Program Design and Management for Transformative Research at the US National Institutes of Health

Japan Science Technology Agency
September 16, 2009

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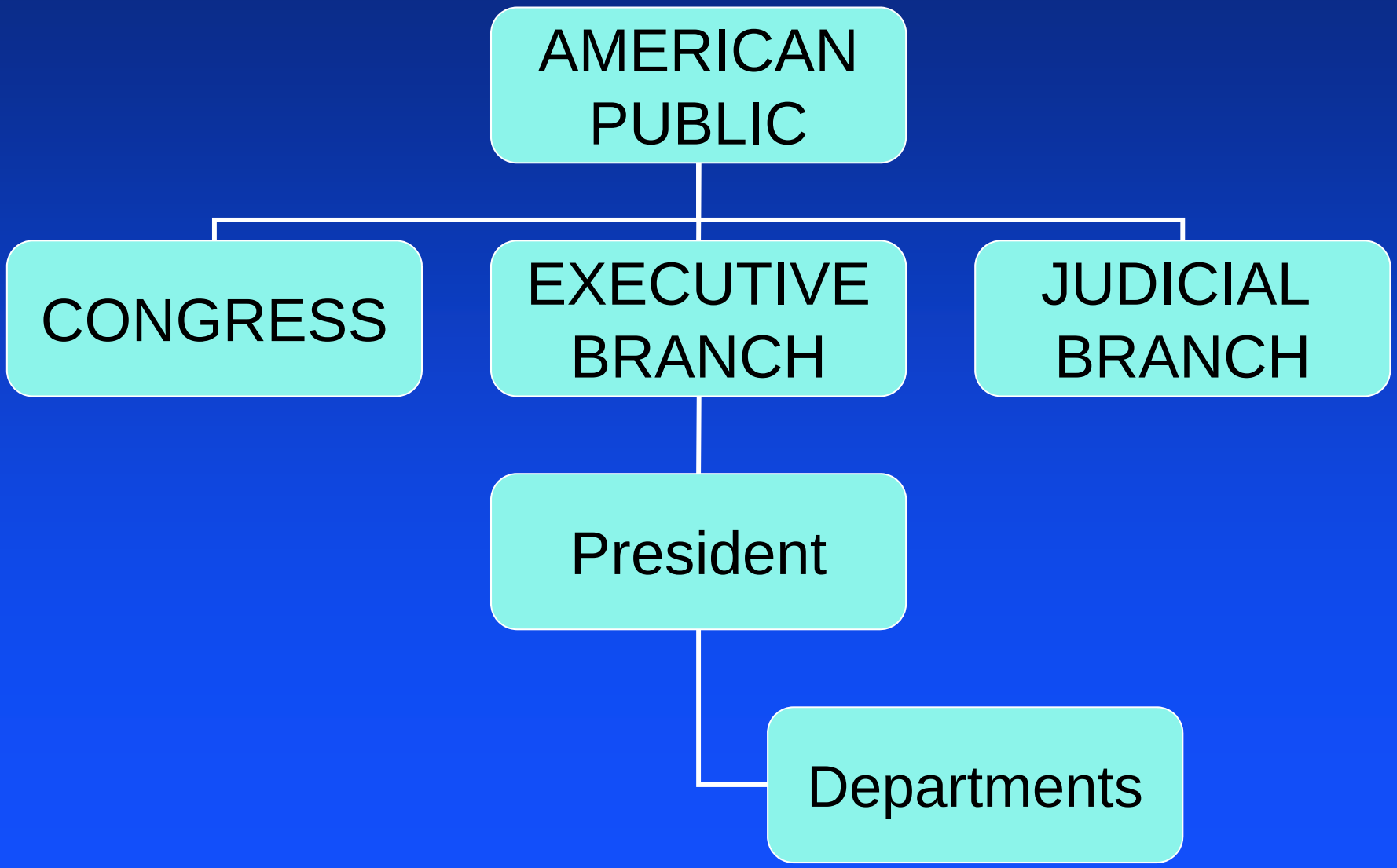
National Eye Institute
National Institutes of Health

National Institutes
Of Health

Department of Health
and Human Services

US Government



Departments in the President's Cabinet

Health and Human Services

FY2009: **$777 Billion**

NIH	30
CDC	6
FDA	3
CMS	669
ACF	51

15 Departments:

Agriculture
Commerce
Defense
Education
Energy
HHS
Homeland Security
Housing and Urban Dev
Interior
Justice
Labor
State
Transportation
Treasury
Veterans Affairs

National Institutes of Health

Biomedical research in the United States supported by the Federal Government

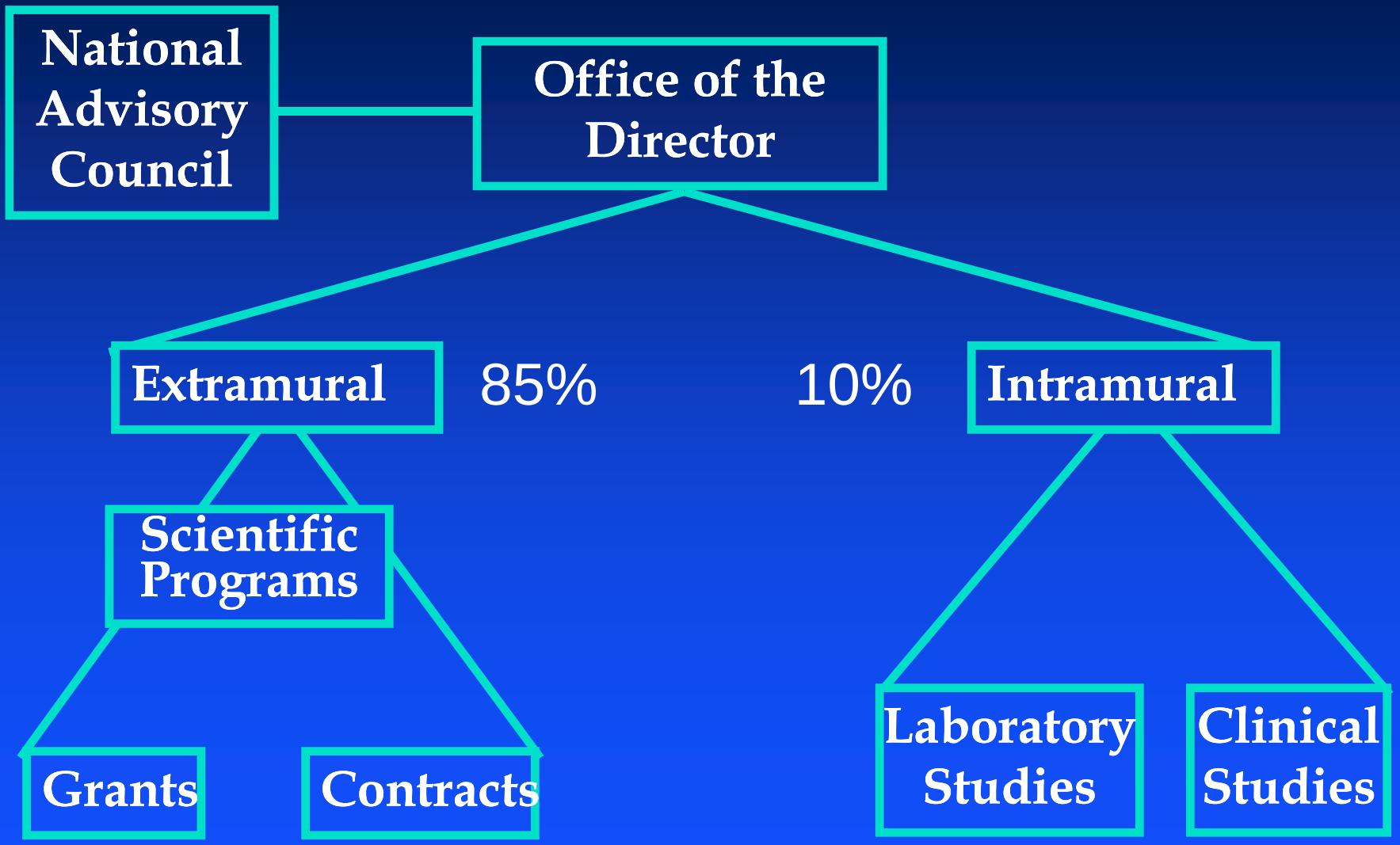
NIH Director, Francis Collins, MD, PhD

National Institutes of Health $30B

OD – No Direct Funding

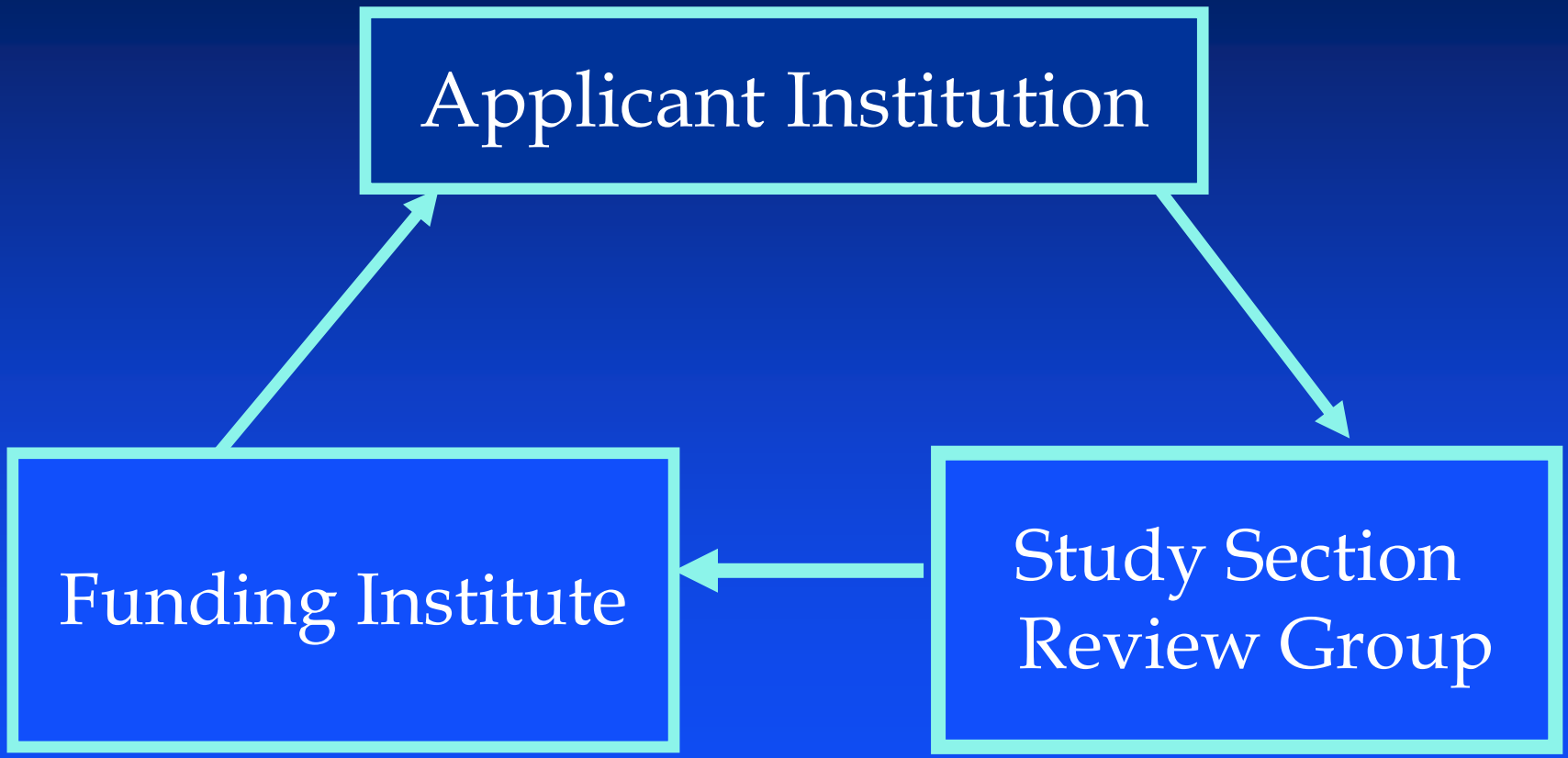
- National Institute on Aging
- National Institute on Alcohol Abuse and Alcoholism
- National Institute of Allergy and Infectious Diseases
- National Institute of Arthritis and Musculoskeletal and Skin Diseases
- **NCI**
- National Institute of Child Health and Human Development
- National Institute on Deafness and Other Communication Disorders
- National Institute of Dental and Craniofacial Research
- National Institute of Diabetes and Digestive and Kidney Diseases
- National Institute on Drug Abuse
- National Institute of Environmental Health Sciences
- **NEI**
- National Institute of General Medical Sciences
- National Heart, Lung, and Blood Institute
- National Human Genome Research Institute
- National Institute of Mental Health
- National Institute of Neurological Disorders and Stroke
- National Institute of Nursing Research
- National Institute of Biomedical Imaging and Bioengineering
- National Center for Complementary and Alternative Medicine
- Fogarty International Center
- National Center for Research Resources
- National Library of Medicine
- National Center on Minority Health and Health Disparities
- Clinical Center
- Center for Information Technology
- **Center for Scientific Review**

A Typical NIH Institute



Typical Peer Review Process

Grant Application Cycle



Applications to NIH

- > 60,000 grant applications are submitted to NIH each year

- 10-25% are funded

10 months to Award a Grant:

Feb	Receipt of Application	CSR
July	Scientific Merit Review	CSR or NEI
Sept	National Advisory Eye Council	NEI
Dec	Notice of Grant Award	NEI

Center for Scientific Review (CSR)

Receipt and Referral

- Receives applications
- Assigns to Scientific Review Panels
- Designates Funding Institute (NEI)

- Scientific Review
- Initial scientific merit review

CSR Study Sections

Scientific Merit Review

- ~25 members
- face-to-face meetings
- 60-100 applications (2 days)
- Scientific Review Officer

5 Review Criteria

Significance

Innovation

Approach

Investigators

Environment

Overall Impact

Summary Statement to Applicant

- Summary of Review Discussion
- Detailed Critiques of Assigned Reviewers
- Priority Score and Percentile Ranking
- Budget Recommendations

National Advisory Council

- Oversight of the Review Process
- Approval Required to Fund a Grant
- Programmatic Considerations

NIH Funds Grants based on

- Scientific merit
- Program considerations
- Availability of funds

What is the Problem?

Innovation?

High Risk / High Reward?

New Opportunities?

NIH Roadmap for Medical Research

Accelerating Medical Discovery to Improve Health

What are today's scientific challenges?

What are the roadblocks to progress?

What do we need to do to overcome roadblocks?

NIH Roadmap Goals

- Accelerate basic research discoveries and speed translation of those discoveries into clinical practice
- Explicitly address roadblocks that slow the pace of biomedical research to improve health
- Develop new ways to fund innovative, potentially transformative research
- Develop programs that no single institute would fund that would be relevant to much or all of NIH

National Institutes of Health

OD – No Direct Funding

- National Institute on Aging
- National Institute on Alcohol Abuse and Alcoholism
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- National Library of Medicine
- National Center on Minority Health and Health Disparities
- Clinical Center
- Center for Information Technology
- Center for Scientific Review

National Institutes of Health

$30,000,000,000

$500,000,000 **1.7% of Total NIH**

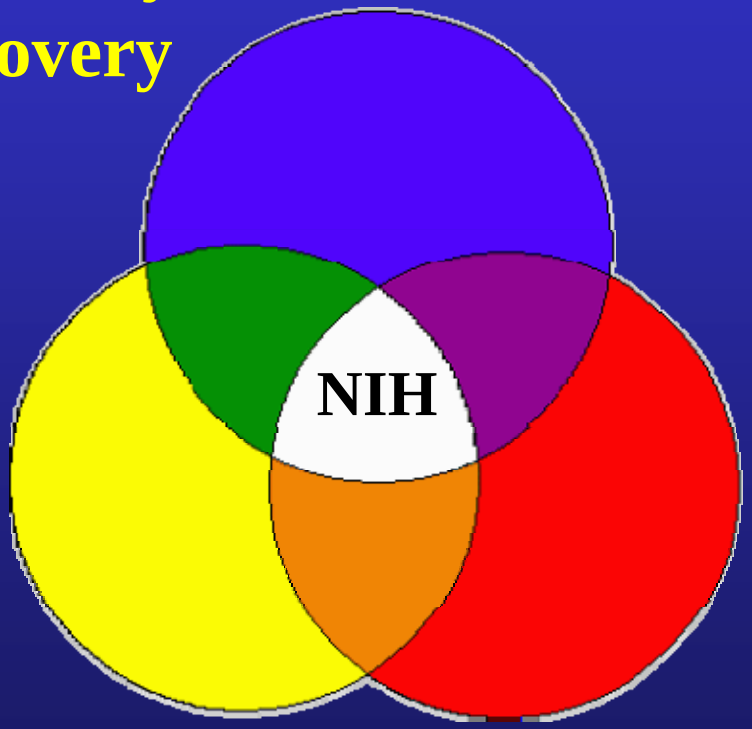
NIH Roadmap for Medical Research

Like JST:

Devote a portion of NIH Budget to new approaches for innovative, transformative programs

What is the NIH Roadmap?

New Pathways to Discovery



Research Teams of the Future

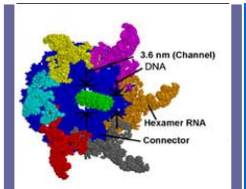
Re-engineering the Clinical Research Enterprise

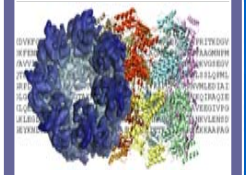
NIH Roadmap for Medical Research

- **New Pathways to Discovery**

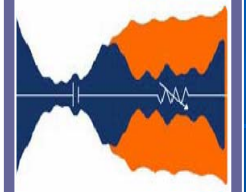
  Molecular Libraries and Imaging
  Building Blocks, Biological Pathways and Networks
  Structural Biology
  Bioinformatics and Computational Biology
  Human Microbiome Project
  Epigenomics
  Nanomedicine

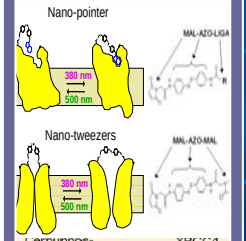
- **Research Teams of the Future**
- **Re-engineering Clinical Research Enterprise**

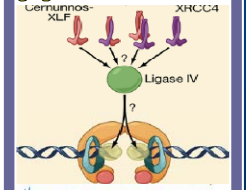




the Cell Propulsion Lab







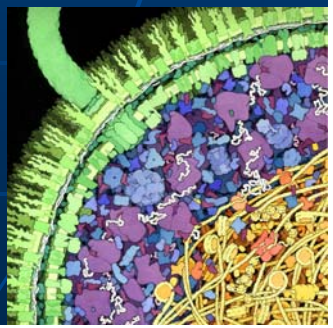
NANOTECHNOLOGY CENTER FOR MECHANICS IN REGENERATIVE MEDICINE

NIH Roadmap FOR MEDICAL RESEARCH

NIH Roadmap

Nanomedicine Initiative

A Novel Program



National Institutes Of Health

Department of Health and Human Services

Nanomedicine?

- Medical diagnosis, monitoring and treatment at the level of single molecules or molecular assemblies that provide structure, control, signaling, homeostasis and motility in cells (Am Acad NM)

- The science and technology of diagnosing, treating and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body (Euro Sci Found)

Nanomedicine

- An outgrowth of nanotechnology
- Application of tools to biological tissue
  - Optical Imaging (contrast agents, single-molecule optics)
  - Probe and Manipulation (AFM)
  - Multifunctional Nanoparticles (gold, silver, hybrid magnetic)
  - Nanostructures (QD, dendrimers)
  - Nanocoatings and films (antibacterial, anti-inflammatory)
  - Nanodevices (sensors using nanotubes)
  - Bottom-up self-assembly

NIH Nanomedicine Roadmap Initiative

How can NIH add value?

What does NIH do best?

Not Nanotechnology

- Physical sciences
- Novel properties of materials (1-100 nm) that lead to novel applications
- Manipulation and control

Not <u>just</u> nanotechnology applied to biology and medicine

- Develop new materials and/or technologies and apply to specific diseases or cell systems
- > $200 million

The NIH Vision
Nanomedicine Roadmap Initiative

- Uncover novel properties; quantitatively characterize these and other known properties of biomolecules and their complexes inside cells.

- Gain an understanding of the engineering principles used in living cells to "build" molecules, molecular complexes, organelles, cells, and tissues

- Develop new technologies, and engineer devices and hybrid structures, for repairing tissues as well as preventing and curing disease

CONTROL AND MANIPULATE BIOLOGY AT THE NANOSCALE IN VIVO

Nanomedicine Development Centers

Challenge #1

Understand a system with such precision (at the nanoscale) to be able to engineer (intracellular) structures in order to address a specific medical problem within 10 years

Challenge #2

Develop a medical research program with basic scientists

Involve clinician scientists early in the research

The Nanomedicine Initiative

Multidisciplinary

– biology, chemistry physics, math and computational science, engineering, clinical

Translational

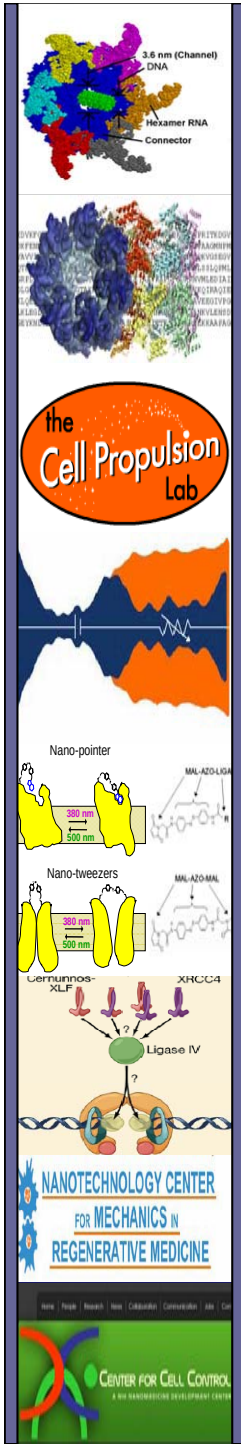
– connects basic scientists with clinicians to develop new knowledge of basic biological mechanisms and transition it to pre-clinical testing within 10 years.

Novel and risky

– proposes new scientific and team science concepts:
engineering biology based on quantitative knowledge
basic science shaped by clinical goals

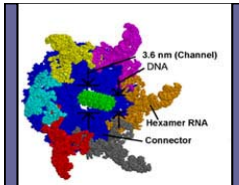
Novel program development and management

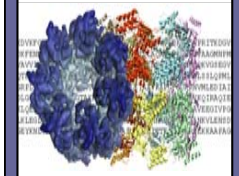
– departs from NIH practices that thwart pursuit of novel, risky projects



Nanomedicine Development Centers

	Total	PIs	Postdocs	Students	Other
Nanomedicine Center for Nucleoprotein Machines	45	10	14	13	8
Center for Protein Folding Machinery	75	16	24	17	18
Nanotechnology Center for Mechanics in Regen. Med.	47	12	19	8	8
The Center for Systemic Control of Cyto-Networks	31	10	8	10	3
NDC for the Optical Control of Biological Function	63	18	13	16	17
Engineering Cellular Control: Synthetic Signaling and Motility	44	13	10	10	11
Phi29 DNA-Packaging Motor for Nanomedicine	39	17	12	8	2
National Center for the Design of Biomimetic Nanoconductors	34	14	12	4	4
Average/NDC	49	14	14	12	10
TOTAL	**344**	**96**	**100**	**82**	**67**





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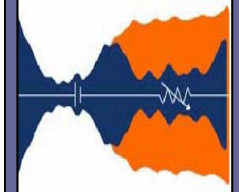
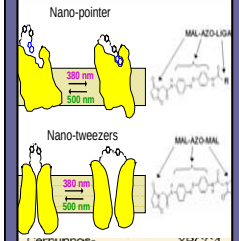
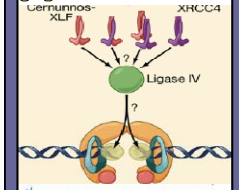






NANOTECHNOLOGY CENTER FOR MECHANICS IN REGENERATIVE MEDICINE

CENTER FOR CELL CONTROL

Nanomedicine Development Centers

Institutions (n=46; 5 foreign)

Baylor College of Medicine	NYU Langone Medical Center	University of Chicago
Caltech	NIST	University of Cincinnati
City of Hope	NYU School of Medicine	University of Heidelberg
CSHL	Purdue University	University of Illinois at Chicago
Columbia University	Rochester University	University of Illinois at U-C
Duke University	Rutgers University	University of New Mexico
Emory University	Sandia National Laboratories	University of Pennsylvania
ETH-Zurich	Scripps Research Institute	University of S. Mississippi
Georgia Institute of Technology	Stanford School of Medicine	University of Washington
German Cancer Research Center	Stanford University	UT MD Anderson
Gladstone	UC Berkeley	UT Southwestern Medical Center
Illinois Institute of Technology	UC Davis	Wabash College
Lawrence Berkeley Lab	UC San Diego	Weill Medical College of Cornell
Ludwig-Maximilians-University	UC San Francisco	Weizmann Institute
MIT	UC Santa Barbara	
Medical College of Georgia	UCLA	

Programmatic Timeline & Challenge

Biological Nanostructures → **Medicine**

Basic science ➡ *engineering* ➡ *biology* ➡ *animal* ➡ *human* ➡ *disease*

Identify novel properties & characterize quantitatively	Understand Design Principles; Develop new technologies	Engineer devices, hybrid structures, intracellular nanomachinery for repairing tissues to treat disease

2006 → 2016

What is Different?

Not a grant, contract or cooperative agreement

Program development

- Input from scientific Community
- 5-page white papers (87)
- Planning awards (20 for $50,000)
- Meeting with applicants, then applications
- Closed competition
- 4 Centers Funded (x2)

What is Different?

Peer Review

special review group (includes NIH staff)

preliminary data not essential

strength of team

different scoring – bins

No council approval

What is Different?

Award management

- flexible resource allocation
  (set aside ~ 20%)
  - Team oversight includes staff, external advisors and center personnel
  - Network of centers is simultaneously collaborative and competitive
  - Programmatic involvement without programmatic control
  - Can increase/decrease number and size of centers

Nanomedicine Development Centers

www.nihroadmap.nih.gov

www.nanomedcenter.org

Other Innovative NIH Programs

Pioneer

New Innovators

TR01

Pioneer Awards

Support Potentially Groundbreaking Ideas

NIH DIRECTOR'S PIONEER A·W·A·R·D

Support individuals with untested, potentially groundbreaking ideas

Application: 3-5 page essay
evidence for innovation

Unique review:
interviews
reference letters

$500,000 (direct) pe year for 5 yrs

Pioneer Awards

Success Rates FY04 –FY08

NIH DIRECTOR'S PIONEER A·W·A·R·D

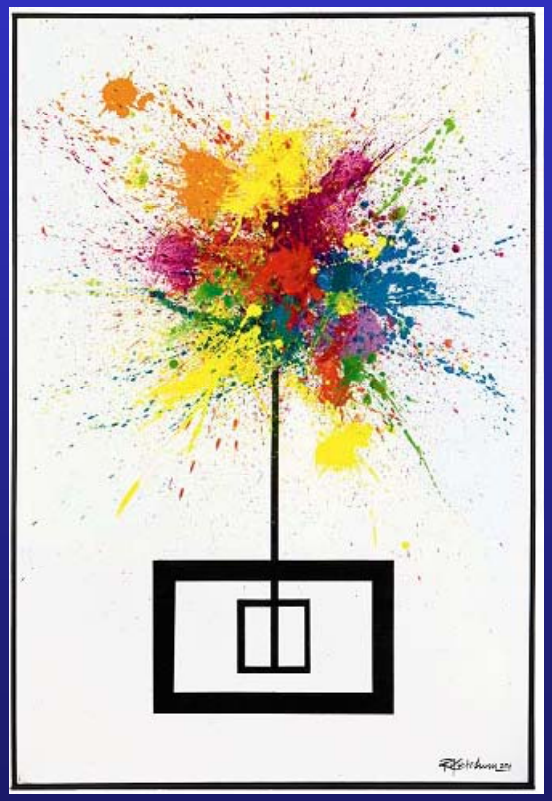
Applications: 1900

Awards: 63

Success Rate: 3.3%

T-R01

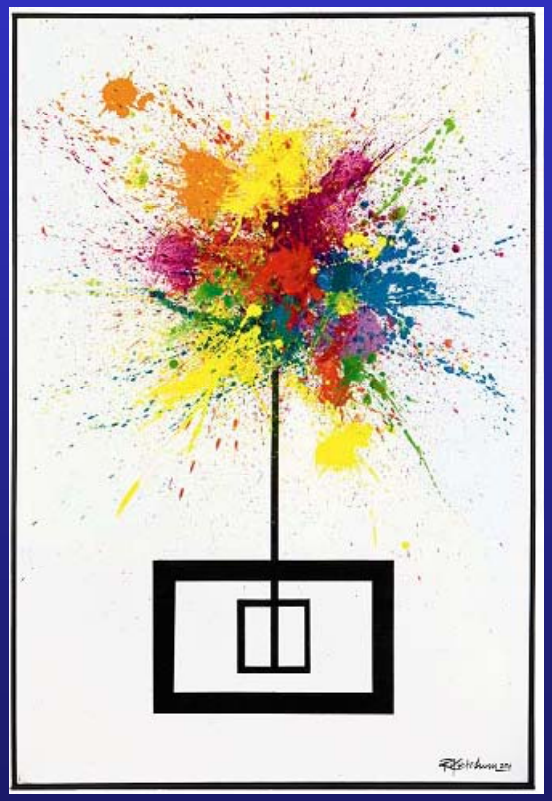
Transformative R01



- Projects with potential to create or overturn fundamental paradigms
- Inventive, innovative, original and/or unconventional (risk)
- Major impact in biomedical or behavioral research
- Open to all fields of interest to NIH
- Budget flexibility allows projects of varying complexities to be supported

T-R01

Transformative R01



8 page application

No preliminary data required

Unconventional review

No budget limit

Program (2009) = $25M

739 Applications Received:
None awarded yet

Thank you to JST !

Questions?

Flexible Research Authority (FRA)

Granted to the NIH by the US Congress:

NIH … may use funds … to enter into transactions (other than contracts, cooperative agreements, or grants) to carry out research in support of the NIH Roadmap Initiative of the Director.

… may utilize such peer review procedures (including consultation with appropriate scientific experts) as the Director determines to be appropriate to obtain assessments of scientific and technical merit. Such procedures shall apply to such transactions in lieu of the peer review and advisory council review procedures that would otherwise be required…

Nanomedicine Development Centers

Filament networks and motors

Cell Propulsion Lab (UCSF, Wendell Lim)

Networks: cytoskeletal proteins and signal transduction
Redesign and reprogram; build artificial cell-like assemblies
Novel therapeutics

Nanotechnology Center for Mechanics in Regenerative Medicine (Columbia University, Michael Sheetz)

Cell mechanotransduction
Force sensing, generating, and bearing systems
Extracellular influences: matrix rigidity, form, and spacing
Immune synapse and stem cell growth and differentiation

Nanomedicine Development Centers

Membranes

Optical Control of Biological Function (UC Berkeley, Ehud Isacoff)

Remote control of molecular function using light:
ligand photoswitches; light-gated peptides
Ion Channels, G-protein coupled receptors, and enzymes
Light-gated channels to restore vision

National Center for the Design of Biomimetic Nanoconductors

(University Illinois Urbana-Champaign, Eric Jakobsson)

Full understanding of membrane function for re-engineering
New membrane channels with designed selectivity
Functional Protocell: nanoporous, membrane-enclosed structure
Drug delivery and disease treatment

Nanomedicine Development Centers

Enzymes and Protein Function

Center for Protein Folding Machinery (Baylor, Wah Chiu)

Network of chaperones for protein folding
Chaperonin - understand to re-engineer
disease targets: neurodegenerative diseases, cataract

Center for Cell Control (UCLA, Chih-Ming Ho)

Signaling pathways monitor and control
Engineering approach to develop algorithms for control
Develop intracellular nanosensors for enzyme activity
Manipulate pathways for wide range of disease treatment

Nanomedicine Development Centers

Polynucleotide manipulation

Center for Nucleoprotein Machines (Ga Inst Tech, Gang Bao)

Non-homologous end joining complex (NHEJ)
Repair DNA double-strand breaks
Examine kinetics of assembly and disassembly to re-engineer specific genetic fix for hemoglobinopathies, neurodegenerative

Phi29 DNA-Packaging Motor (Univ. Cincinnati, Peixuan Guo)

Bacteriophage motor packages DNA in capsid
Isolate, characterize and incorporate into delivery device
Therapeutic cargo: DNA, RNA or drugs.

Implementation
Nanomedicine Development Centers

	Phase 1 = $81.5M Total					
	FY 04	**FY 05**	**FY 06**	**FY 07**	**FY 08**	**FY 09**
# Centers		**4**	**8**	**8**	**8**	**8**
$ Million	**1.5**	**6**	**12**	**12**	**25**	**25**