# Nanoscience and Nanotechnology Research for Biology and Medicine



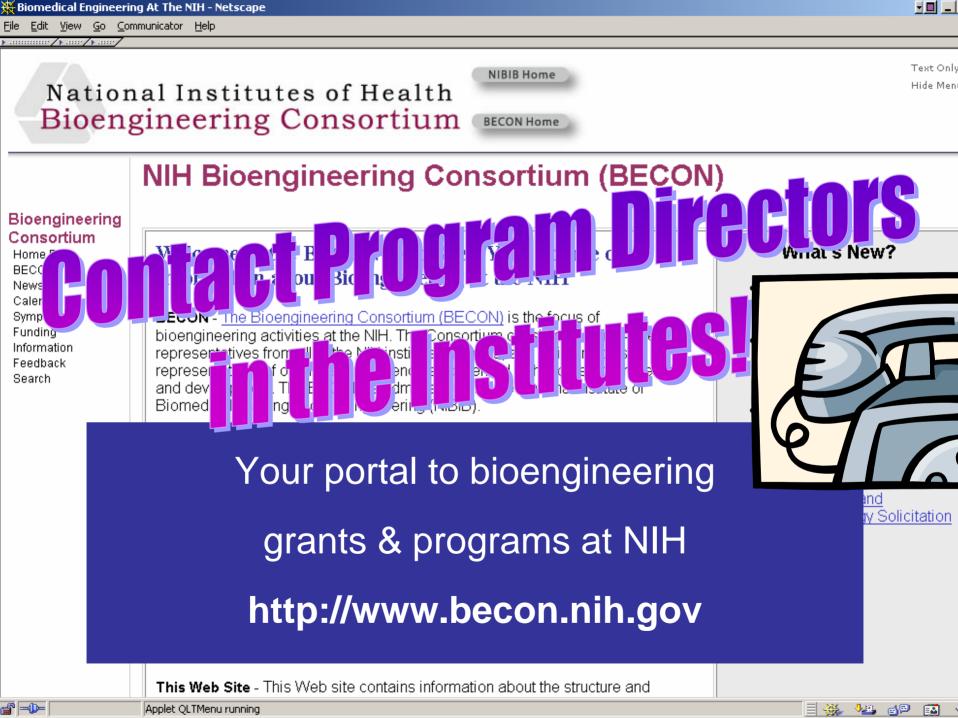




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BRP Grantee Meeting Bethesda, 15-16 August 2005









NIH supports nanoscience and nanotechnology research in the context of many programs.

While in some of those programs/projects, the focus may be on the nano-research *per se*, in other cases the nano-research may be a component of a larger project with broader goals.

Several examples are provided here, to demonstrate support for the breadth of potential applications of nanotechnology for understanding, diagnosing and treating disease.





### Program announcements issued through BECON:

- Nanoscience and Nanotechnology in Biology and Medicine
- Bioengineering Nanotechnology Initiative (SBIR)
- Exploratory/Developmental Bioengineering Research Grants
- Bioengineering Research Grants
- Bioengineering Research Partnerships
- Mentored Quantitative Research Career Development (K25)
- Awards under these programs are listed on the BECON web site: www.becon.nih.gov/nano.htm





# Nanoscience and Nanotechnology in Biology & Medicine

- i) create & use structures, devices & systems that have novel properties and functions because of their small size, to achieve a fundamental understanding of biological processes or for disease detection, therapy, or prevention; ii) conceive, fabricate and test devices to detect and analyze nanoscale entities of relevance to biomedicine; iii) study biological systems at the nanoscale to develop nanotechnologies and nanostructured materials for use in biomedicine.
- Encourages team approach to nanotechnology research.
- R01 (research project).
- R21 (exploratory/developmental) if little preliminary data and potential for groundbreaking impact. R21s are for up to 3 years, up to \$125,000 per year direct cost.
- Review panel dedicated to this program announcement.
- Application Receipt: February 18 & August 18, through 2006
- http://grants.nih.gov/grants/guide/pa-files/PAR-03-045





# Nanoscience and Nanotechnology in Biology & Medicine

- 20 awards in FY 2004 10 R21, 10 R01
  - 8 NIBIB
  - 4 NIGMS
  - 4 NHGRI
  - 2 NCI
  - 1 NIA
  - 1 NIDCR
- \$4.8 million





### Bioengineering Nanotechnology Initiative (SBIR)

- Nanotechnology is emerging as a field critical for enabling essential breakthroughs that may have tremendous potential for affecting biomedicine.
- Encourages team approach to nanotechnology research
- Phase I may request up to 2 years, \$200,000 per year
- Phase II may request up to 3 years, \$400,000 per year
- Applications Receipt per SBIR:
   April 1, August 1 and December 1
- Competes with other SBIR applications
- http://grants.nih.gov/grants/guide/pa-files/PA-02-125



# BIOENGINEERING RESEARCH SUPPORT



# Bioengineering Research Partnerships

- For basic and applied research by a multi-disciplinary team applying an integrative, systems approach to develop knowledge and/or methods to prevent, detect, diagnose, or treat disease or to understand health and behavior.
- Partnership must include bioengineering expertise and basic biology and/or clinical expertise.
- Identify lead investigators in Abstract
- Maximum request = \$2M per year for five years
- Need approval >6 wks before submission if request >\$500,000 direct cost

  Reviewed in Special Emphasis Panels
- Research Project (R01) mechanism
- Application receipt: January 21, August 20 (2004 through 2006)
- http://grants.nih.gov/grants/guide/pa-files/PAR-04-023.html



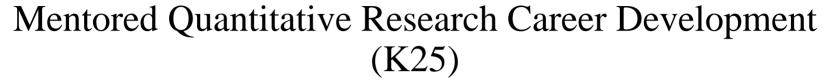
# BIOENGINEERING RESEARCH SUPPORT



# Bioengineering Research Grants

- For basic and applied multi-disciplinary research that addresses important biological or medical research problems.
- Hypothesis-driven, discovery-driven, developmental, or design-directed research.
- Multi-disciplinary research performed in a single laboratory or by a small number of investigators that applies an integrative, systems approach to develop knowledge and/or methods to prevent, detect, diagnose, or treat disease or to understand health and behavior.
- Research Project (R01) mechanism
- Applications Receipt: February 1, June 1, and October 1
- http://grants.nih.gov/grants/guide/pa-files/PA-02-011.html (will be re-issued)





- For research-oriented physical/mathematical scientists and engineers to engage in supervised study & research leading to increased competence to perform biomedical, behavioral, bioengineering or bioimaging research.
- PI's on NIH grants are not eligible
- Up to five years of support, NIH/IC limit on salary, \$40,000 supplies/personnel/travel/tuition
- Requires commitment of 75% of effort
- Application Receipt: February 1, June 1, and October 1
- http://grants.nih.gov//grants/guide/pa-files/PA-02-127.html



### **Tissue Engineering**

### Functional Tissue Engineering of Musculoskeletal Tissues



- To stimulate innovative research that will enhance our understanding of functional tissue engineering of musculoskeletal tissues (articular cartilage, ligaments, tendons, bone, meniscus, intervertebral disc and skeletal muscle).
- NIAMS, NICHD, NIDCR
- http://grants.nih.gov/grants/guide/pa-files/PA-02-014.html

### Novel Approaches to Corneal Tissue Engineering



- To explore new approaches that could lead to enhanced engineering of corneal tissues, includes studies of early developmental processes to delineate the interactions between individual corneal tissue layers, the biomechanical properties of the stroma, cellular control of matrix deposition, control of corneal growth and maturation, and studies of synthetic replacement materials.
- NFI
- http://grants.nih.gov/grants/guide/pa-files/PA-02-053.html



### **Diagnostics & Therapeutics**

### Novel Technologies for in vivo Imaging

- For the development and delivery of novel image acquisition or enhancement technologies and methods for biomedical imaging and image-guided interventions and therapy, and which may incorporate limited pilot or clinical feasibility evaluations using either pre-clinical models or clinical studies. This initiative will facilitate the proof-offeasibility, development, and delivery of novel imaging technologies and limited evaluation studies to show proof-of-concept and functionality.
- NCI
- http://grants.nih.gov/grants/guide/pa-files/PA-04-095.html

### Speech Processor Optimization for Cochlear Implants

- To advance the design of speech processors for cochlear implants. The goal of this RFA is to support the development of innovation and enhancements for cochlear implants that will increase the level of patient performance. The research may involve conceptualization, design, fabrication, and/or testing of algorithms for evoking neural activity with cochlear implants.
- NIDCD
- http://grants.nih.gov/grants/guide/rfa-files/RFA-DC-04-001.html



# NHGRI DNA Sequencing Technology Development "\$100,000 and \$1000 genome"



### Capillary/microchannel integrated system, near-term

Jovanovich/Mathies/Barron

(Microchip Biotechnologies, Inc.)

Gorfinkel (SUNY Stony Brook)

Kellogg (Network Biosystems)

Microfluidic device

Fair (Duke U))

#### SBS/polony integrated systems, near-term

Costa/Smith (Agencourt Personal Genomics)

Lohman/Margulies (454 Life Sciences)

Church (Harvard Med)

#### **SBS/polony component**

Benner (U of Florida)

Ju (Columbia U)

Metzker (Baylor/LaserGen)

Ronaghi (Stanford U)

Williams, P (Arizona State U)

#### **SBS** single-molecule

Quake (Stanford U) Williams, J (LiCor Inc.)

### -9 → \$20 m over life of grants

#### Free-running polymerase

Hardin (VisiGen)

-9 Turner (Nanofluidics)

### Sequencing-by-hybridization/denaturation

Huang (UCSC) Mishra (NYU)

### **Biological nanopore**

Ghadiri/Bayley (Scripps/Oxford)

#### Synthetic nanopore

- **-9** Collins (U of Maine)
- **-9** Davis (Stanford U)
- **-9** Ramsey (U of North Carolina)
- -9 Golovchenko/Branton/Deamer (Harvard)
- **-9** Timp (UIUC)

#### Nanopore with modified analyte

- **-9** Benner (U of Florida)
- **-9** Marziali (U of British Columbia)
- -9 Meller (Rowland Inst)
  Ju (Columbia)

#### Other near-field sensing of unmodified DNA

- **-9** Lindsay (Arizona State U)
- -9 Lee (Oak Ridge Nat'l Lab)



# NIDCR Salivary Diagnostics Program

- Development of Technologies for Saliva/Oral Fluid Based Diagnostics
- to encourage outstanding multidisciplinary research aimed at the development of new technologies or the advancement of existing technologies for simultaneous multi-analyte detection in saliva and other oral fluids
- ■7 U01 awards



# Nanotechnology at NHLBI

- NHLBI held a Working Group in 2003 to assess the potential of nanotechnology for heart, lung, blood and sleep diseases. The Working Group identified 4 areas where nanotechnology could have an immediate impact:
  - Targeted therapeutics
  - Tissue engineering to replace defective valves, damaged heart muscle, clogged blood vessels
  - Molecular imaging
  - Biosensors and diagnostics



# Nanotechnology at NHLBI

- An NHLBI RFA for multidisciplinary Programs of Excellence in Nanotechnology was funded in 2005, awarding \$54 million over 5 years.
  - Washington University
  - Georgia Tech
  - Burnham Institute
  - Massachusetts General Hospital



# Nanotechnology at NHLBI

- A new initiative to support innovative nanotechnology research for the diagnosis and treatment of heart, lung, blood and sleep disorders
  - has been developed and approved by the NHLB Advisory Council
  - and is currently under consideration for release.

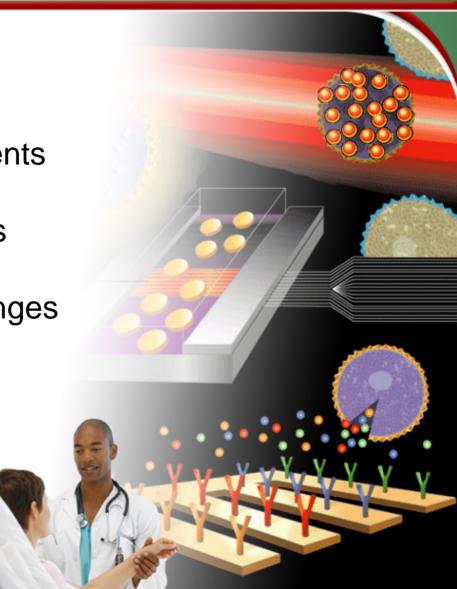
# Alliance for Nanotechnology in Cancer

- \$144.3M initiative launched in September 2004
- Designed to "ignite" nanoproduct development and commercialization
- Encompasses public and private sectors
- Emphasizes cross-disciplinary collaborations
- Participates in the National Nanotechnology Initiative (NNI)



### **Alliance Goals**

- Early detection
- Real-time efficacy assessments
- Delivery of multiple therapies
- Monitoring of molecular changes
- Symptomatic management
- Targeted discovery



## **Alliance Strategies**

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

# Nanotechnology Characterization Laboratory

### Mission:

- Perform and standardize the preclinical characterization of nanomaterials developed by academic, government, and industrial researchers
- Accelerate use of nanoparticles for drug delivery, as image contrast agents, and for diagnostics
- Collaborate with other government agencies to leverage resources and expertise

# How the Alliance Applies Systems-level Approaches

- 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

### **Alliance Milestones**

### Centers of Cancer Nanotech Excellence selections

Announcement: Fall 2005

### Fellowships in Cancer Nanotech

RFA receipt date: Nov. 16, 2005

### Nanotech Characterization Lab

Accepting nanomaterials to characterize

### Nano Cancer Gov Website

 Available for the latest info on funding opportunities and nanotech news



National Cancer Institute

ncl.cancer.gov



# NANOTECHNOLOGY RESEARCH ENVIRONMENT, HEALTH, AND SAFETY



# National Toxicology Program Toxicological Evaluation of Nanoscale Materials

- NIEHS/NIH, NIOSH/CDC, NCTR/FDA
- Nanoscale materials activities initiated 2002
- Size- and composition-dependent biological disposition of nanoscale crystalline fluorescent semiconductors.
- Short- and long-term studies of one or more carbon-based nanoscale materials (e.g., SW- or MW-nanotubes, fullerenes)
- Evaluate role of core and surface composition in possible immunotoxicity of the above (quantum dots and CNTs)
- Phototoxicology studies of representative nanoscale metal oxide particles used in industrial setting and consumer products (e.g., TiO<sub>2</sub>)
- Skin uptake, inhalation, and oral routes of exposure



# NANOTECHNOLOGY RESEARCH ENVIRONMENT, HEALTH, AND SAFETY



- FY06 Joint solicitation on health and environmental effects of manufactured nanomaterials
- EPA, NIEHS, NIOSH (CDC), and NSF



## NIH NANOSCIENCE/NANOTECHNOLOGY NANOMEDICINE NCI ALLIANCE **CONTACTS**

**National Cancer Institute** 

**NCI Alliance for Nanotechnology** 

**National Eye Institute** 

National Heart, Lung, and Blood Institute

**National Human Genome Research Institute** 

**National Institute on Aging** 

National Inst of Alcohol Abuse and Alcoholism Karen Peterson

**National Inst of Allergy and Infectious Diseases** 

Nat'l Inst of Arthritis & Musculosk & Skin Diseases

National Institute for Biomedical Imaging and Bioengineering

**National Institute of Child Health and Human Development** 

National Inst on Deafness & Other Communication Disorders

National Institute of Dental and Craniofacial Research

National Inst of Diabetes and Digestive and Kidney Disorders

**National Institute on Drug Abuse** 

**National Institute of Environmental Health Sciences** 

**National Toxicology Program** 

**National Institute of General Medical Sciences** 

**National Institute of Mental Health** 

Nat'l Inst of Neurological Disorders and Stroke Joe Pancrazio

Center for Scientific Review

Clinical Center

Dan Gallahan

**Greg Downing, Travis Earles** 

Richard Fisher, Paul Sieving

**Denis Buxton** 

**Jeff Schloss, Allison Peck** 

Winifred K. Rossi

Maria Giovanni

Jim Panagis, Kuan Wang

Bill Heetderks, Peter Moy

**Louis Quatrano** 

Roger Miller

Eleni Kousvelari

Maren Laughlin

**Tom Aigner** 

David Balshaw, Sally Tinkle

John Bucher, Nigel Walker

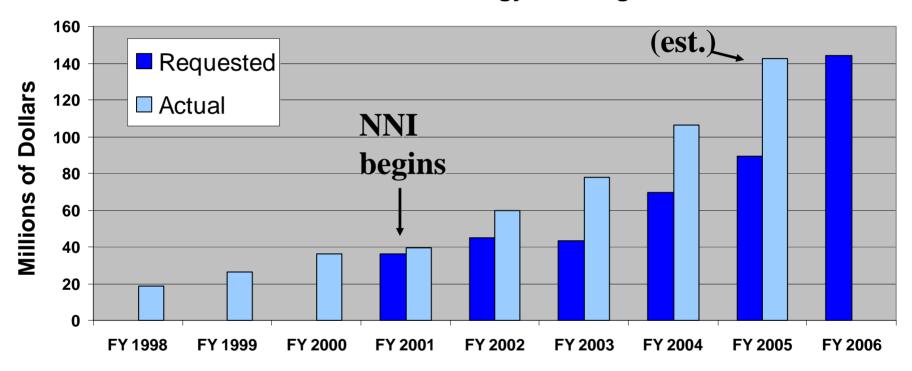
**Cathy Lewis** Mike Huerta

John Bowers

King Li



### **NIH Nanotechnology Funding**



SBIR/STTR

FY	2001	2002	2003	2004
\$M	4.4	7.9	7.2	11.9

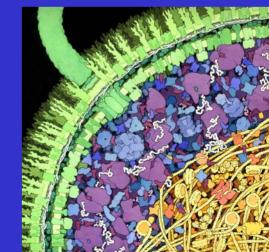


# National Nanotechnology Initiative (NNI) Advances in Biomedicine and Healthcare

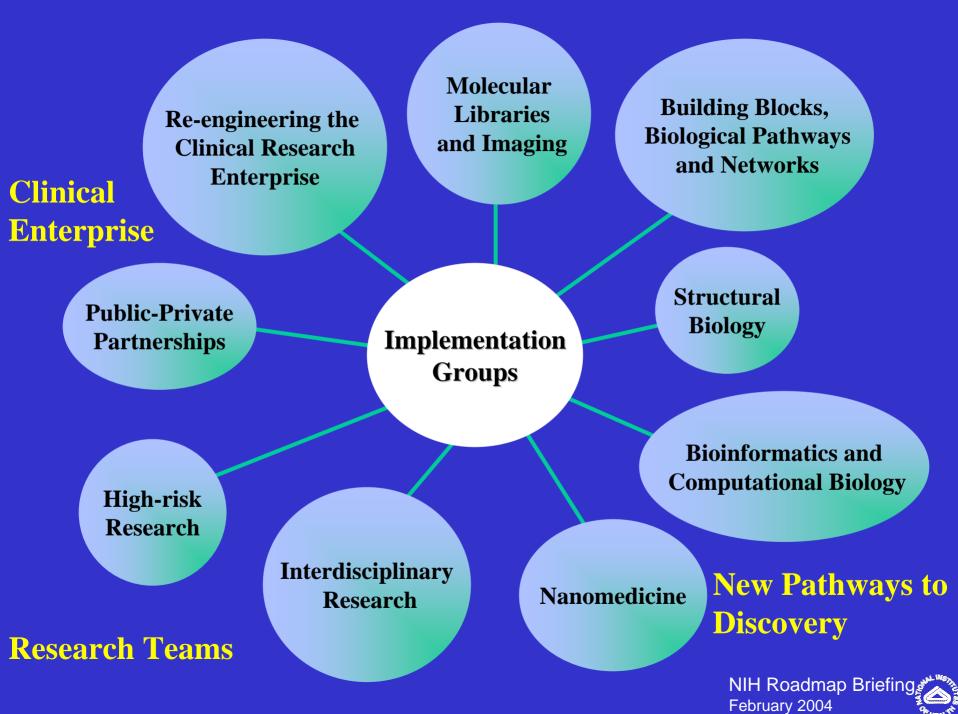
- Detecting Disease Before Health Has Deteriorated
  - Imaging
  - Sensors
- Implants to Replace Worn or Damaged Body Parts
  - Controlling interactions of synthetic and inorganic materials with the body, for effective integration
- Delivery Of Therapeutics
  - Particle Size
  - Targeting
- Research Tool correlates of the above



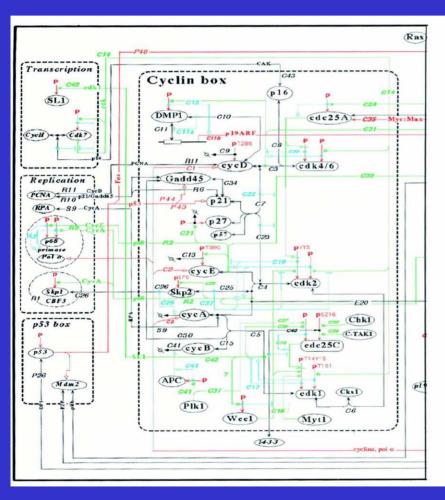
# NANOMEDICINE ROADMAP INITIATIVE

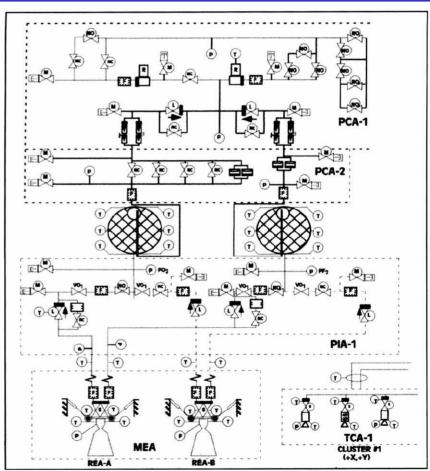






# Need to understand biological systems





# The Biological Data Of The Future

- Destructive
- Qualitative
- Uni-dimensional
- Low temporal resolution
- Low data density
- Variable standards
- Non cumulative

- Non-destructive
- Quantitative
- Multi-dimensional and spatially resolved
- High temporal resolution
- High data density
- Stricter standards
- Cumulative

# **Nanomedicine Development Centers**

### The NIH Vision

- Characterize quantitatively the physical and chemical properties of molecules and nanomachinery in cells;
- Gain an understanding of the engineering principles used in living cells to "build" molecules, molecular complexes, organelles, cells, and tissues; and
- Use this knowledge of properties and design principles to develop new technologies, and engineer devices and hybrid structures, for repairing tissues as well as preventing and curing disease.

# Beginning a ten-year process

- We need a more quantitative analysis of biomolecules and their interrelationships.
- To understand design, we need to measure physical parameters such as force, stoichiometry of subunits, kinetics, material requirements, energy utilization and transduction.
- Collecting this comprehensive data set requires:
  - a coordinated effort to develop uniform standards,
  - a lexicon of engineering terms and definitions applicable to biological processes and structures, and
  - data systems to collect and analyze the data.

# Beginning a ten-year process continued...

- As we develop this lexicon we will discover gaps in our ability to collect essential data.
- To complete the analyses, new tools and strategies will be discovered and applied.
- The endpoint of this activity will be a characterization of biomolecular systems in a format that will interface seamlessly with engineering specifications required to create blueprints for the design of new nanomachines or structures.

# Scope of centers

- multidisciplinary -- biology, physics, chemistry, engineering, math, computational, clinical...
- biomedical focus of model system/theme -- e.g.,
  - pathway, motor system, transport
  - cell type, disease model
- toxicity, biocompatibility -- goal is to develop particles, materials and devices that can be used in vivo.
- broad (but not comprehensive) technological approach
- generality of tools (broadly applicable)
- design of tools: throughput, comprehensive measurement (à la HGP)
- operate as network of centers

# NANOMEDICINE ROADMAP INITIATIVE

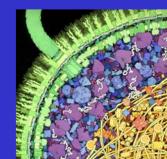


Nanotechnology Tools

**Biology**Medicine

Design principles of subcellular nanosystems

Nanotechnology Tools



# Status of the initiative

- 20 planning awards made in September 2004
- Meeting of awardees in Spring
- Limited competition for Centers awards
  - \$6 M annual investment in Centers in FY 2005
- Open competition for Centers awards
  - \$6 M annual additional in Centers in FY 2006



# From white paper instructions...

...NIH intends that the Nanomedicine Roadmap Initiative projects should depart from established, ongoing projects and should propose truly novel approaches, breaking new scientific and technical ground. Our primary goal is to stimulate new ideas and directions that would not be likely to receive funding in routine grant solicitations.