

National Cancer Institute

# NCI Director's Update

Dr. John E. Niederhuber  
Director, National Cancer Institute

National Cancer Advisory Board  
June 11, 2009

U.S. DEPARTMENT  
OF HEALTH AND  
HUMAN SERVICES

National Institutes  
of Health

# NCI-June 2009

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- Most-challenging issues
  - American Recovery and Reinvestment Act of 2009
  - ‘Managing’ the FY09 budget
  - Planning for 2010 and 2011
  - Developing the trans-NIH cancer strategic plan

# The American Recovery and Reinvestment Act of 2009



**Tuesday, Feb. 17, 2009**



# \$10.4 Billion to NIH

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- \$7.4 billion: Institutes and Centers
  - \$1.267 billion to NCI
- \$1 billion: extramural construction
- \$500 million: NIH construction
- \$300 million: shared instrumentation
- \$400 million: comparative effectiveness research (\$400M HHS; \$300M AHRQ)
- \$800 million: NIH Office of the Director



# NCI ARRA Goals

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- Meet the “jobs” goal of ARRA
- Fund the best new science
- Model one-time dollars to soften out-year problems
- Invest in science that will make a difference for patients

# Supporting Individual Investigators

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- **16th percentile: 2009 RPG payline from appropriated funds**
- **16th to 18th percentile: 4-year grants through stimulus, followed by appropriated dollars**
- **18th to 25th percentile: Mix of 2-year and 4-year grants (stimulus for first 2 years)**

# Raising the Payline

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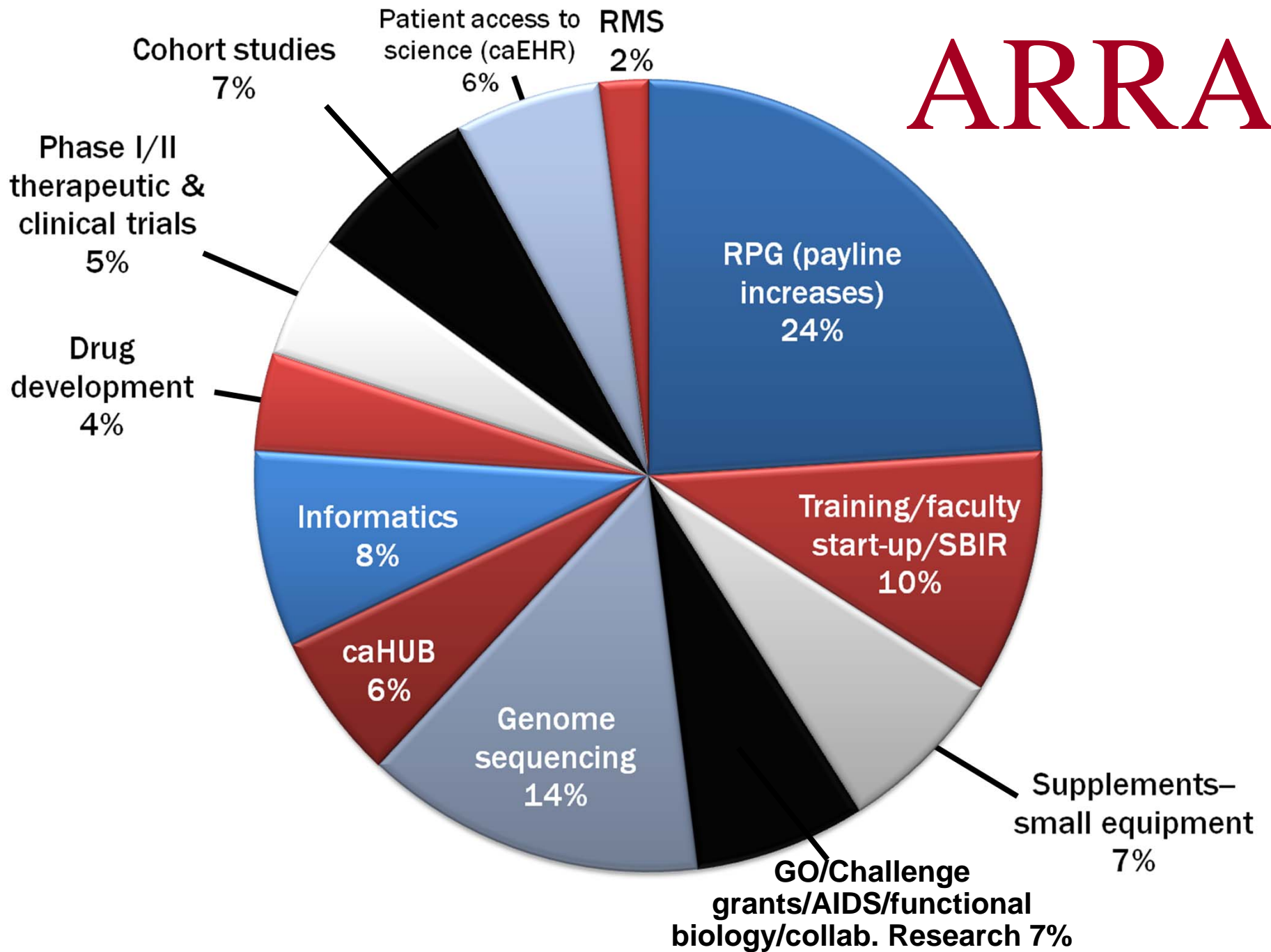
- Raising the RPG payline to the 25th percentile:
  - To date, 156 RPGs have been funded out of the 384 eligible (about 40% of eligible RPGs)
  - After NCAB takes action on grants today, NCI will be able to move toward having them awarded and on the way to grantees by month's end



# ARRA Funding Applications Received

Funding Opportunity	NIH total	NCI total	Status
NCI - Activities to Promote Research Collaborations		~167	Closed
Challenge Grants	~20,000	~4,398	Closed
Competitive Revisions	~2,123	~500	Closed
GO Grants	~2,500	~568	Closed
P30 Staff Grants	~550	~56	Closed
Administrative Supplements		2,500–3,000	Some closed 6/1; remainder for FY09 close 7/1

# ARRA



# ARRA Process

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- **Nearly 50 ARRA funding announcements have been posted and made available to the community to apply for NCI support**
- Grants ready to award are submitted weekly through NIH to the White House
  - **After inclusion on the weekly list, generally about 2 weeks until the grant is officially awarded**



# Obligating ARRA Funds

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- ARRA funds need to be spent by the end of next year — FY2010
- We are on target to accomplish the task
- Grant specialists have been assigned to work on ARRA awards as their sole responsibility
- Like other ICs, NCI must administer its annual appropriation, as well

# NCI FY 2009 Operating Budget Development

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<b>FY 2008 operating budget (with \$25M supplemental)</b>	<b>\$4,830,647</b>
<b>FY 2009 Omnibus Appropriations Bill</b>	<b>\$4,968,973</b>
<b>Difference, FY08 to FY09</b>	<b>\$138,326</b>
<b>Percent change, FY08 to FY09</b>	<b>+2.9%</b>

(dollars in thousands)

# NCI FY 2009 Operating Budget: NCI Operating Policies

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- NCI operating policies
  - 3% inflationary adjustments on non-competing grants
  - Award at full commitments of record for categorical (non-modular) grants
  - No cut to modular non-competing RPGs
  - NCI to award more competing RPGs than FY 2008 (1,284 to 1,412)
    - Will hit NIH target for competing new investigator R01s

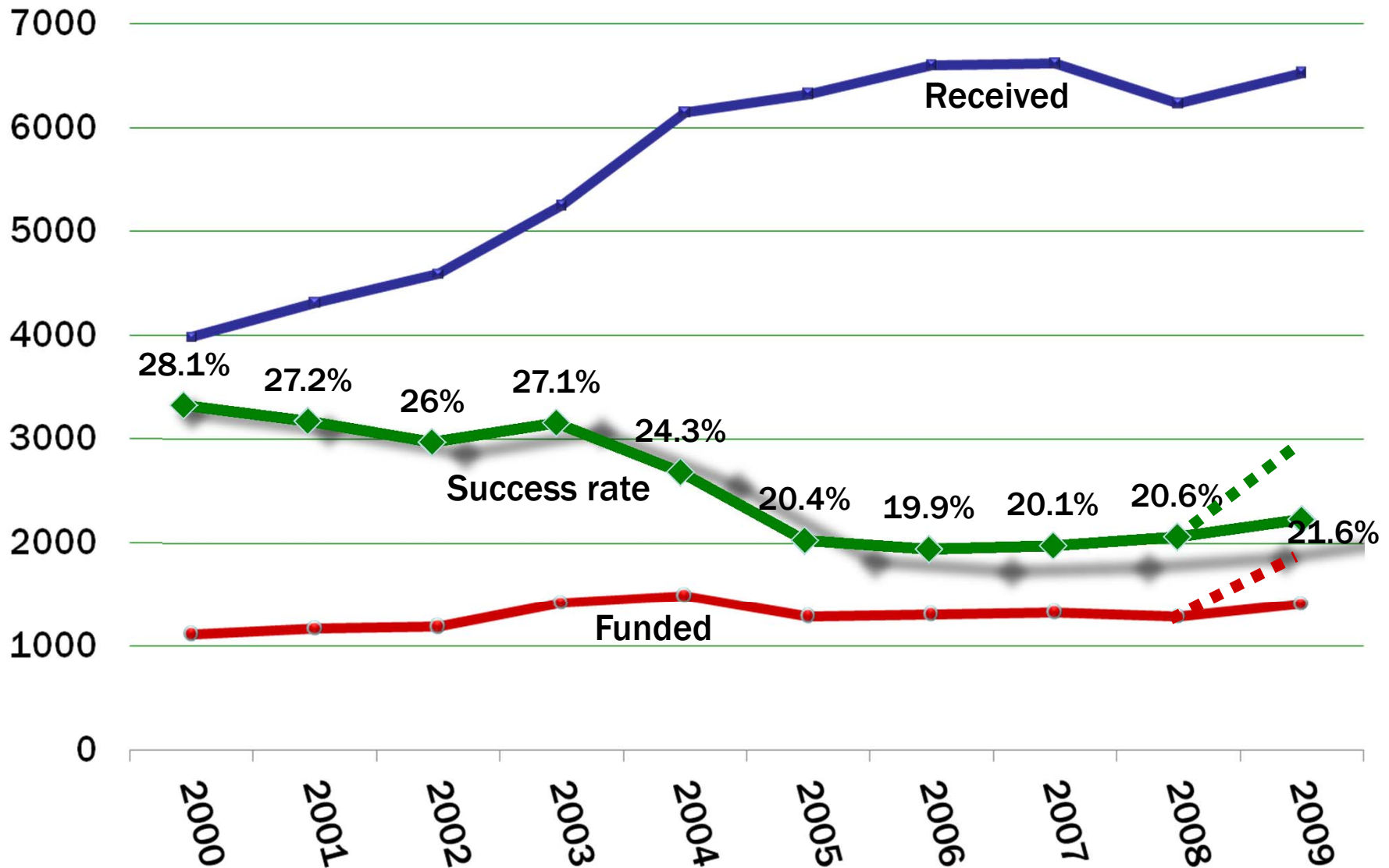


# NCI FY 2009 Operating Budget: NCI RPG Policies

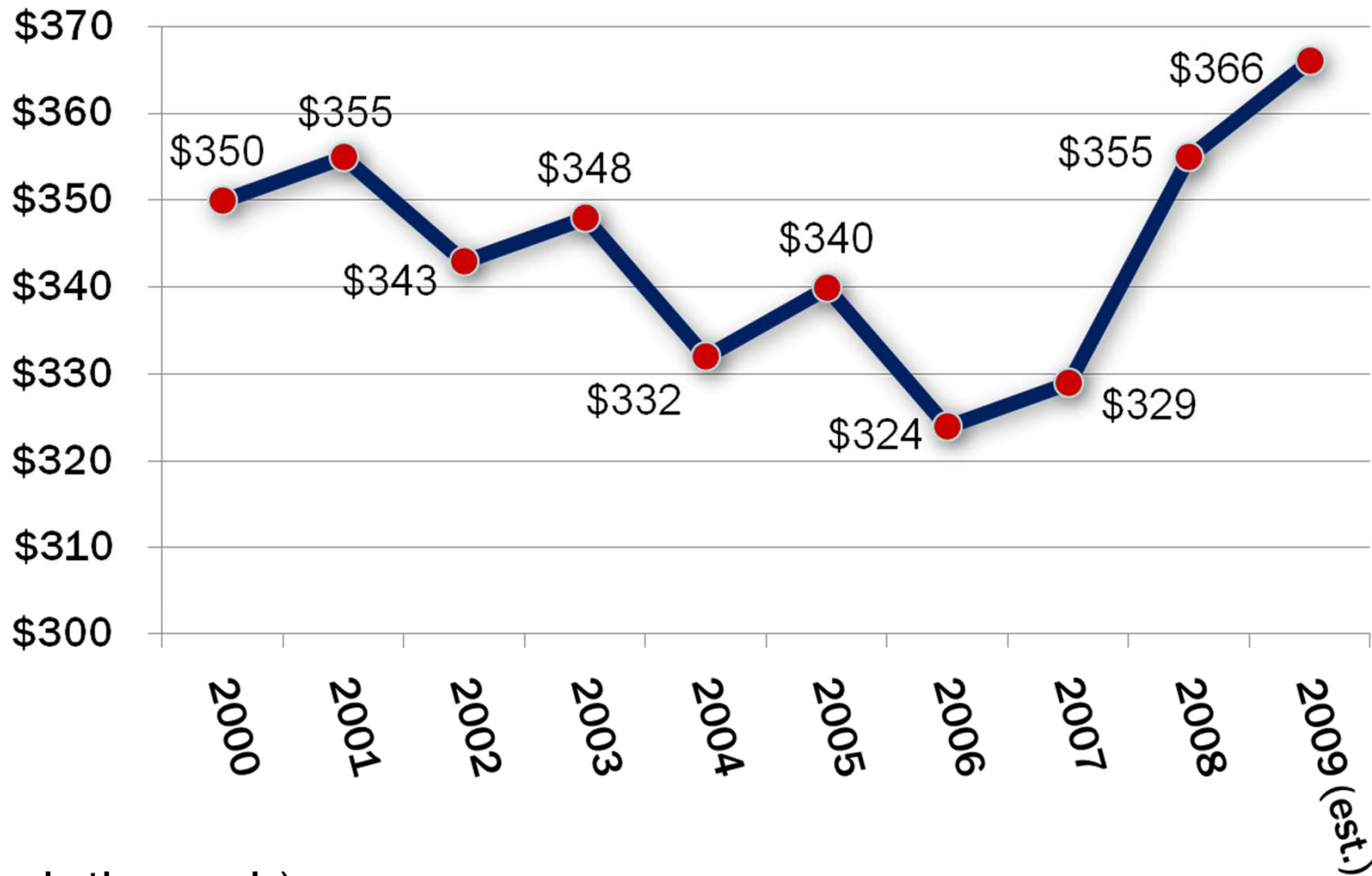
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- NCI RPG policies
  - 3% above current levels for Type-2 (last year's grant award, in most cases) for competing continuing grants
    - Unless PI requested less than 3% or peer review recommended less than 3%
  - 5% above current levels for grants recommended for 7 modules or fewer
  - ~17 % cut from Type-1 level requested (or approved by peer review)

# Competing RPGs



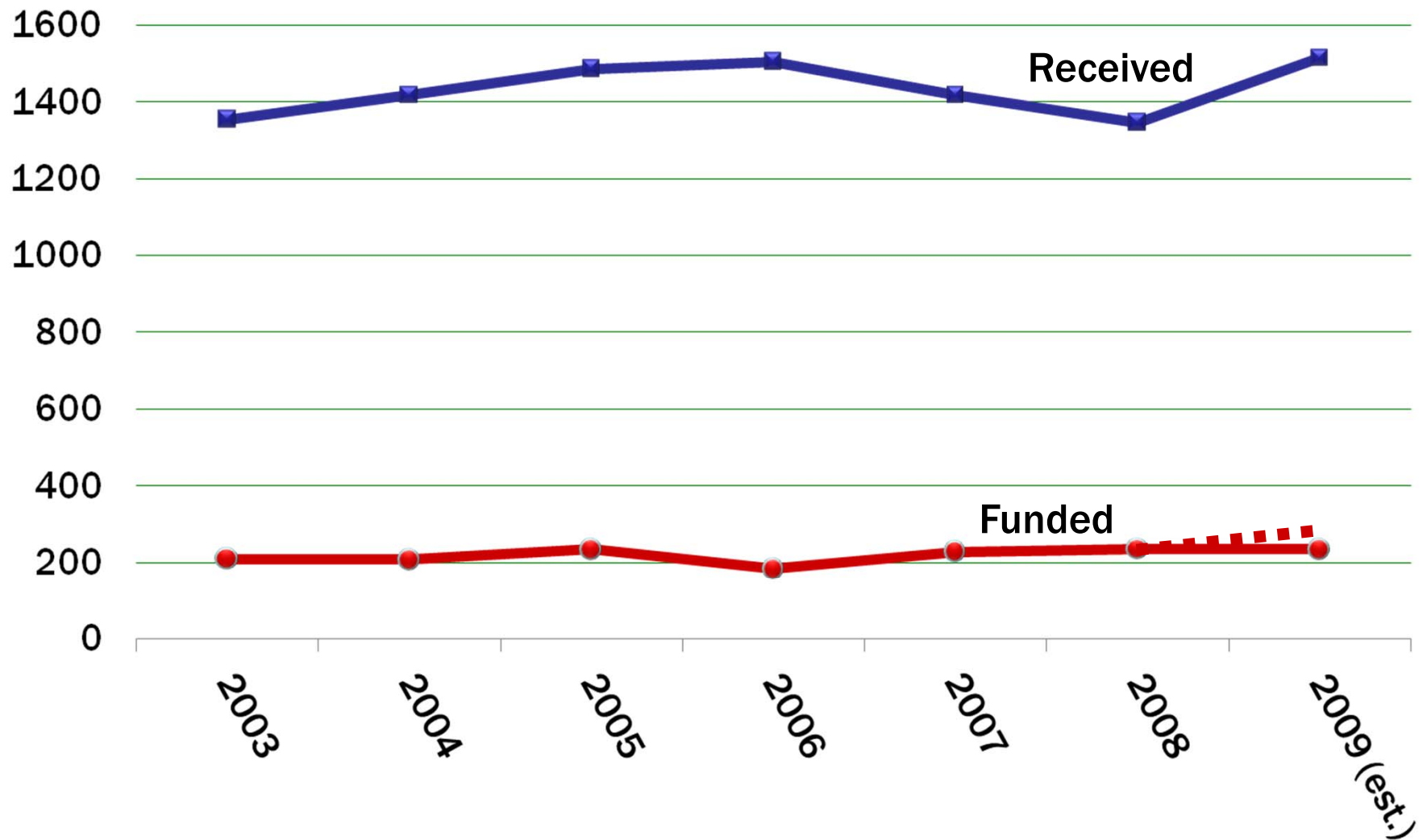
# Average Cost of Competing RPGs



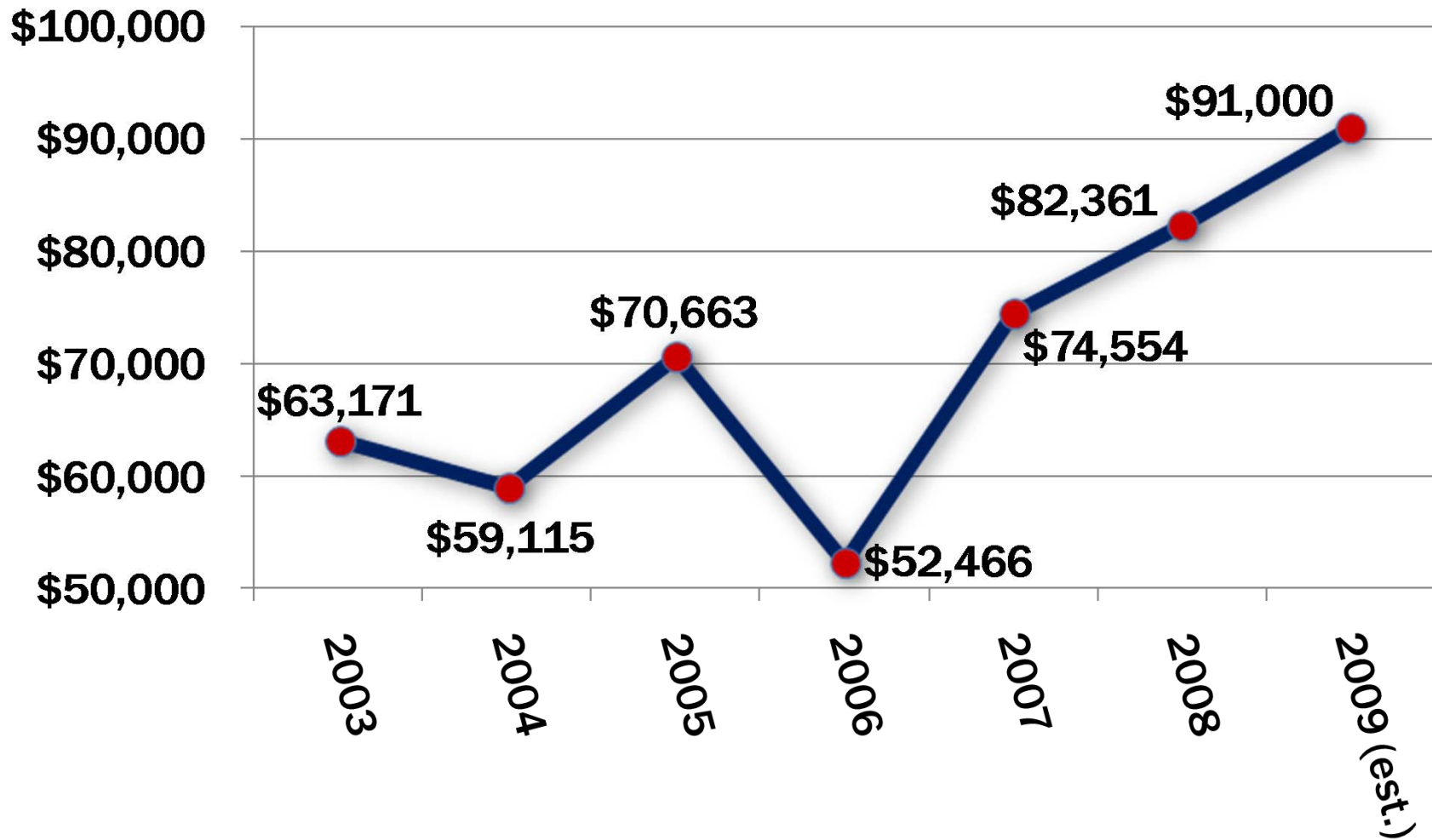
(Dollars in thousands)



# \*R01 First-time Investigator Awards



# \*R01 Awarded Dollars



(Dollars in thousands)

# New NCI-Designated Cancer Centers

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University of Maryland  
**Marlene and Stewart  
Greenebaum Cancer Center**



**Kevin J. Cullen,  
MD  
Director**



Medical University of  
South Carolina  
**Hollings Cancer Center**



**Andrew S.  
Kraft, MD  
Director**



Emory University  
**Winship Cancer  
Institute**



**Brian Leyland-  
Jones, MD, PhD  
Director**



## Cancer Centers designated in 2007:

- Stanford Comprehensive Cancer Center
- Dan L. Duncan Cancer Center, Baylor

# FY2010 President's Budget Proposal

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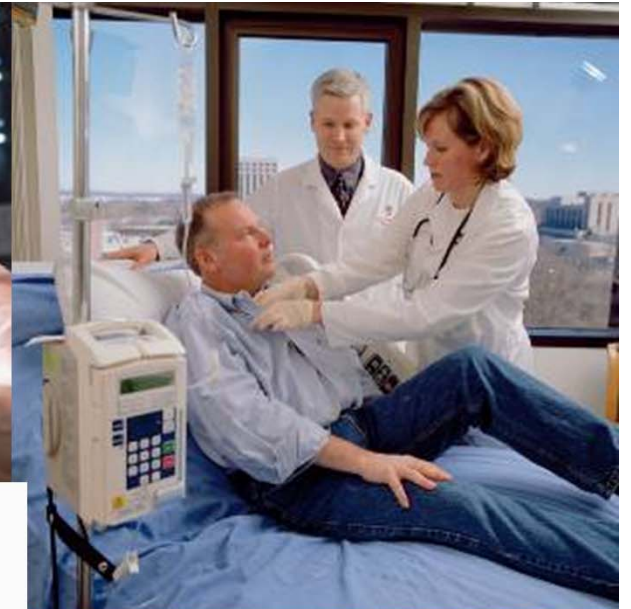
- “The President proposes to invest over \$6 billion for cancer research across NIH, reflecting the first year of an eight-year strategy to double cancer research by FY 2017.”
  - \$5.15 billion for NCI
    - ~3.5% (\$181 million) increase

# Developing the Trans-NIH Cancer Strategic Plan

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- **Drs. Niederhuber and Katz (NIAMS) appointed by NIH to chair committee to develop plan**
- **All ICs conducting cancer research submitted information (24 of 27 NIH ICs)**
- **Report currently being written and edited**
- **To be submitted to NIH June 24**

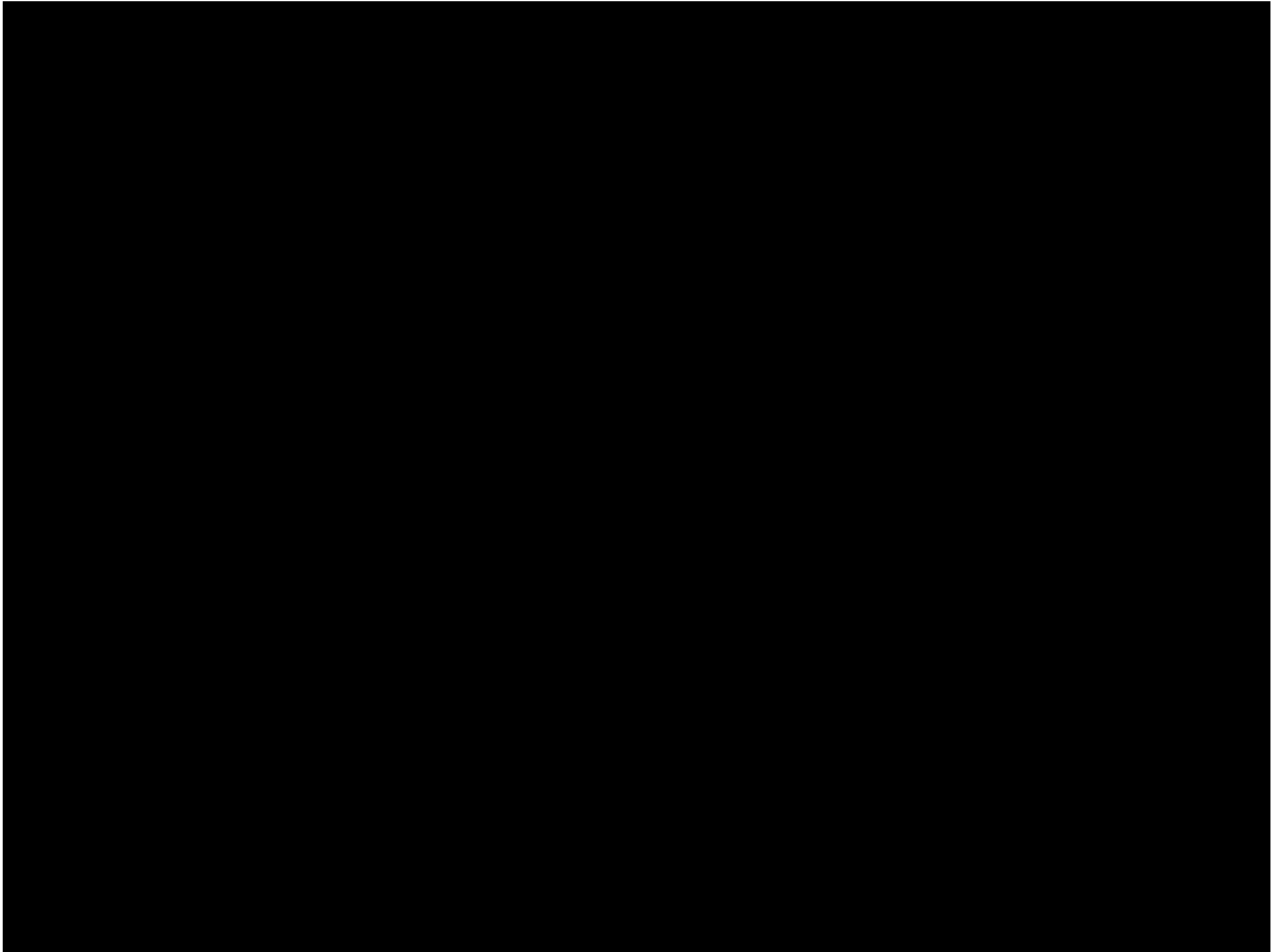




[www.cancer.gov](http://www.cancer.gov)





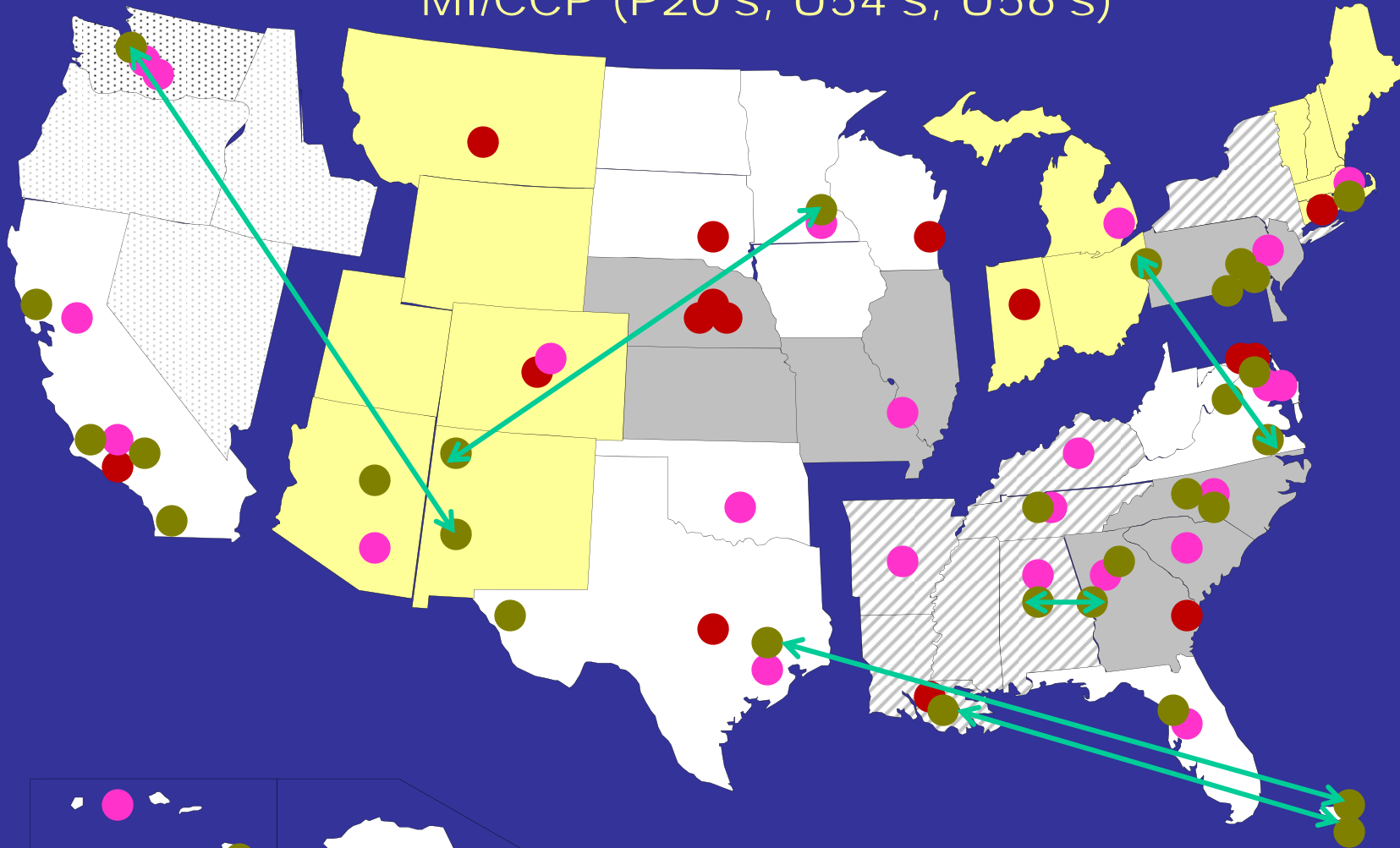


# Areas of Concern

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- **Two communities that are less than happy**
  - **Cancer Centers**
  - **Cooperative Groups**

NCCCP pilot sites  
CNP's  
MI/CCP (P20's, U54's, U56's)



- - CNP
- - NCCCP
- - MI/CCP

# FY09 Centers Budget

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- **FY09 centers budget ~\$271 million**
  - ~\$10 million (4%) increase
- **Currently funding 65 centers**
- **Funding is premised — as in years past — on merit, as determined by priority score in peer review**

# Wish Lists for Funding

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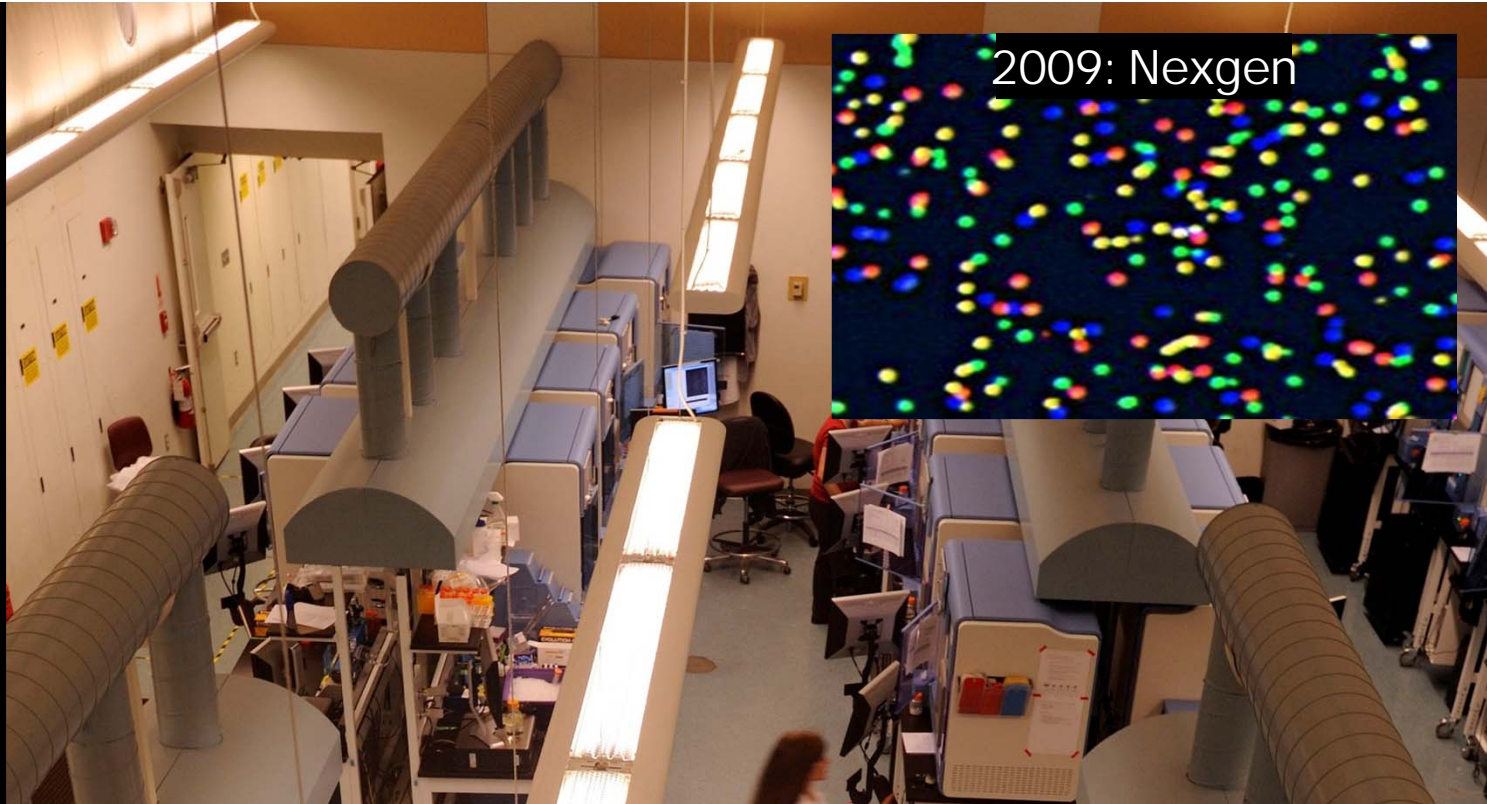
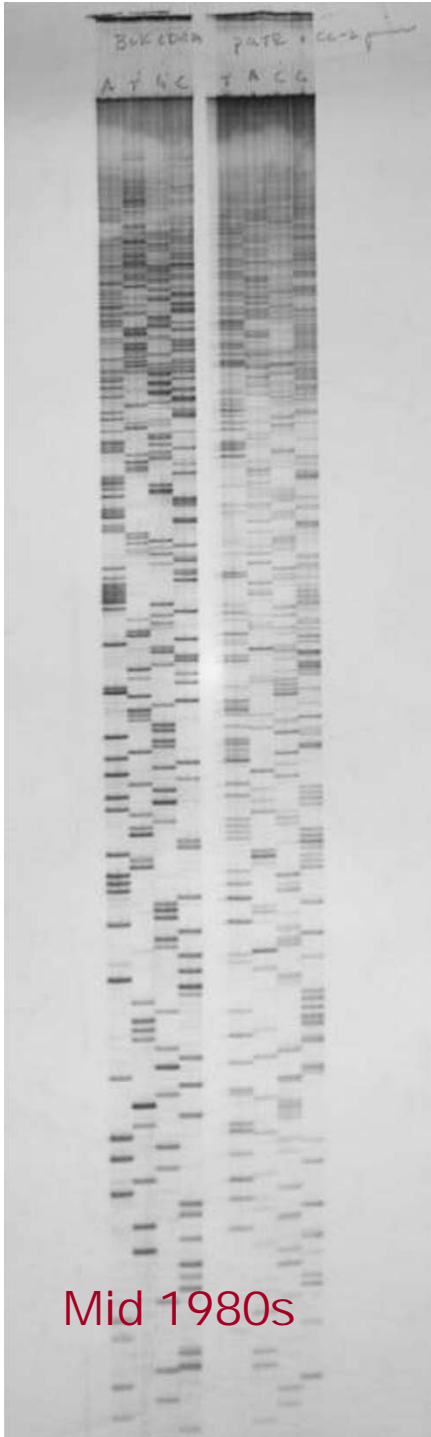
- At Executive Committee retreat, each division, office, or center presents requested increases
- EC members prioritize the NCI requests
- List is ranked, based on combined scores
- NCI director uses prioritized list and presentation information to make allocation decisions

# Accountability and Transparency

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**“And we expect you, the  
American people, to  
hold us accountable for  
the results.”**

**President Obama**

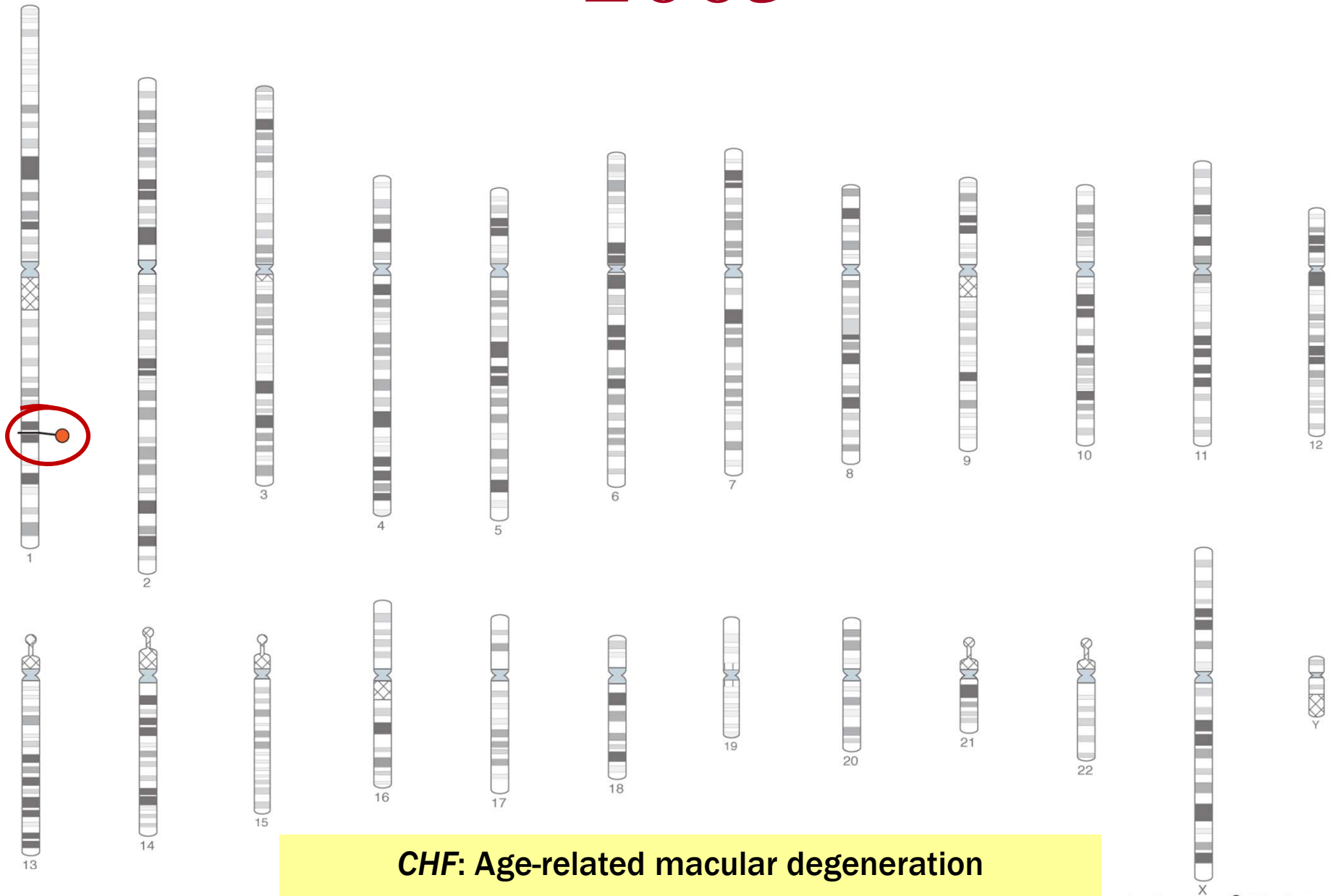


# An Unprecedented Era of Discovery

A transformation in medicine

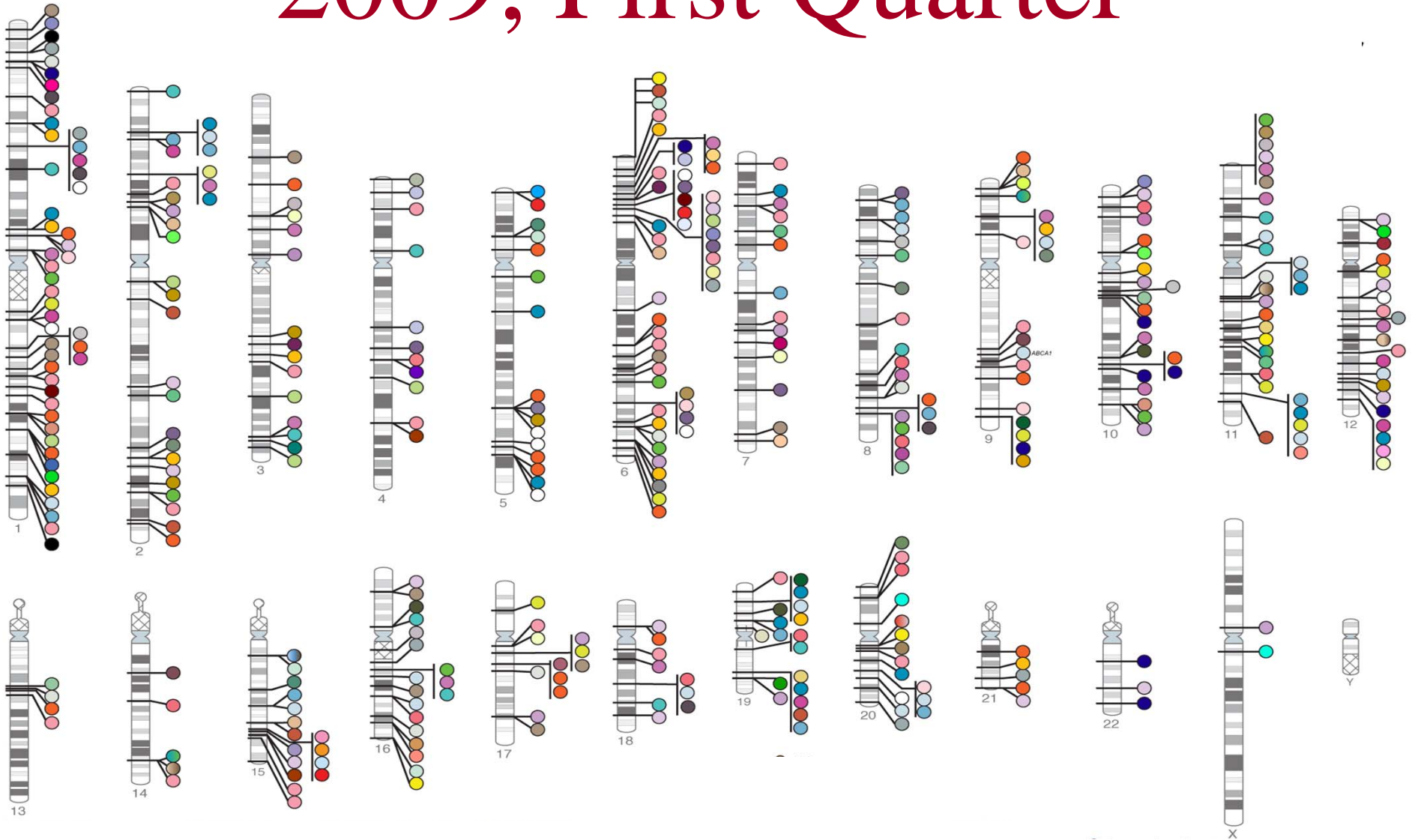


# 2005



**CHF: Age-related macular degeneration**

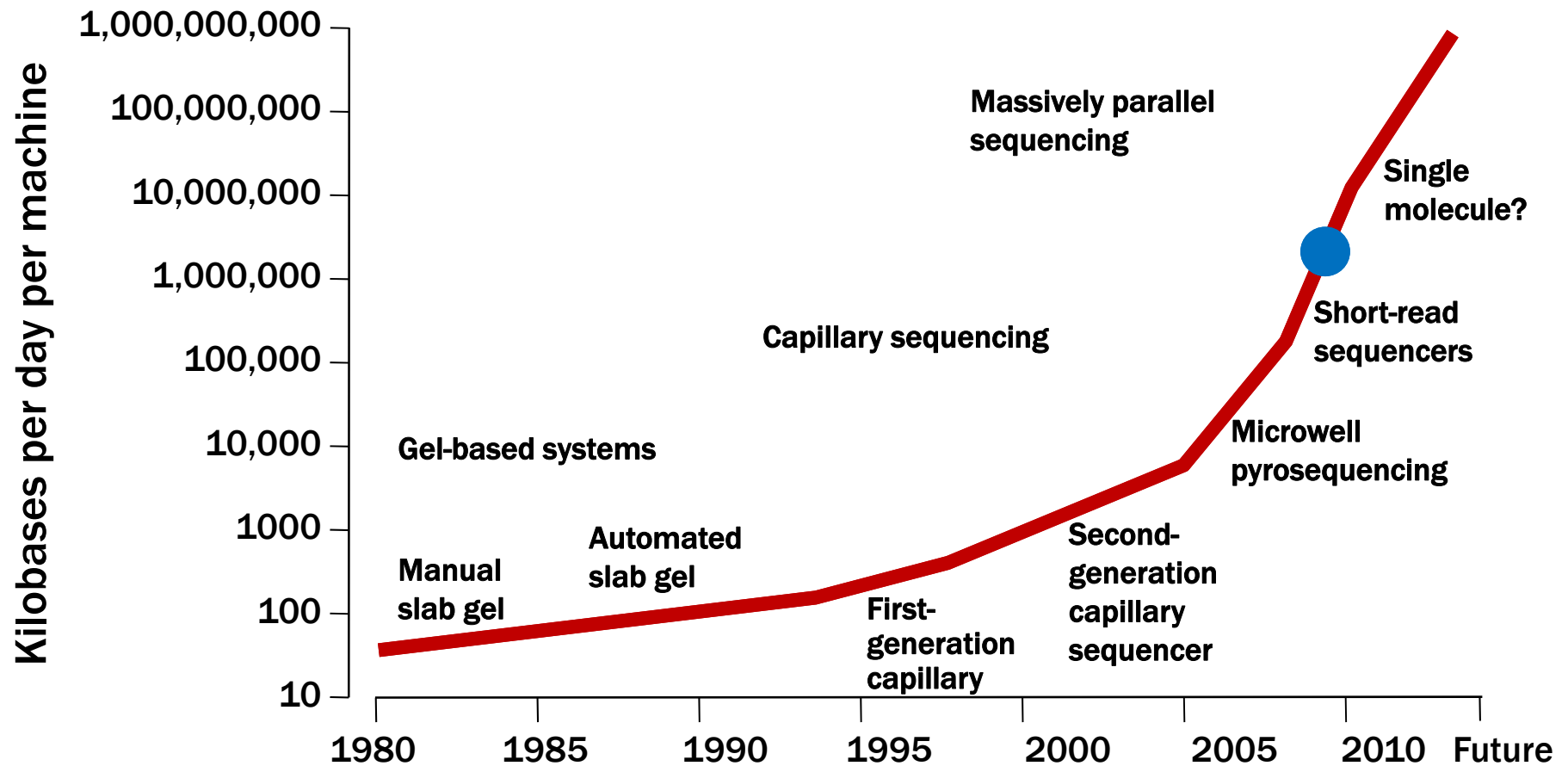
# 2009, First Quarter



Currently, more than 400 loci associated with disease

# Sequencing Output

(currently 1-2 Gb per machine per day)



# Cost of Sequencing

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ABI 3730XL



454



Illumina



ABI SOLiD



Cost of human genome (30x coverage)

**\$100,000 by late 2009**

**\$30,000 by late 2010**

- **Costs in samples; cost in analysis**
- **Optimizing density**
- **Whole-genome vs. whole-exome**

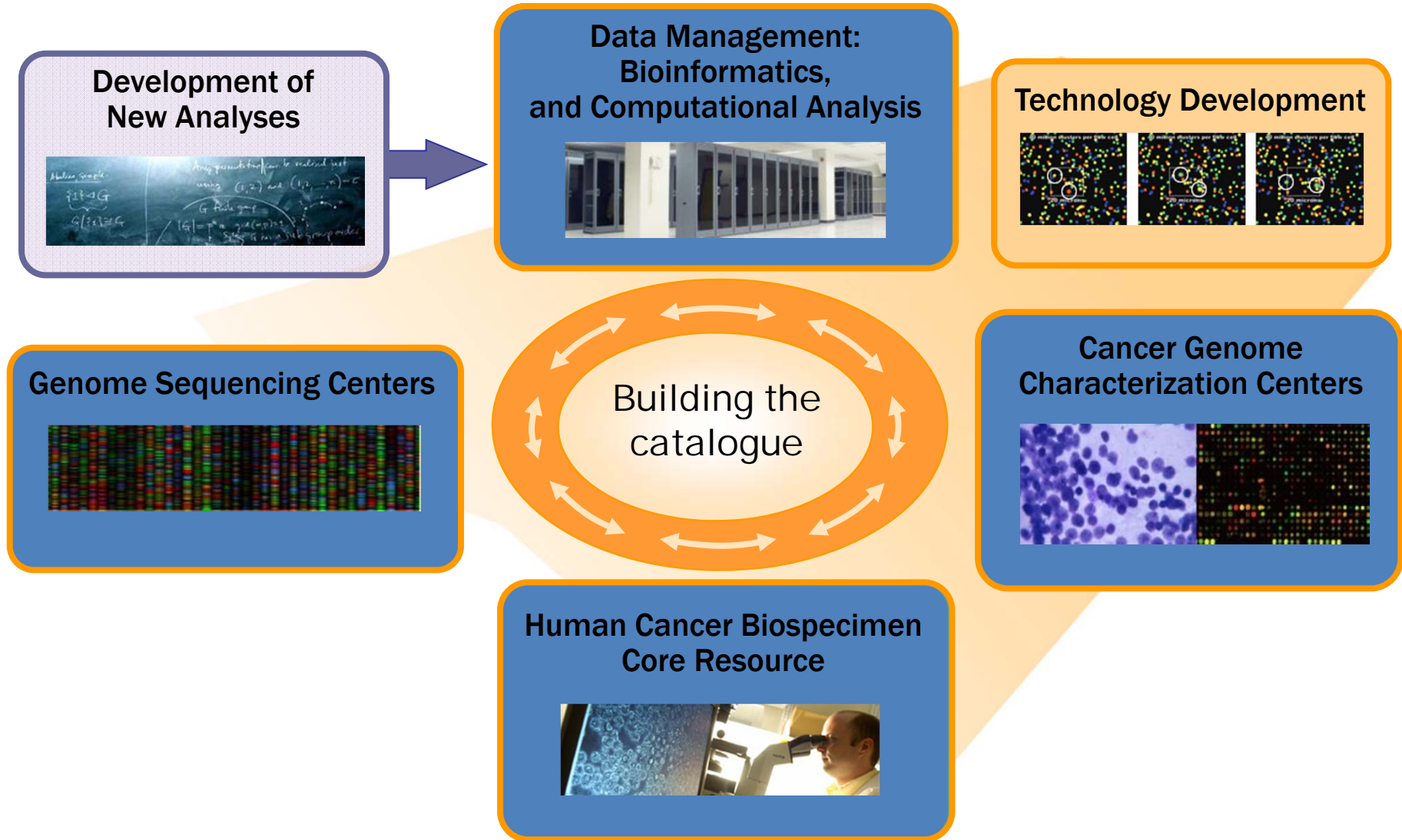
# Building the Catalogue

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- **NexGen sequencing**
  - \$1,000 genome within 5 years
- **Germline regions predict risk**
  - SNPs, large cohorts, CGEMS
- **High throughput screens for RNAi**
  - Profiling, epigenetic regulation
- **Systemically monitor protein translation**
  - Ribosome profiling based on deep sequencing
- **Single circulating cell capture and analysis**
  - Microfluidics, nanotechnology



# The Cancer Genome Atlas Pilot Network (TCGA)



# The Cancer Genome Atlas

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- Pilot includes glioblastoma, ovarian and lung cancers
- Glioblastoma (80 percent tumor purity, with matched normal controls)
  - Genomic analysis of 214 patient cases; 168 patient cases sequenced
  - Identified NF1, Erbb2, and PIK3R1 as highly associated with GBM (EGFR, p53)
  - At least 4 subtypes emerging
- New data integration and analysis underway





# TCGA: Ovary

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- Genomic analysis of 238 patient cases to date
- Six whole genomes and five exomes sequenced by next generation sequencing methods
- P53 mutated (some multiple mutations) in 100% of ovarian cancers studied
- BRCA2 highly associated with ovarian cancer samples
- Extraordinarily large number of chromosomal rearrangements associated with ovarian cancer

# Causal, But Challenging Targets

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- **Transcription factors**
- **Oncogenes (*K-RAS*)**
- **Regulatory RNAs**
- **Protein – protein interactions**
- **Chromatin**

# Facilitating Patient-Centered Cancer Research

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**Changing how we get the  
latest therapies to cancer  
patients is not a goal.**

**It is a necessity.**

# 21st Century Drug Development

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## Creating the repair manual

- Derive a functional understanding of the causal defect/dependence; e.g. Wnt, P13K, NF- $\kappa$ B...
  - Distinguish passenger defects from true drivers
- Determine dependence of cancer cells and micro-environment cells on genes that are amplified, translocated, mutated or epigenetically altered
  - “Oncogene addiction”
- Find genes to which cancer cells are addicted but that are not mutated, translocated or amplified
  - “Non-oncogene addiction”

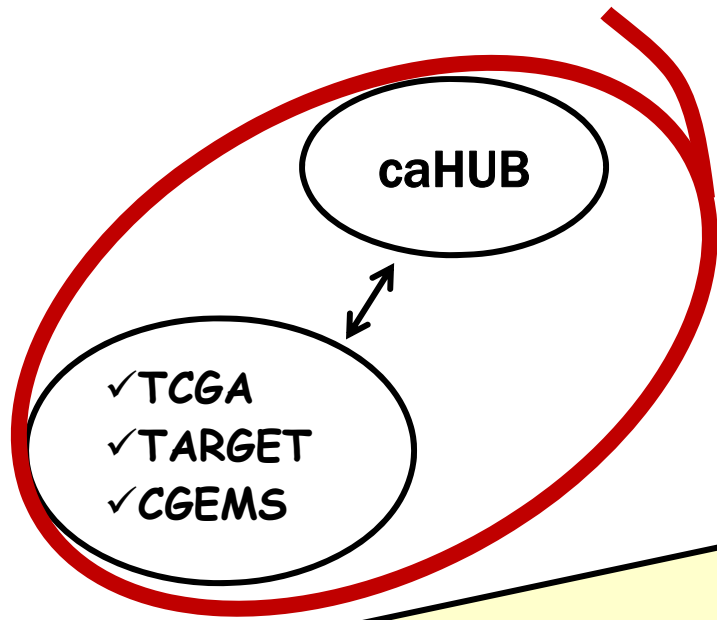
# NCI Therapeutics Platform



**Translational Science**  
From Genomics to Therapy

- Small molecules
- Biologics
- Biomarkers

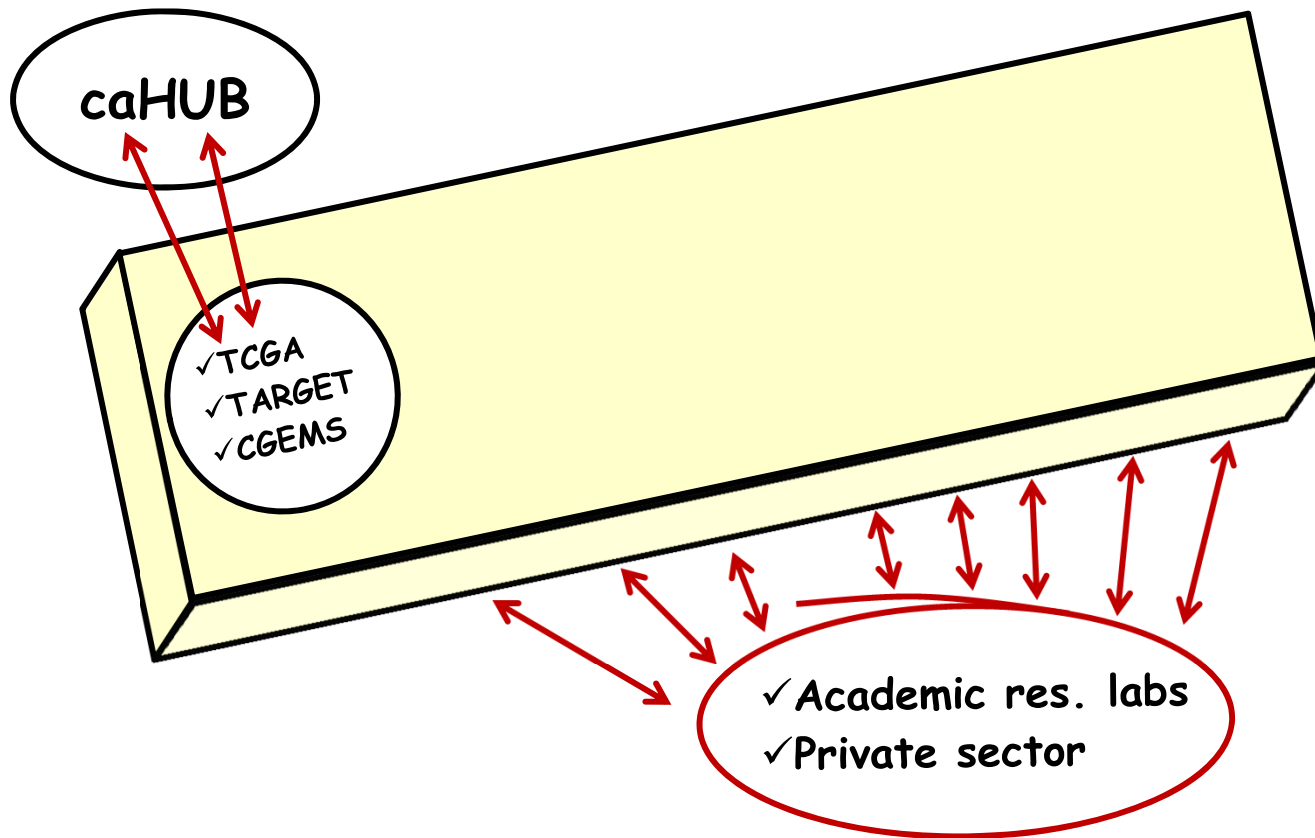
# NCI Therapeutics Platform



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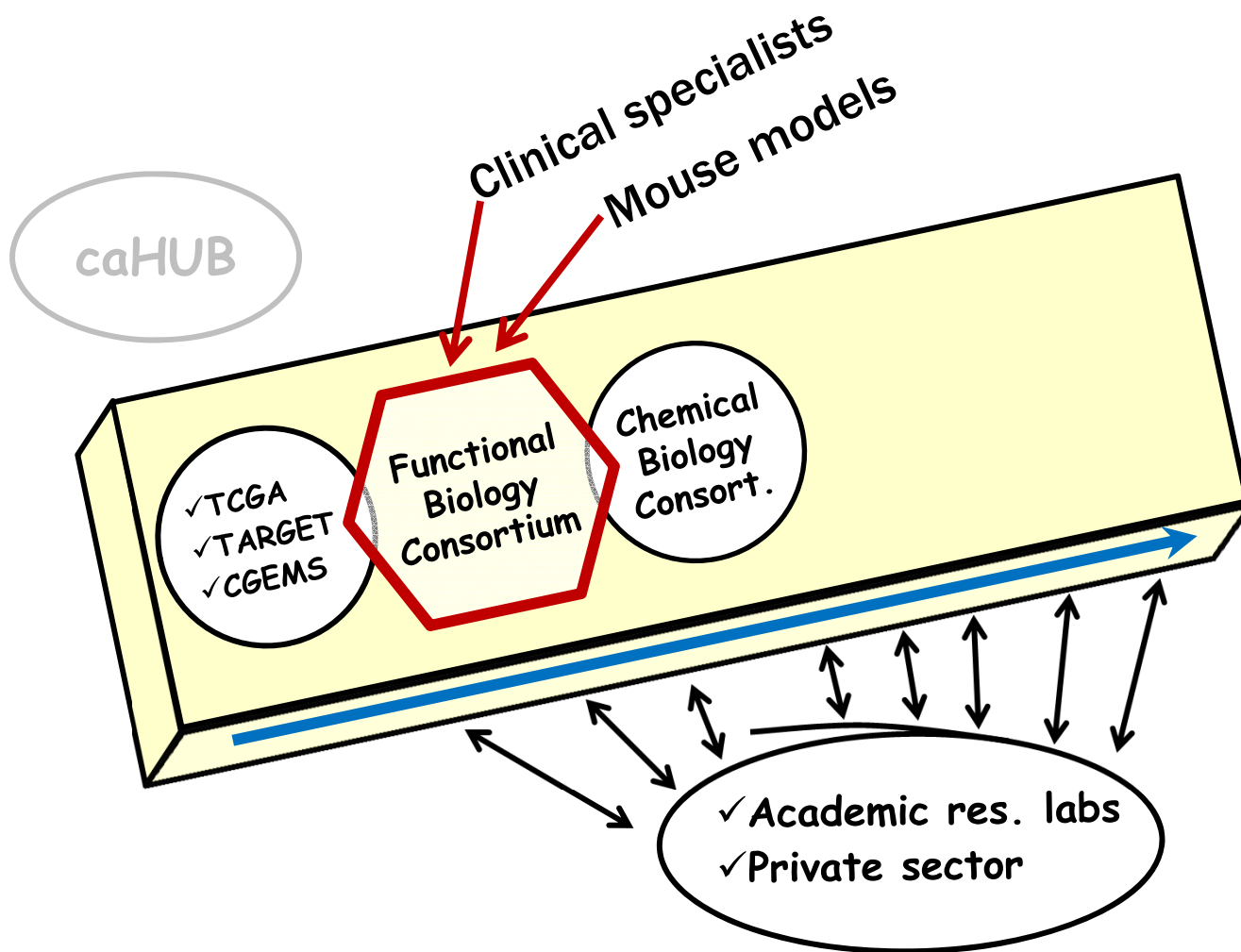
- Small molecules
- Biologics
- Biomarkers

# NCI Therapeutics Platform

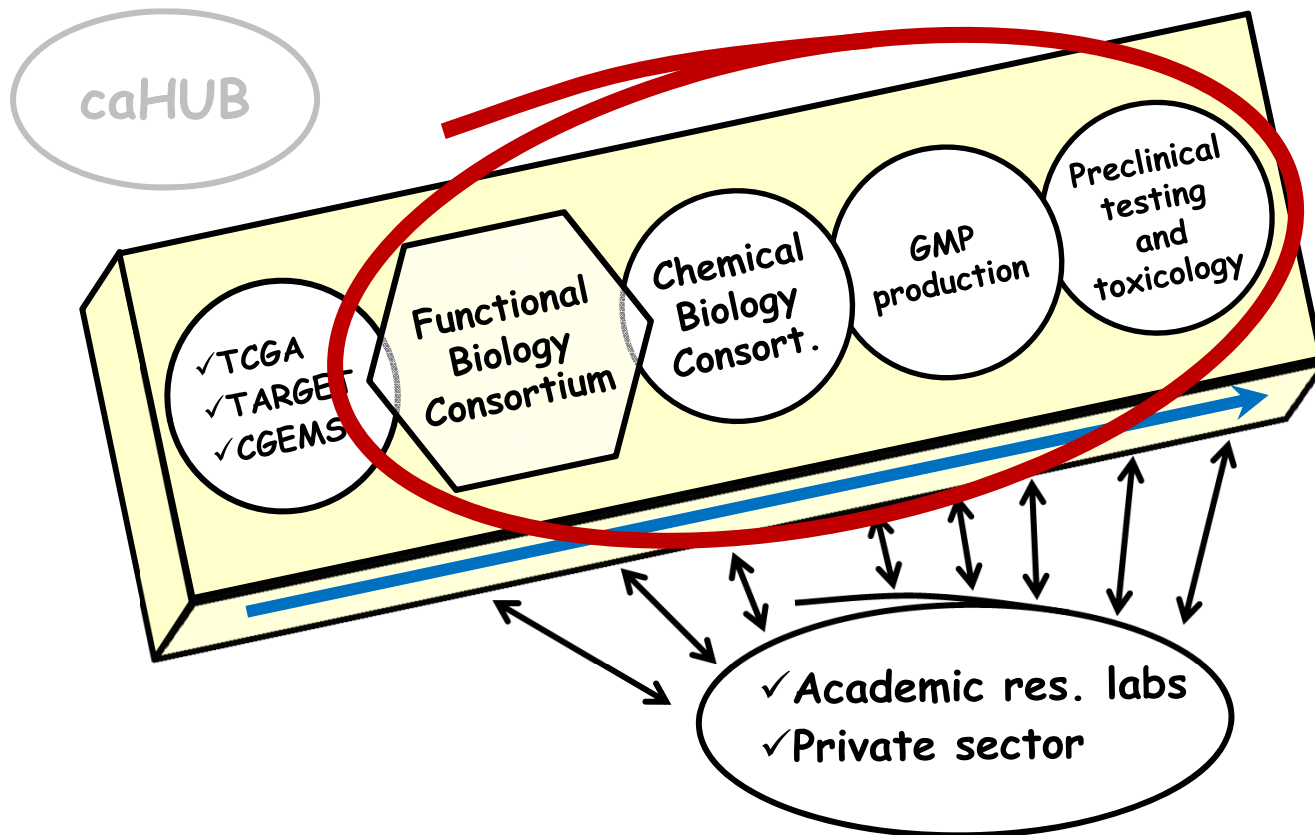




# NCI Therapeutics Platform



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# NCI Therapeutics Platform

## CLOUD COMPUTING

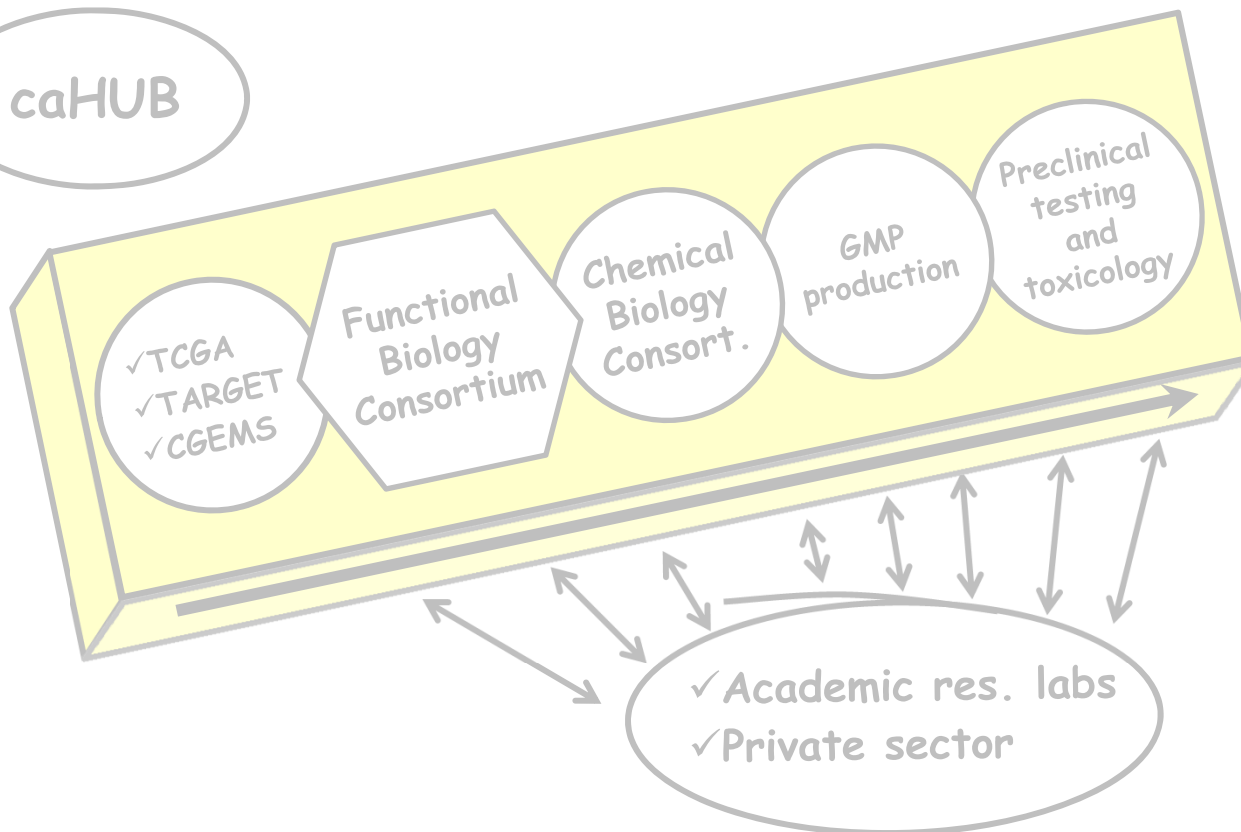
- ✓ Patient data
- ✓ Cancer electronic health record
- ✓ Data management, storage and analysis
- ✓ Science data (national cohort)

↕ Patient selection

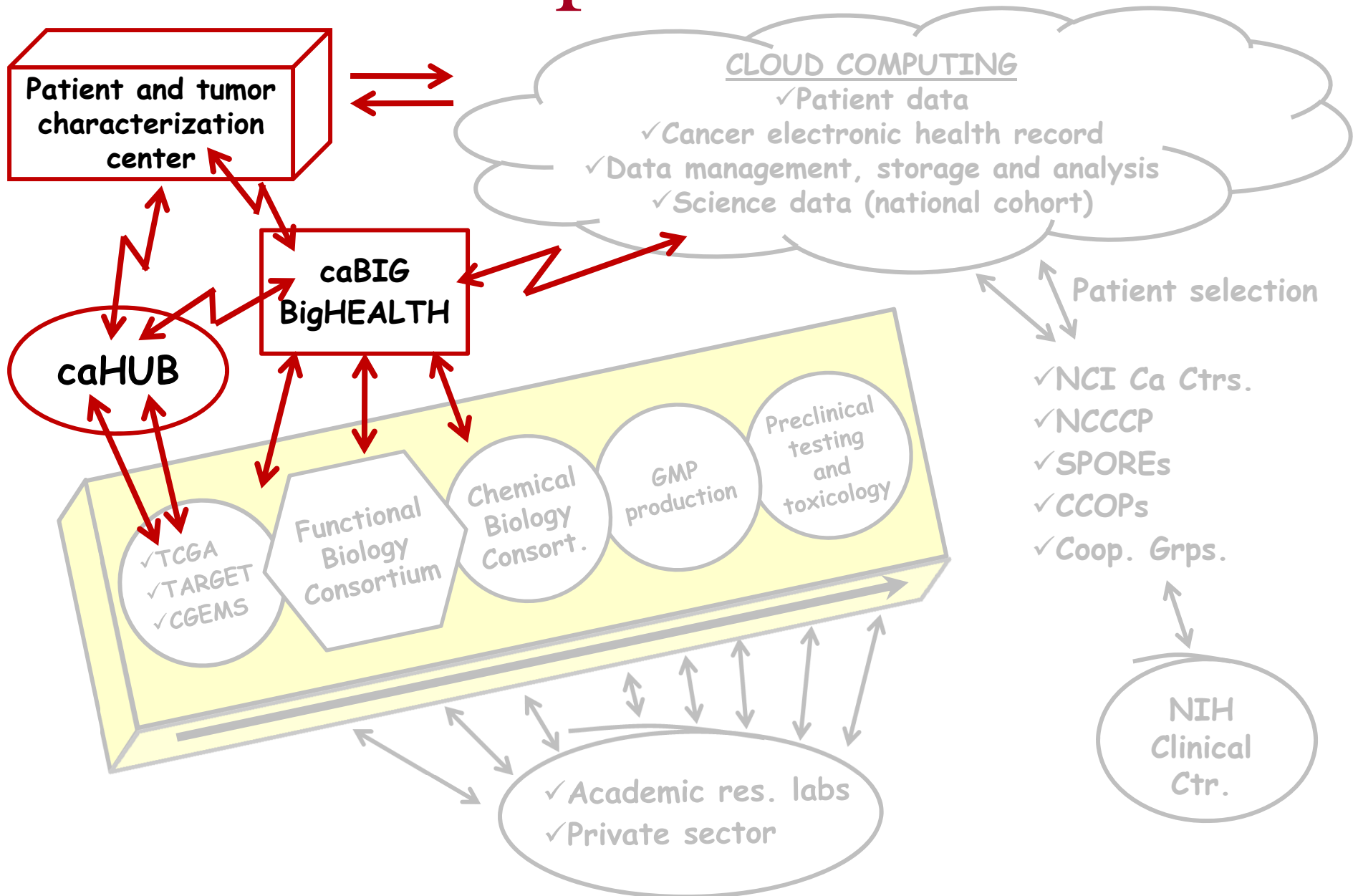
- ✓ NCI Ca Ctrs.
- ✓ NCCCP
- ✓ SPOREs
- ✓ CCOPs
- ✓ Coop. Grps.

↕  
**NIH  
Clinical  
Ctr.**

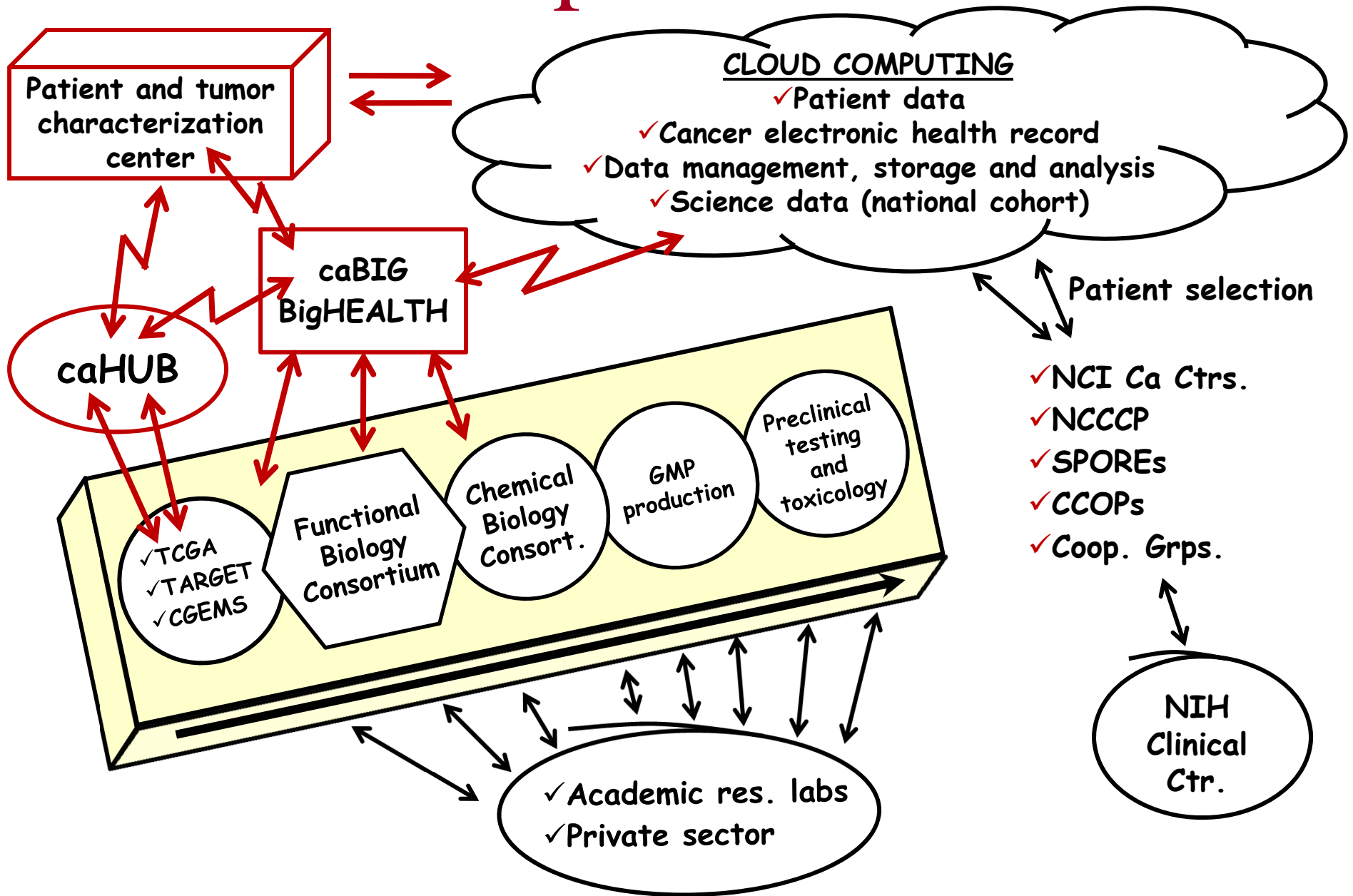
caHUB



# NCI Therapeutics Platform



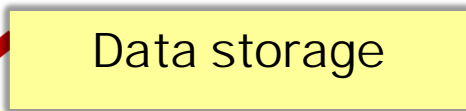
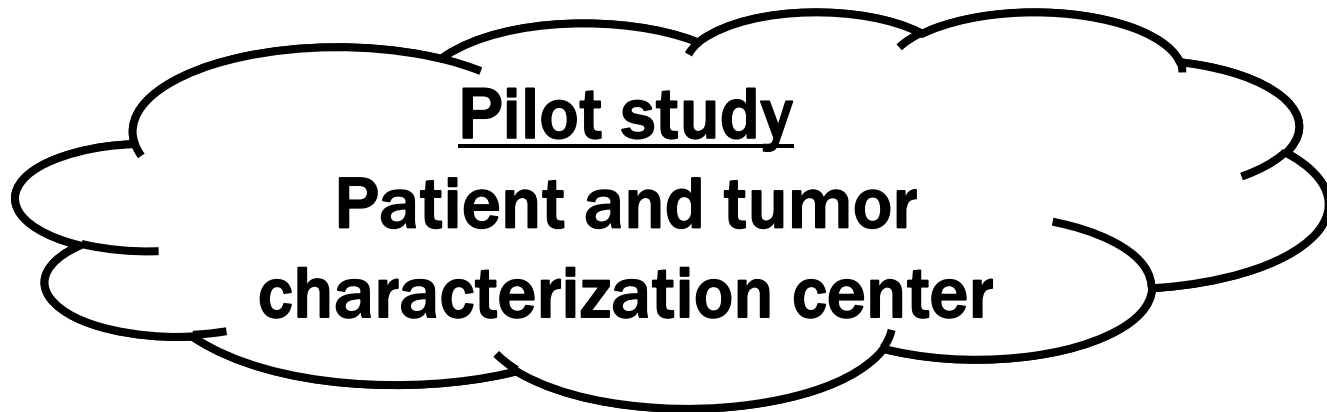
# NCI Therapeutics Platform



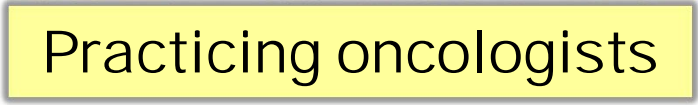
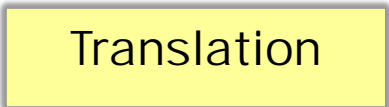
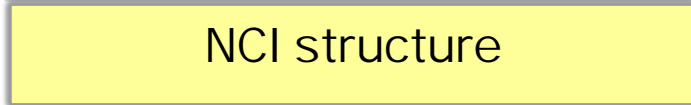
# Personalized Cancer Medicine Hypothesis

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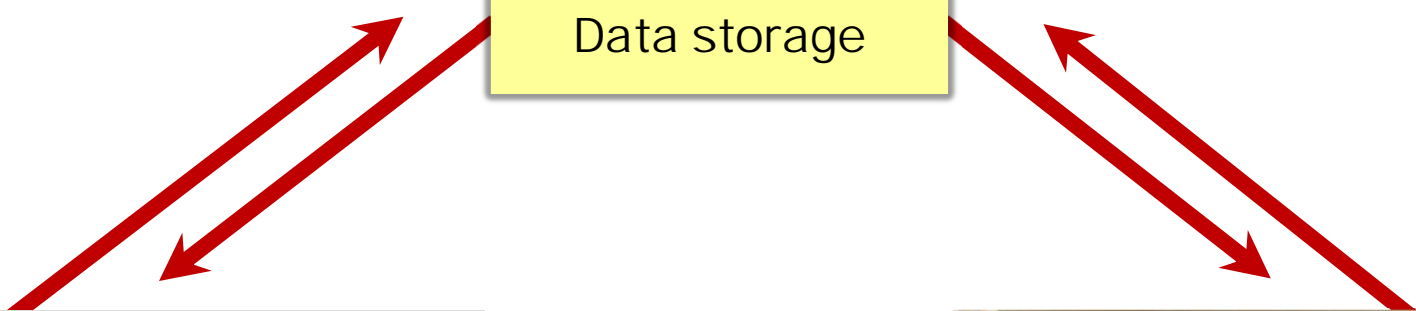
- Documentation of drug target's expression/activity increases the **likelihood of efficacy for a drug designed to extinguish the target**
  - e.g., HER2/herceptin in breast cancer
- Knowledge of the target's signaling circuitry can further inform the deployment of drugs
  - e.g., K-RAS status for EGFR inhibitors



- **NCI Cancer Centers**
- **NCCCP**
- **SPOREs**
- **CCOPs**
- **Cooperative Groups**

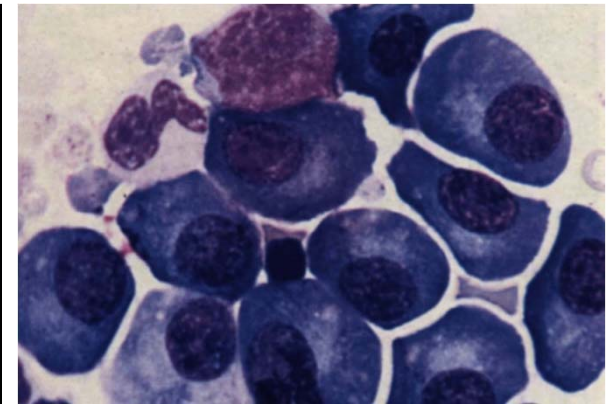
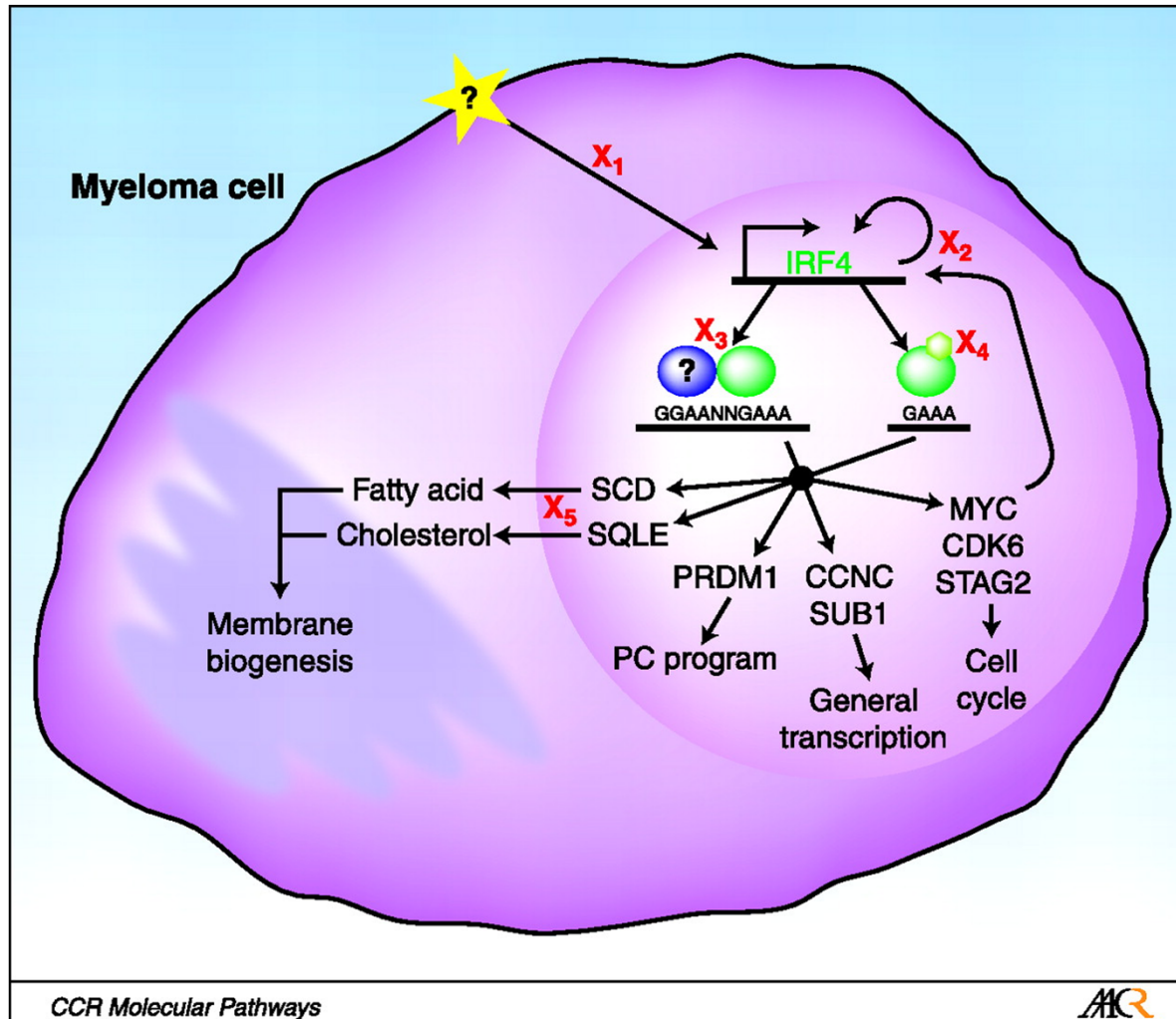


**Point of Care Diagnostics**





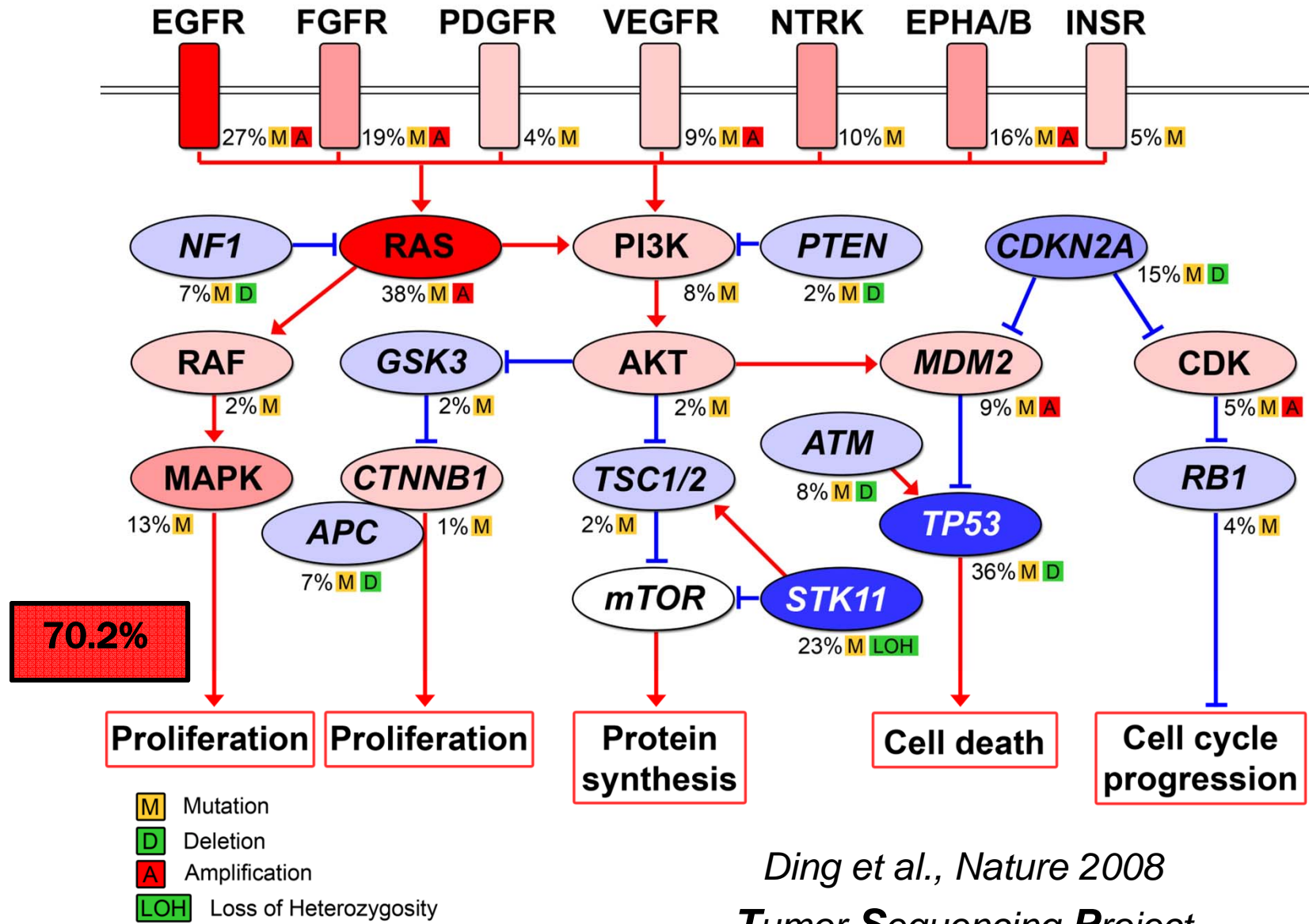
# IRF4 Inactivation in Multiple Myeloma



- Myeloma cells are addicted to IRF4 expression
- Even a modest decrease in IRF4 levels leads to cell death

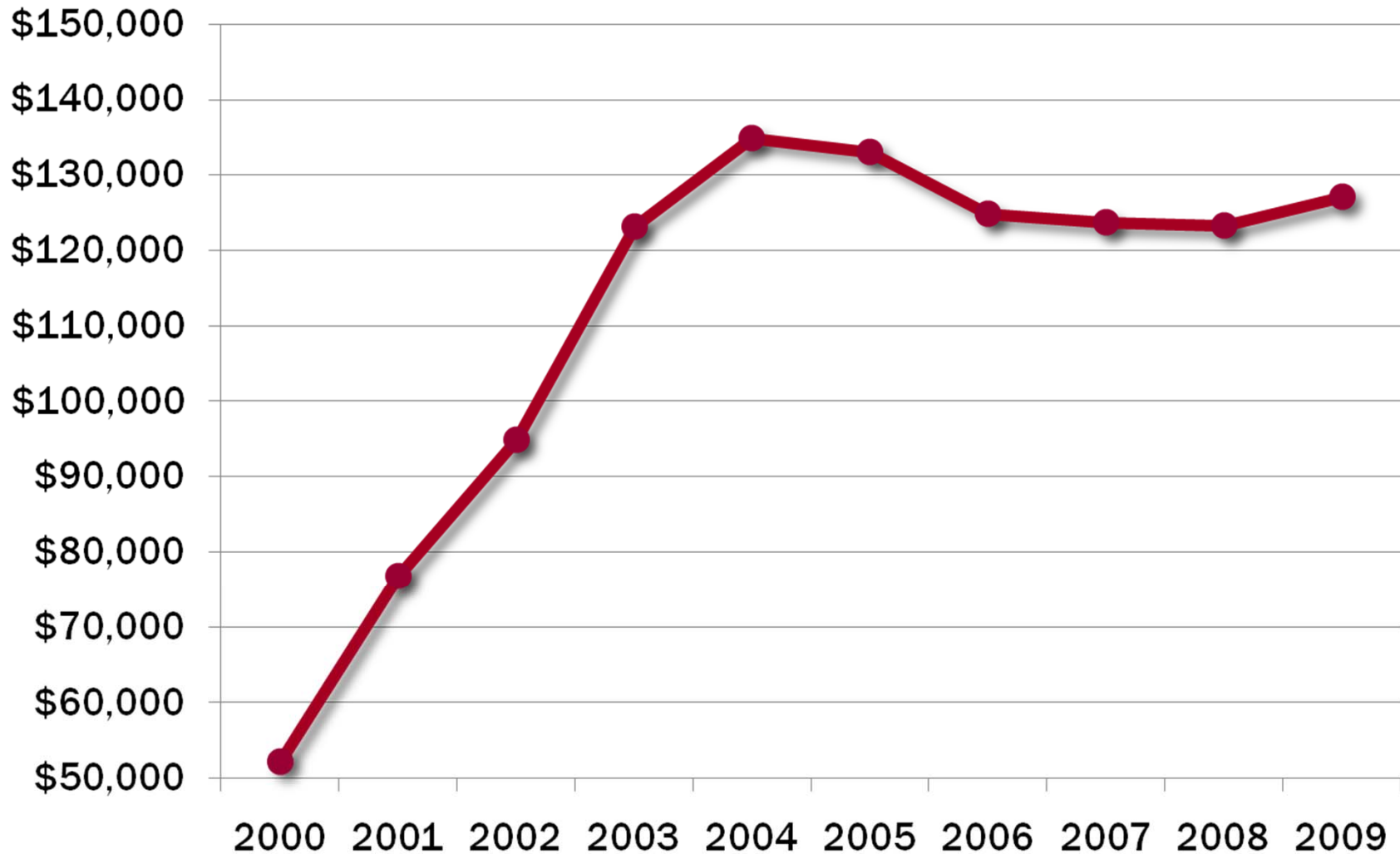


# Altered Core Signaling Pathways in Lung Cancer



Ding et al., Nature 2008  
 Tumor Sequencing Project

# SPOREs Funding



(Dollars in thousands)

# Summary

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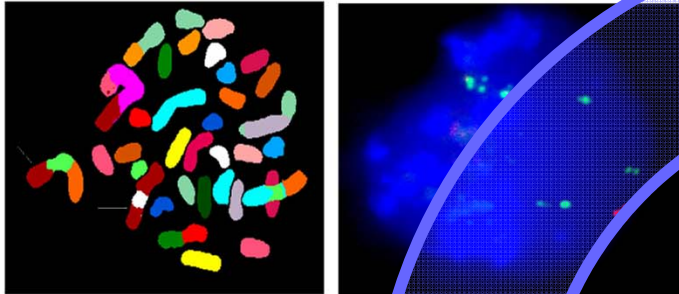
- Whole genome sequencing a part of all cancer research in 5 years; a part of all patient care in 10 years
- Personal genomics will lead to a transformation of medicine
- Web-like connectivity of information is key to achieving personalized medicine
- Government and the private sector must seek new types of collaborations

# Atlas = integration...

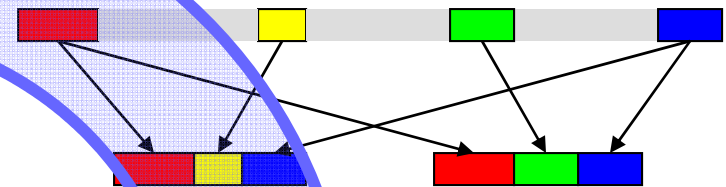
THE CANCER GENOME ATLAS



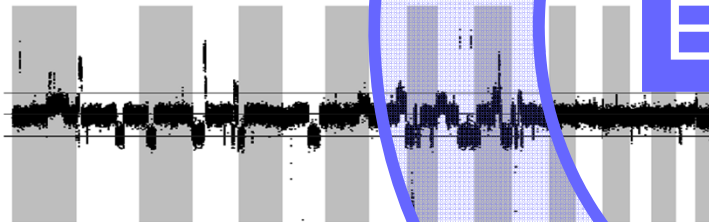
Aneuploidy; Re-arrangement;  
Translocation



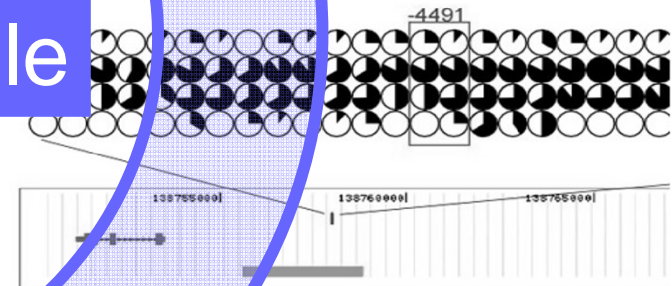
Gene Splicing Alterations



Copy number aberrations

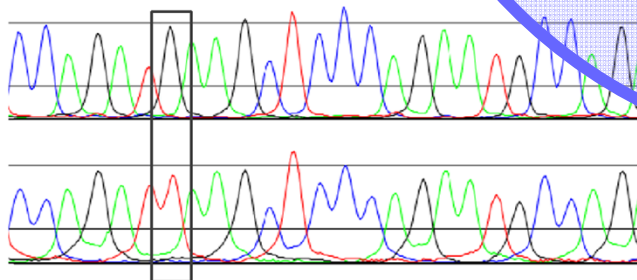


Methylation or  
histone modification

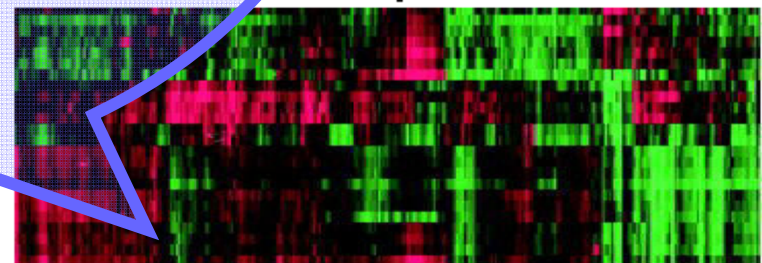


Each Sample

Somatic mutations



Altered expression



Adopted from Cameron Brennan

# ARRA Funding to Cancer Centers

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- **69% (\$35,963,666) of NCI ARRA funds awarded to date have gone to investigators at institutions home to NCI-designated Cancer Centers**
  - **63% of all grants awarded**



# Obama Administration

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**Kathleen Sebelius**, Secretary of Health and Human Services



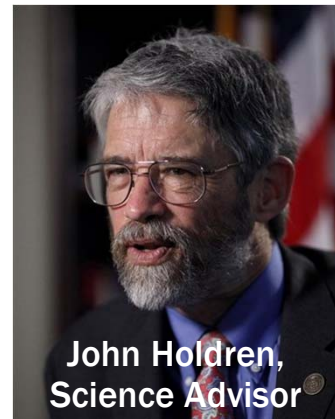
**William V. Corr**, HHS deputy secretary



**Dr. Thomas Frieden**, director, CDC



**Dr. Margaret Hamburg**, FDA commissioner

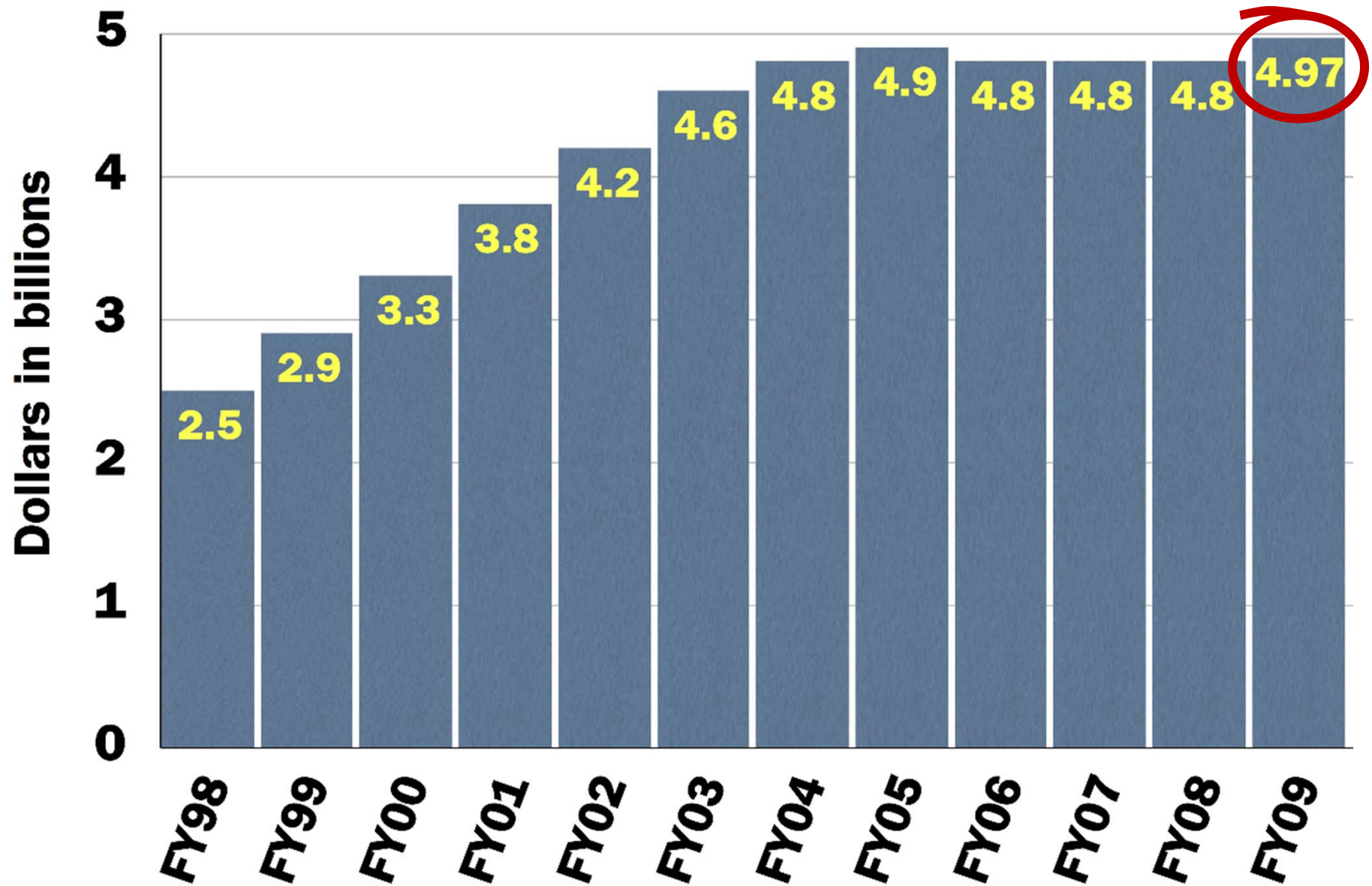


**John Holdren**, Science Advisor

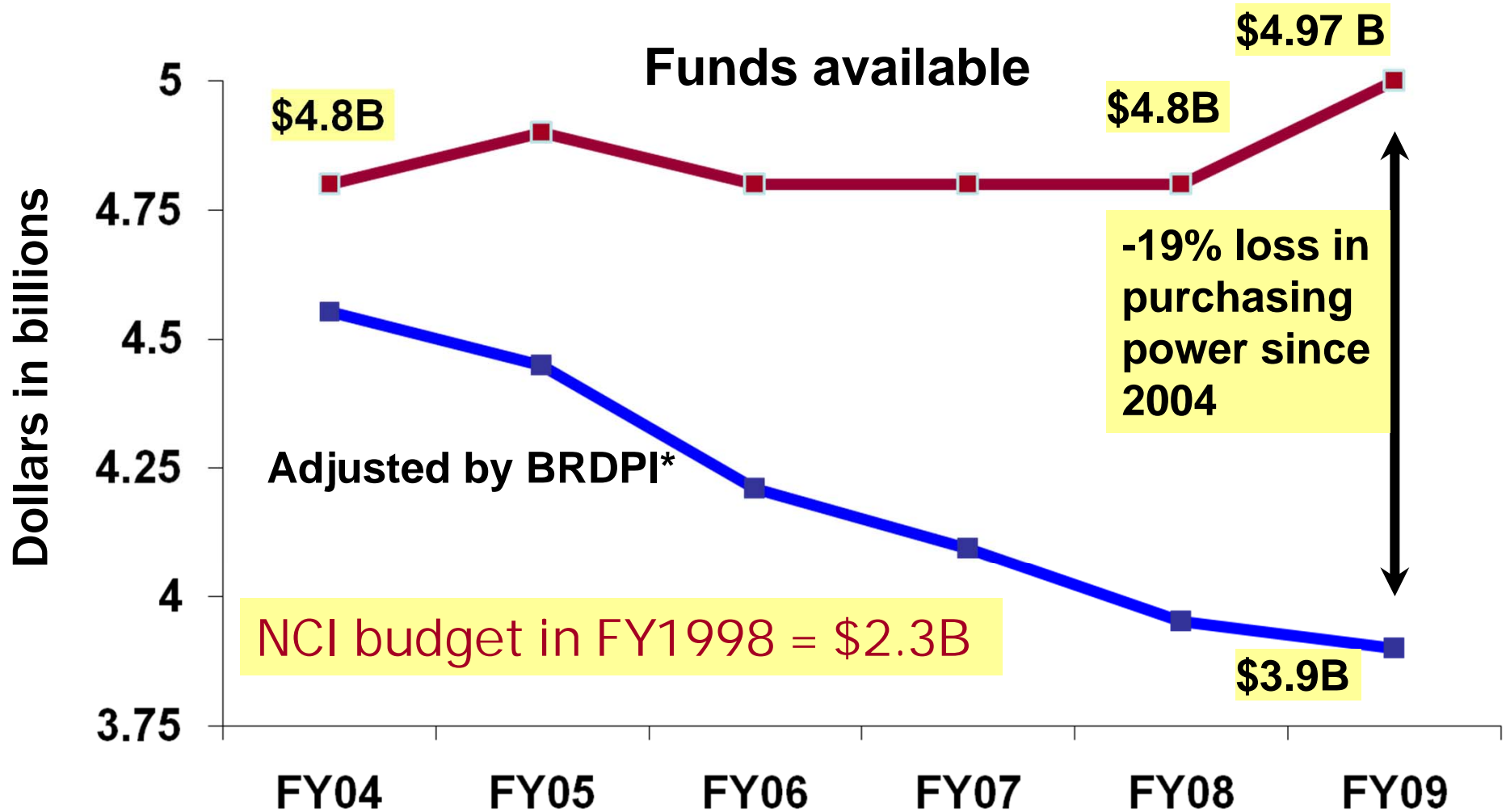


**Steven Chu**, Energy Sec.

# NCI's Congressional Appropriations



# NCI's Challenge



\* BRDPI: Biomedical Research and Development Price Index **~3.4%**  
(<http://officeofbudget.od.nih.gov>)



# NCI FY 2009 Operating Budget Development

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	<b>Amount (in thousands)</b>	<b>Percent change</b>
<b>Subtotal Available</b>	<b>\$138,326</b>	<b>2.86%</b>
<b>NIH Taps/Assessments</b>	<b>-20,000</b>	
• Rare and Neglected Diseases Initiative	<b>-4,920</b>	
	<hr/> <hr/>	
<b>Subtotal Available</b>	<b>113,406</b>	<b>2.35%</b>

# NCI FY 2009 Operating Budget Development

	<u>Amount</u> <u>(in thousands)</u>	<u>Percent</u> <u>change</u>
<b>Subtotal Available</b>	\$113,406	2.35%
<b>NCI-wide Requirements:</b>		
• Mandated Salary Increases	- 30,000	
• Rent/Lease/Utilities/Renovations Incr	- 30,000	
• Small Business Program Increase	-2,700	
• RPGs 16th percentile	-60,703	
• AIDs redirection	-15,000	
<b>NCI Director's Reserve</b>	<u>- 25,000</u>	
<b>Subtotal Available</b>	- 49,997	-1.03%

# NCI FY 2009 Operating Budget Development

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	<u>Amount (in thousands)</u>	<u>Percent change</u>
<b>Subtotal Available</b>	- \$49,997	- 1.03%
<b>Potential Recoveries/Redeployments:</b>		
• Phaseouts/Reductions/one shots from DOCs	48,059	
• Noncompeting RPGs	2,790	
• NCI-Frederick Redeployment	7,800	
	<hr/> <hr/>	
<b>Available for New Initiatives/ Expansions/Restorations</b>	<b>\$8,652</b>	+0.1%