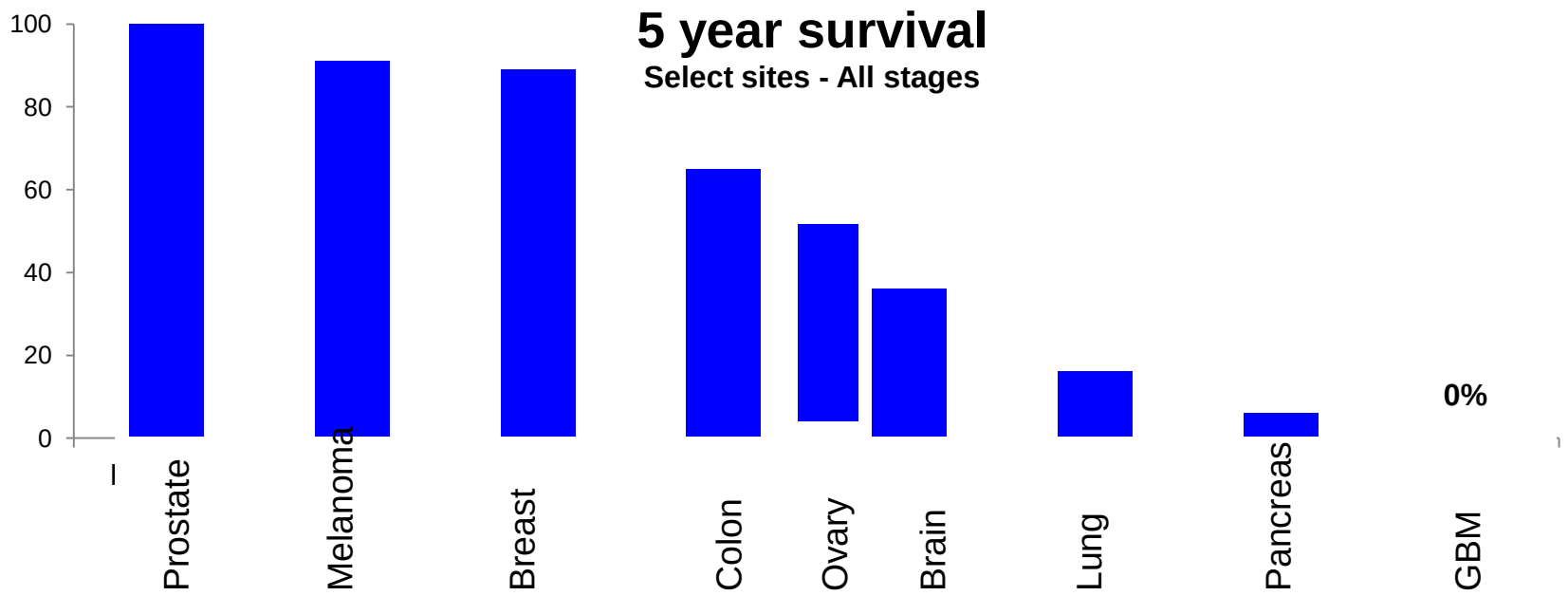
Challenge areas:

- Early diagnosis using in vitro assays and devices or in vivo imaging techniques
- Multifunctional nano-therapeutics and post-therapy monitoring tools
- Devices and techniques for cancer prevention and control

The ANC's development model calls for the most promising strategies discovered and developed by ANC grantees to be handed off to for-profit partners for effective clinical translation and commercial development.

Focus on cancers with low survival rates such as brain, lung, pancreas, and ovarian cancer

5 year Survival for Different Cancers
Rationale Behind Tumor Type Selection



CA Cancer J Clin. 2010 Sep-Oct;60(5):277-300

Focus program on cancers with low survival rates such as brain, lung, pancreas, and ovarian cancer. These were also first four cancers sequenced by TCGA.


GORDON RESEARCH CONFERENCES
Colby College
CANCER NANOTECHNOLOGY
From Basic Concepts to Clinical Applications
Chair: Piotr Grodzinski
July 17-22, 2011

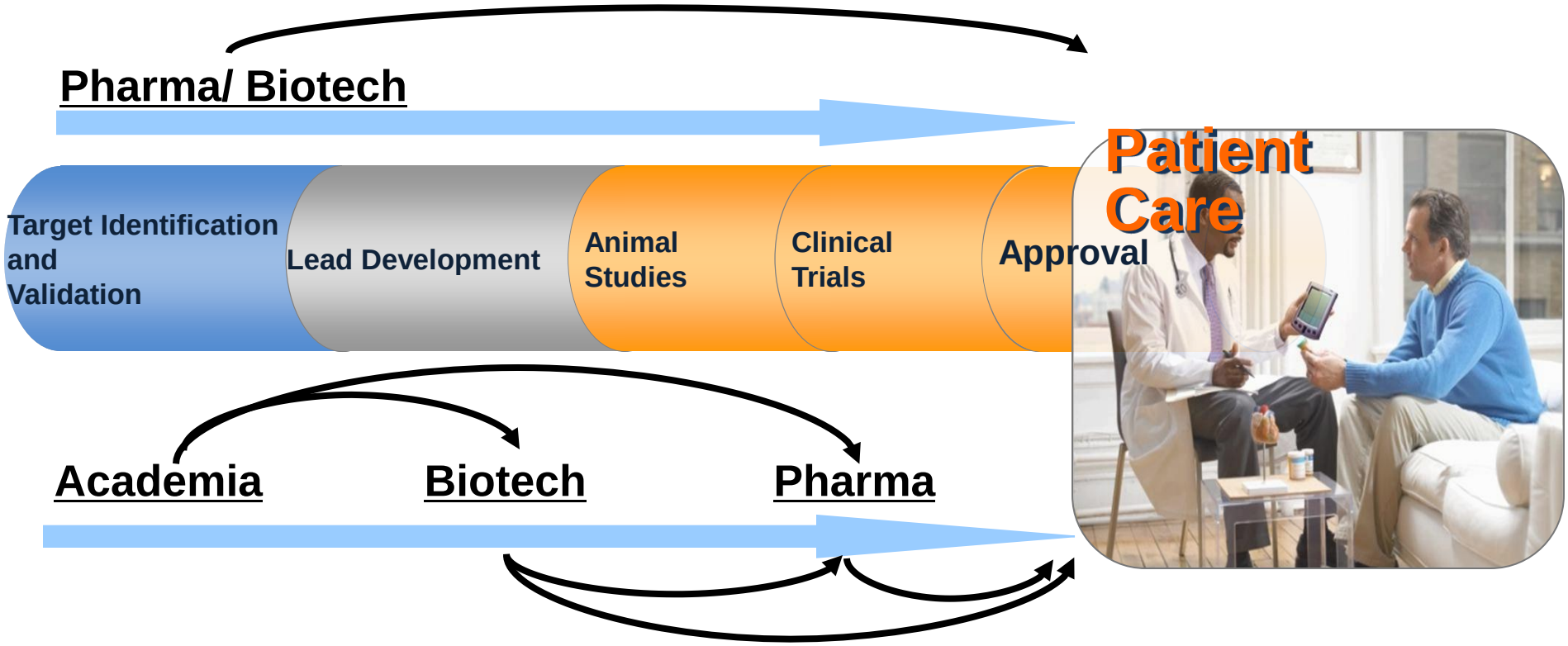
Translating to the Clinic

- Value proposition of nanotechnology in cancer – why would oncologist care?
  - defining compelling applications
- Building research community
- Discovery research OK, but we want to benefit the patient - translate

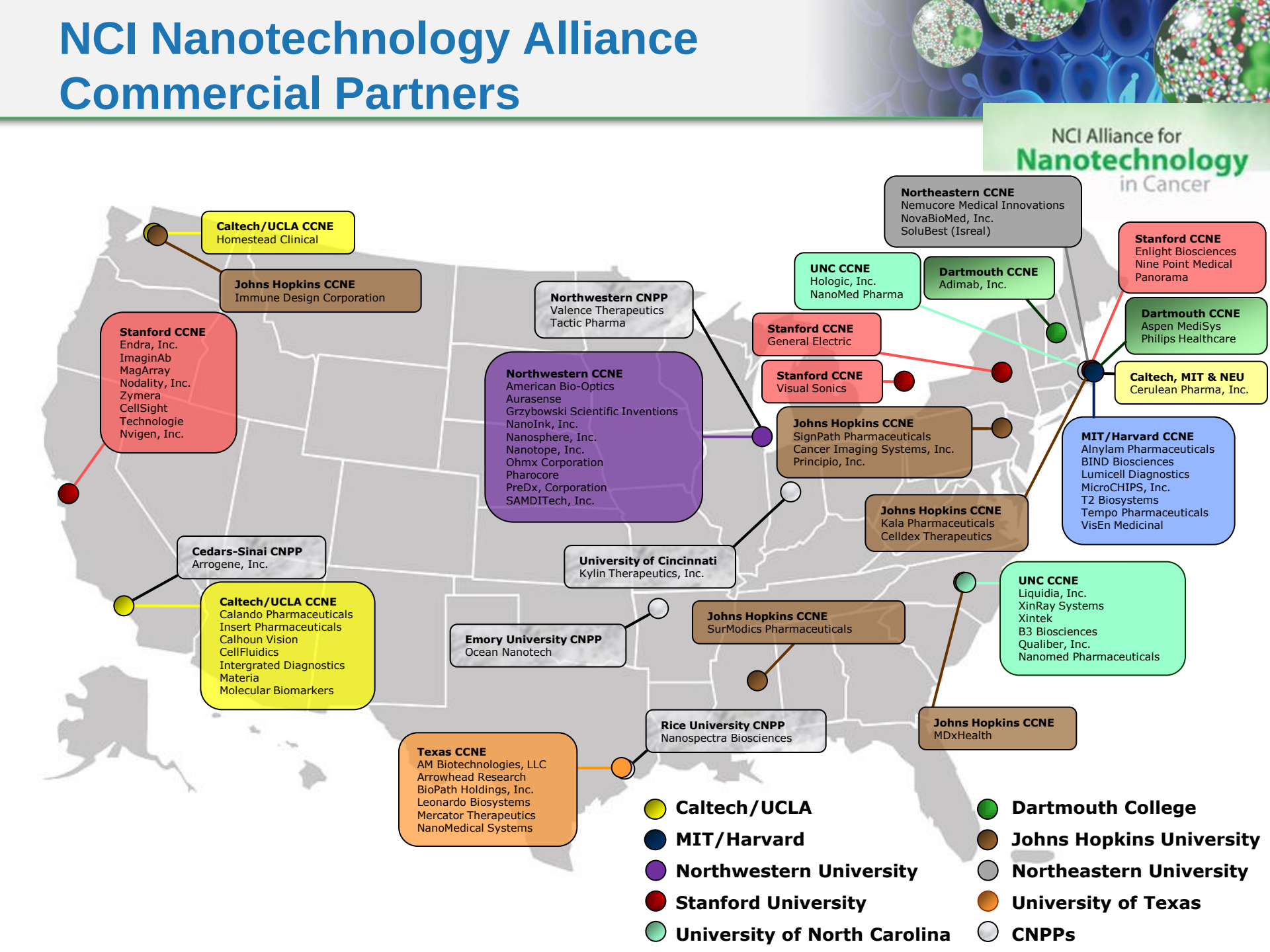
- Translation is hard and expensive
  - it costs ~$2M to scale-up and stabilize materials manufacturing to be ready for IND application
  - limited capital available before reaching clinical trial stage – infamous 'valley-of-death' for start-up companies
  - re-defining roles of academia, industry, and government in the continuum of funding and performing technology development
  - engaging larger pharmaceutical and biotech companies

Current Industry Trends in R&D Development and Commercialization

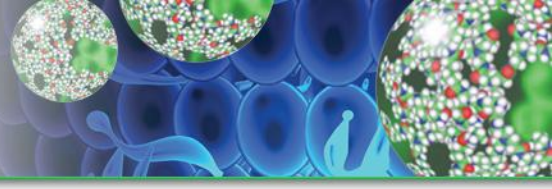
Outsourcing, In- and out-licensing
Mergers & Acquisitions



NCI Nanotechnology Alliance Commercial Partners



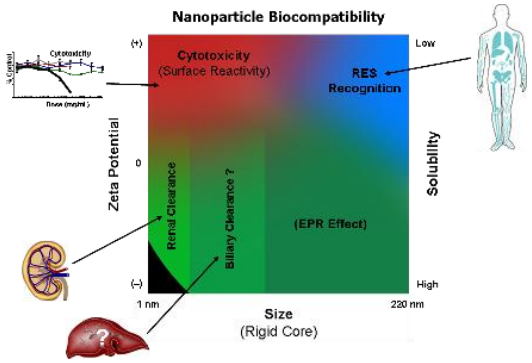
Nanotherapeutics Approved for Oncological Applications



- **Abraxane®** (albumin-bound paclitaxel, Abraxis BioSciences). FDA approval in 2005 for metastatic breast cancer
- Liposomal:
  - **Doxil®** (liposomal-PEG doxorubicin; Ortho Biotech/ Schering-Plough). FDA approval in 1995 for HIV-related Kaposi's sarcoma, metastatic breast cancer, metastatic ovarian cancer
  - **DaunoXome®** (liposomal daunorubicin; Gilead Sciences/ Diatos). FDA approval in 1996 for HIV-related Kaposi's sarcoma
  - **Myocet®** (liposomal doxorubicin; Zeneus). FDA approval is pending for metastatic breast cancer
- Polymeric:
  - **Genexol-PM®** (Methoxy-PEG-poly(D,L-lactide) taxol; Samyang, Korea). Approved in S. Korea for metastatic breast cancer. Phase II for pancreatic cancer in the US
  - **Oncaspar®** (PEG–L-asparaginase; Enzon). FDA approval in 2006 for Acute Lymphoblastic Leukemia

Several companies are close to filing IND applications with FDA for nanotechnology products

Nanotechnology Characterization Laboratory: Serving the Community



Near capacity, Identifying trends, more mature concepts

’09-’11

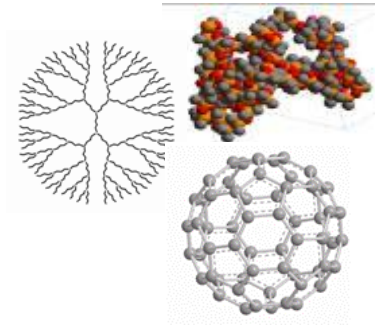
ANNEX 2
NATIONAL CANCER INSTITUTE
NANOTECHNOLOGY CHARACTERIZATION LABORATORY
MATERIAL TRANSFER AGREEMENT
The National Cancer Institute (NCI) Nanotechnology Characterization Laboratory (NCL) has been designed to investigate the use of nanoparticulate material for the advancement of cancer research. This Material Transfer Agreement (MTA) permits the exchange of materials and associated information between NCI and the party defined below as "Provider."

Characterization, SAR studies, support of early development

’07-’08

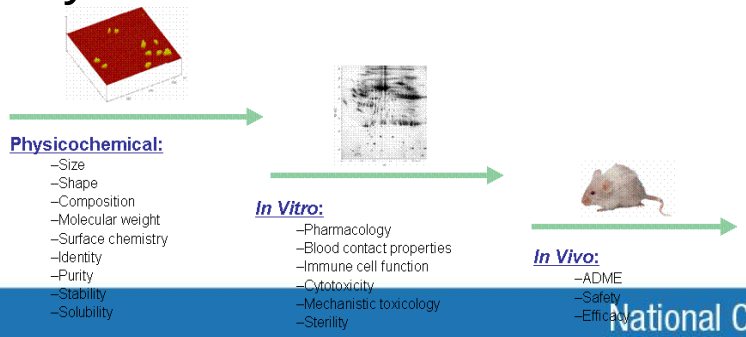
Receipt of materials

’06



Development of assay cascade

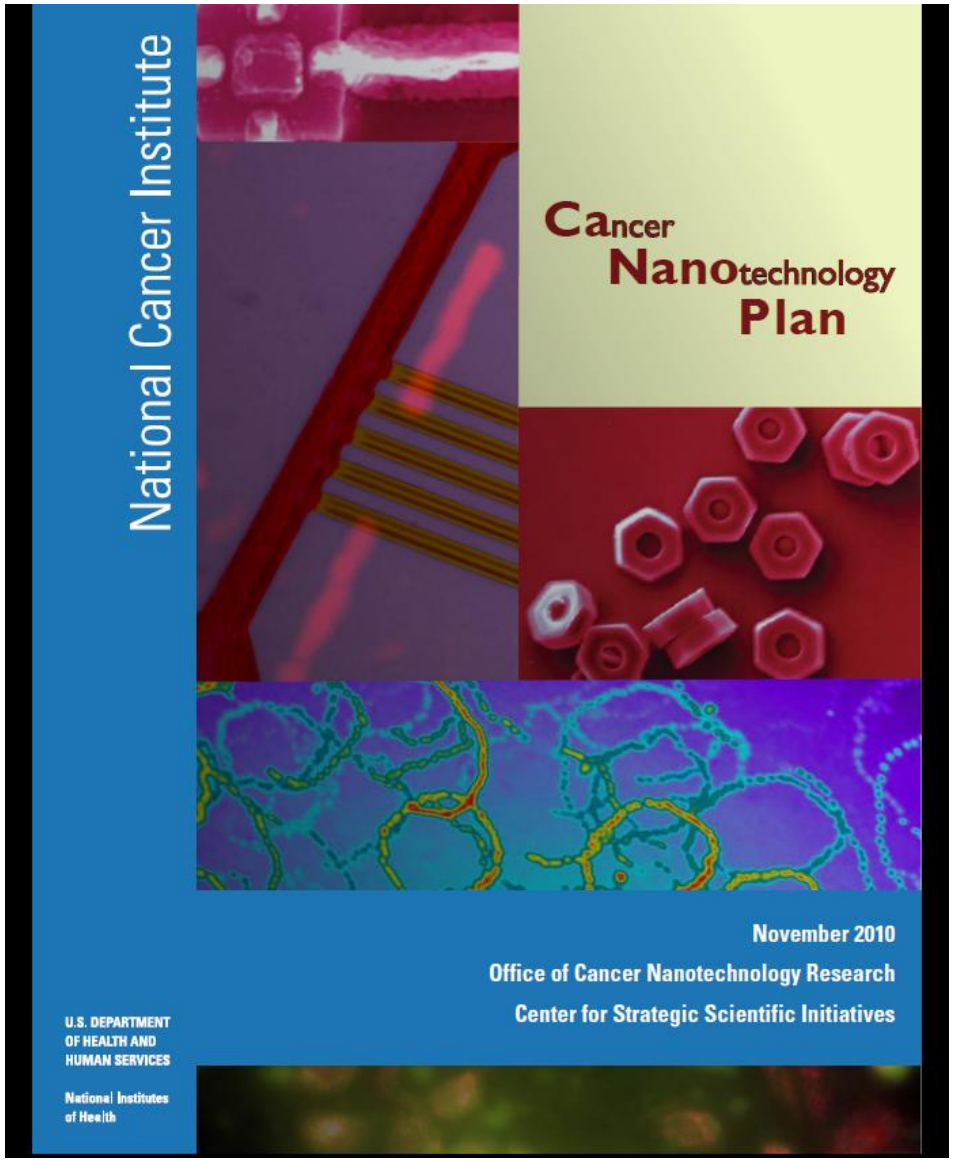
’05



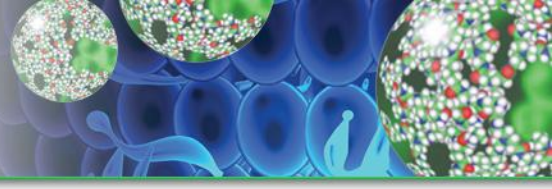
Initiation and planning

’04

Forward Strategies



High Impact Cancer Nanotechnology Goals

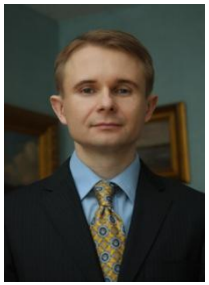


- Early diagnosis of cancer in pre-metastatic stage:
  - point-of-care nano-devices for broad medical applications including cancer using unprocessed bodily fluids, with multiplex capabilities and rapid analysis;
  - diagnostic and post-therapy monitoring nano-devices for interrogation of circulating tumor cells;
- Successful delivery of therapies based on siRNA and other difficult to deliver molecules;
- Novel nanoparticle-based chemotherapeutic formulations with lower toxicity and higher efficacy;
- Theranostic constructs for diagnosis and subsequent localized therapy;
- Effective diagnosis and delivery of therapies to brain, ovary, and pancreas.

Office of Cancer Nanotechnology Research

Dorothy Farrell

Nicholas Panaro



Krzysztof Ptak

Sara Hook

Sandra Chapman

George Hinkal

Consultants:
Subhas Malghan – FDA
Uma Prabhakar – formerly J&J