National Cancer Institute

NCI Director's Update

Dr. John E. Niederhuber
Director, National Cancer Institute

Board of Scientific Advisors
March 8, 2009

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

NCI – March 2010

- NCI FY 2010 operating budget and the President's budget for FY 2011
- Report on National Cancer Advisory Board Working Groups
- Executive Committee Retreat

NCI FY 2010 Operating Budget Development

FY 2009 operating budget (not including ARRA) (+ARRA $6,223,448)	$4,966,931
FY 2010 appropriation	5,103,388
Difference, 2009 to 2010	+136,457
Percent change, 2009 to 2010	+2.7%

(dollars in thousands)

NCI FY 2010 Operating Budget: Infrastructure

Budget increase available	+$136,457
• Taps and assessments	-17,100
▪ Est. increase, NIH taps ($15,000)	
▪ NIH Director's 1% transfer authority (?)	
▪ HHS Secretary's transfer authority (?)	
▪ Genes, Env. & Health Initiative ($2,100)	
• Mandated salary increases (2.4%)	-21,400
• Rent/lease/utilities/renovations increase	-10,000
• Small business program increase	-2,000
• ATRF start-up and operating costs	-2,317
Subtotal available	+$83,640

(dollars in thousands)

NCI FY 2010 Operating Budget: Science

Subtotal available	+$83,640
• RFAs approved to go to BSA & publish	-156,762
▪ RPGs ($96,530)	
▪ Other research grants ($9,947)	
▪ Division controllable ($50,285)	
• NCI Director's Reserve	-25,000
• AIDS target increase	-6,248
• Latin America breast cancer pilot	-1,400
Subtotal available	-$105,770

(dollars in thousands)

NCI FY 2010 Operating Budget: Recoveries

Subtotal available	-$105,770
• Recoveries from divisions and offices	+74,155
Subtotal available	-$31,615

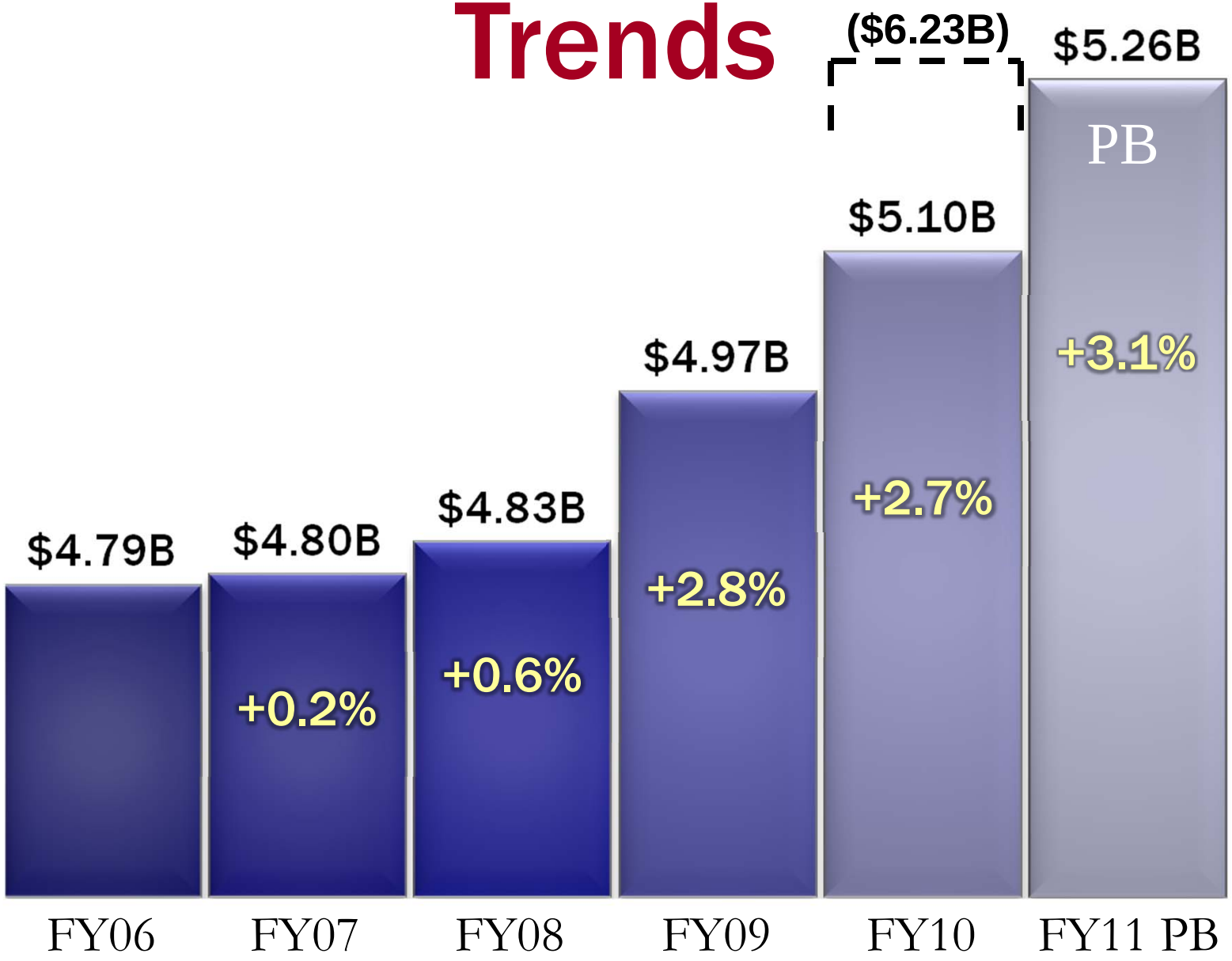
(dollars in thousands)

NCI FY 2010 Operating Budget: Additional Requests

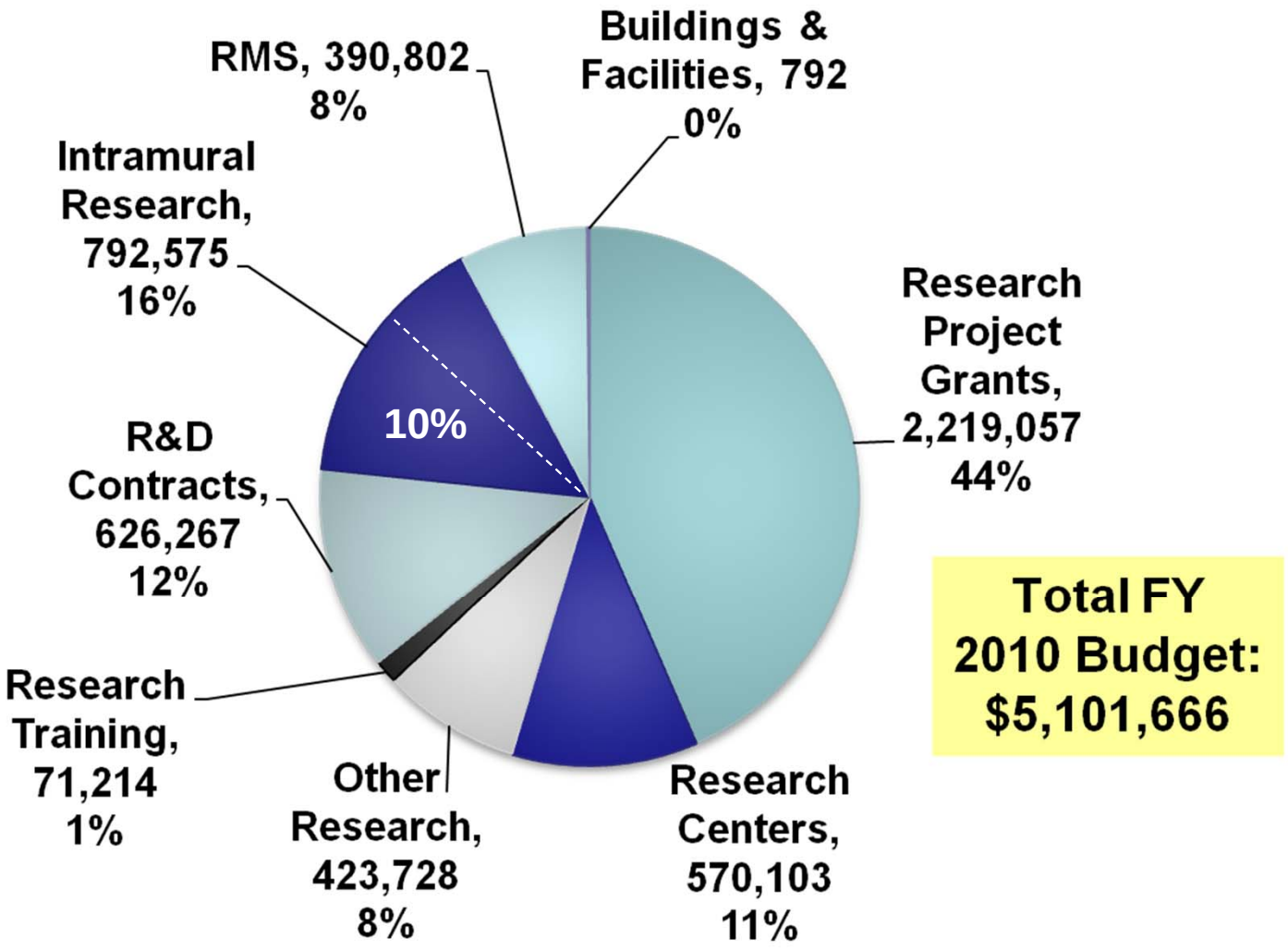
Subtotal available	-$31,615
• Division, Office, and Center requests	-265,259
▪ High priority list ($91,968)	
▪ Research ($76,077)	
▪ Infrastructure ($22,268)	
▪ Facilities ($74,946)	
Total, including all requests	-$296,874

(dollars in thousands)

NCI Appropriated Budget Trends

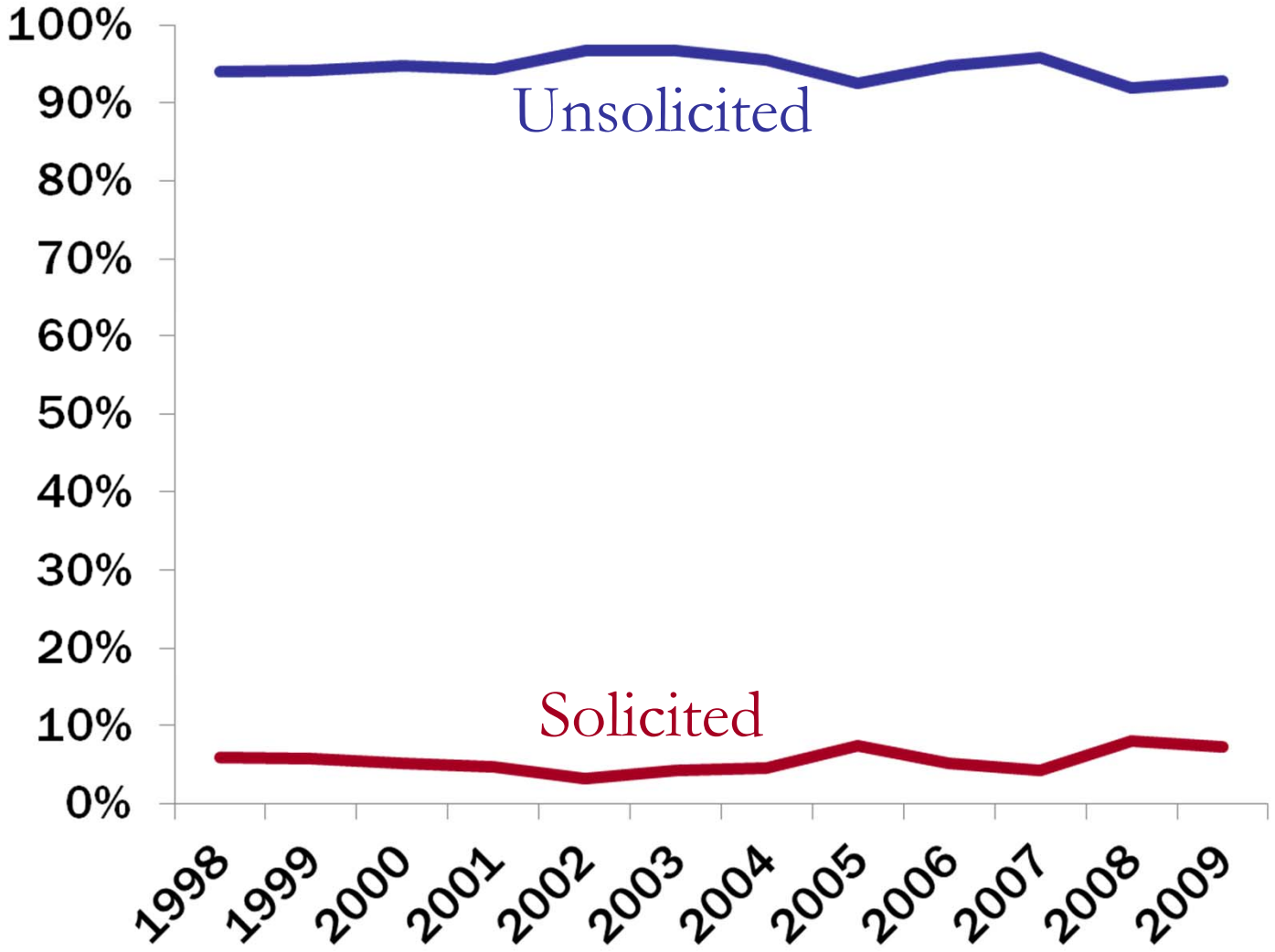


NCI FY 2010 Budget by Mechanism



(dollars in thousands)

Unsolicited RPGs Far Outnumber Solicited



The President's 2011 Budget Proposal

"To accelerate progress in biomedical research, NIH investments will focus on priority areas including genomics, translational research, science to support health care reform, global health, and reinvigorating the biomedical research community."

The Federal Budget for Fiscal Year 2011 Feb. 1, 2010

The President's 2011 Budget Proposal

"The Budget includes $6.036 billion to support a range of bold and innovative cancer efforts…"

- Initiation of 30 new drug trials in 2011
- Doubling of the number of novel compounds in Phase 1–3 clinical t
- Complete a compre mutations for the 2 within 10 years

NCI allocation in the President's Budget for 2011: $5.260 billion.

National Cancer Institute

The Nation's Investment in Cancer Research

AN ANNUAL PLAN AND BUDGET
PROPOSAL FISCAL YEAR 2011

Connecting the Nation's Cancer Community

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

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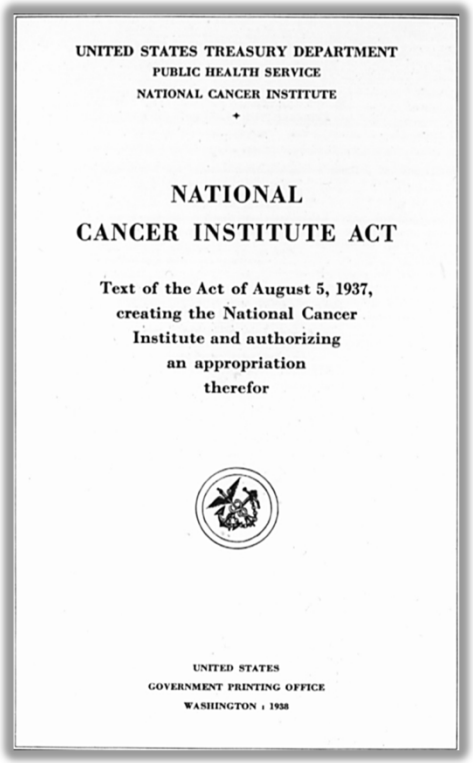
- Executive Committee Retreat

NCAB Working Groups

- Working group on The Cancer Genome Atlas (TCGA)
  - Chair: Dr. Jennifer Pietenpol, director of the Vanderbilt-Ingram Cancer Center
- Ad hoc Working Group to Create a Strategic Scientific Vision for the National Cancer Program and review of the National Cancer Institute
  - Co-chairs: NCAB members William Goodwin, Robert Ingram, and Dr. Bruce Chabner; and Dr. Phillip Sharp, Former NCAB Chair

The National Cancer Act

- 1912: Congress establishes the U.S. Public Health Service
- 1922: Cancer research is initiated within the PHS
- 1937: Congress establishes the National Cancer Institute within the Public Health Service
- 1948: Congress establishes the National Institutes of Health


UNITED STATES TREASURY DEPARTMENT
PUBLIC HEALTH SERVICE
NATIONAL CANCER INSTITUTE

NATIONAL
CANCER INSTITUTE ACT

Text of the Act of August 5, 1937, creating the National Cancer Institute and authorizing an appropriation therefor

UNITED STATES
GOVERNMENT PRINTING OFFICE
WASHINGTON : 1938

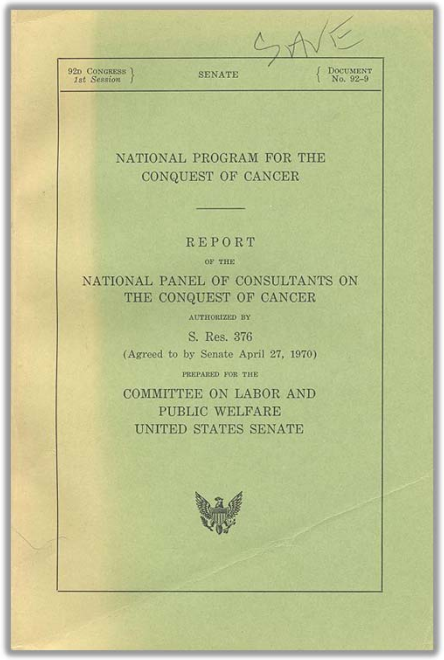
The National Cancer Act 1971

- Senate authorizes a "Panel of Consultants on the Conquest of Cancer"
  - Panel recommends the NCI as the logical organization to administer a National Cancer Program — to be strengthened, upgraded and freed from the constraints of HEW, PHS and NIH

Sen. Ralph Yarborough of Texas, panel chair

Authority of the Director

- To acquire, construct, improve, repair, operate and maintain cancer centers, laboratories, research and other facilities and equipment
- To appoint advisory committees to advise him with respect to his functions
- To accept voluntary and uncompensated services


92D CONGRESS 1st SESSION | SENATE | DOCUMENT No. 92-9

NATIONAL PROGRAM FOR THE CONQUEST OF CANCER

REPORT
OF THE
NATIONAL PANEL OF CONSULTANTS ON THE CONQUEST OF CANCER
AUTHORIZED BY
S. Res. 376
(Agreed to by Senate April 27, 1970)
PREPARED FOR THE
COMMITTEE ON LABOR AND PUBLIC WELFARE
UNITED STATES SENATE

Charge to the Working Group

"Review the NCI current operating structure and strategic vision — to assess the effectiveness of the scientific programs and business management structure of the NCI, in order to determine the gaps and opportunities for delivering scientific progress in understanding, diagnosing, treating, and preventing cancer."

Working Group Membership and Process

- Broad representation from academia, industry, and advocacy communities
- Three face-to-face meetings using panel discussion on special authorities, relationships to other agencies, strategic scientific vision, organizational structure, training, advocacy, global health
- Sub-working Groups will review basic, translational, clinical, population-based scientific programs
- Report to the Activities and Agenda NCAB Subcommittee in September 2010

NCI – March 2010

- NCI FY 2010 operating budget and the President's budget for FY 2011
- The National Cancer Advisory Board
- Executive Committee Retreat

NCI EC Scientific Retreat

Goals:

"To inform NCI's leadership about the directions that its cancer research efforts should take to maximize the impact of personalized medicine in clinical care and public health, within the context of current cancer research opportunities, patient care priorities and the health care environment."

NCI EC Scientific Retreat

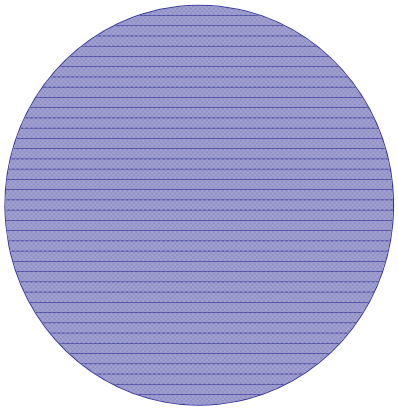
Agenda:

- ✓ Current Realities and the Future of Personalized Cancer Medicine
  - –Croyle, McClellan, Khoury, Fouad, Thun, Simone, Freedman
- ✓ Informing the Cancer Biological Space – Genomics and Beyond
  - –Barker, DePinho, Carr, Hill, Hillis, Tlsty, Lowy
- ✓ Creative Thoughts on How to Translate Genomics for Patient Benefit
  - –Helman, Wiltrout, Sawyers, Trent, Mirkin, Norton
- ✓ "A New Biology for the 21st Century"
  - –Yamamoto
- ✓ Role of Computational Sciences, Systems Biology and Modeling
  - –Singer, Friend, Buetow, Califono, Cantley, Nevins, Mills


Clinical annotation is key
Somatic epigenomics
Germline Susceptibility
Phenotypic Clinical Annotation

TCGA – the example

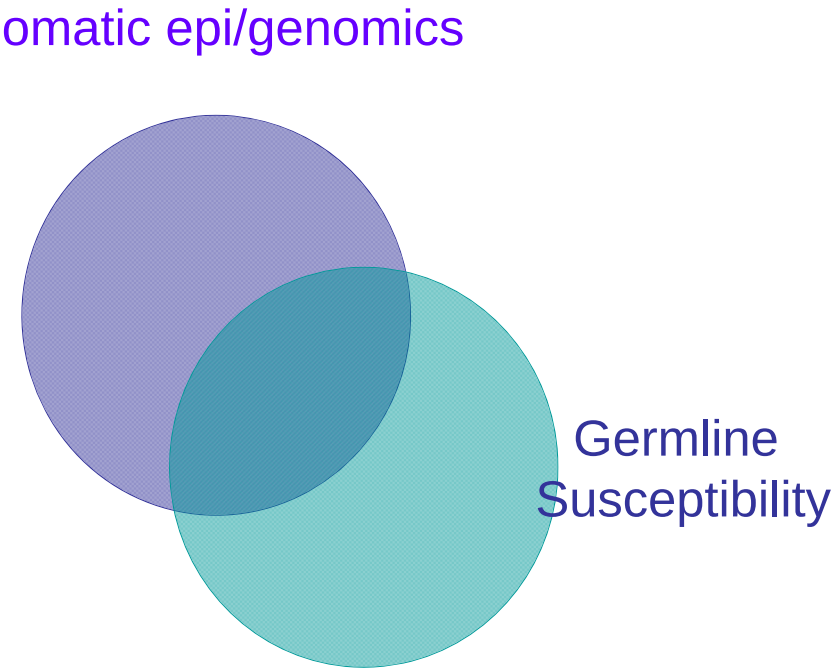
Somatic epi/genomics



- Clinically annotated robust cohort of high-quality biospecimens
- Multi-dimensional characterization
- Integrative analyses

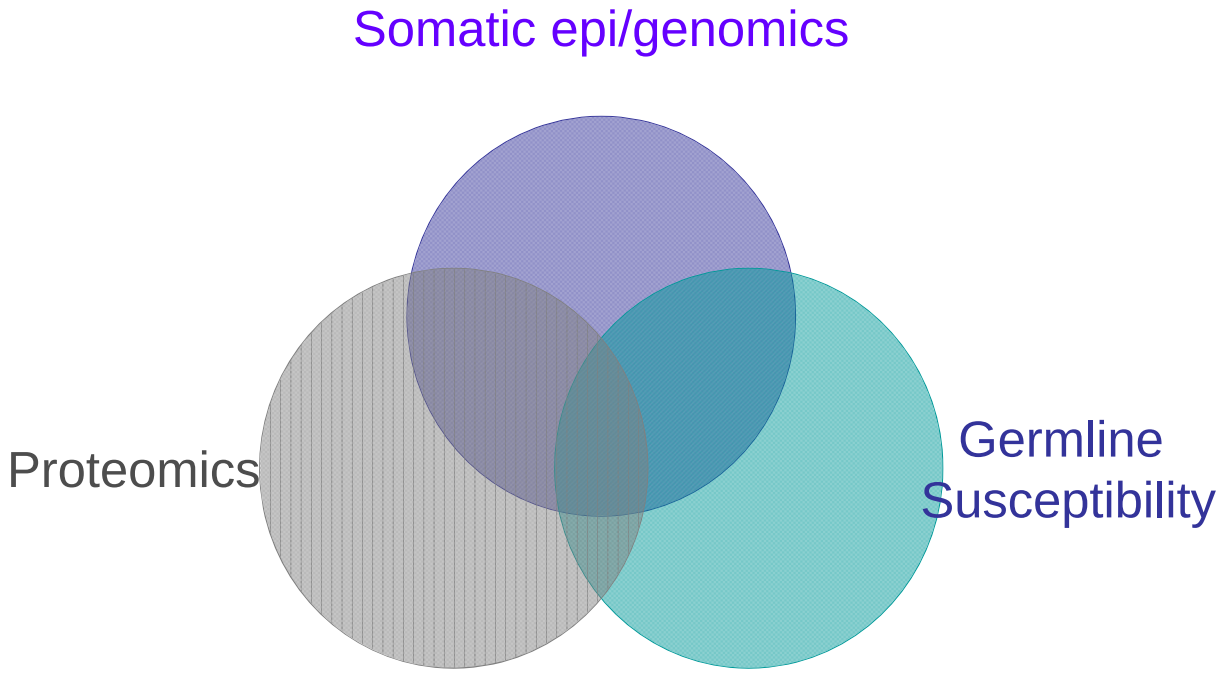
➔ What is it missing?

Somatic vs Germline



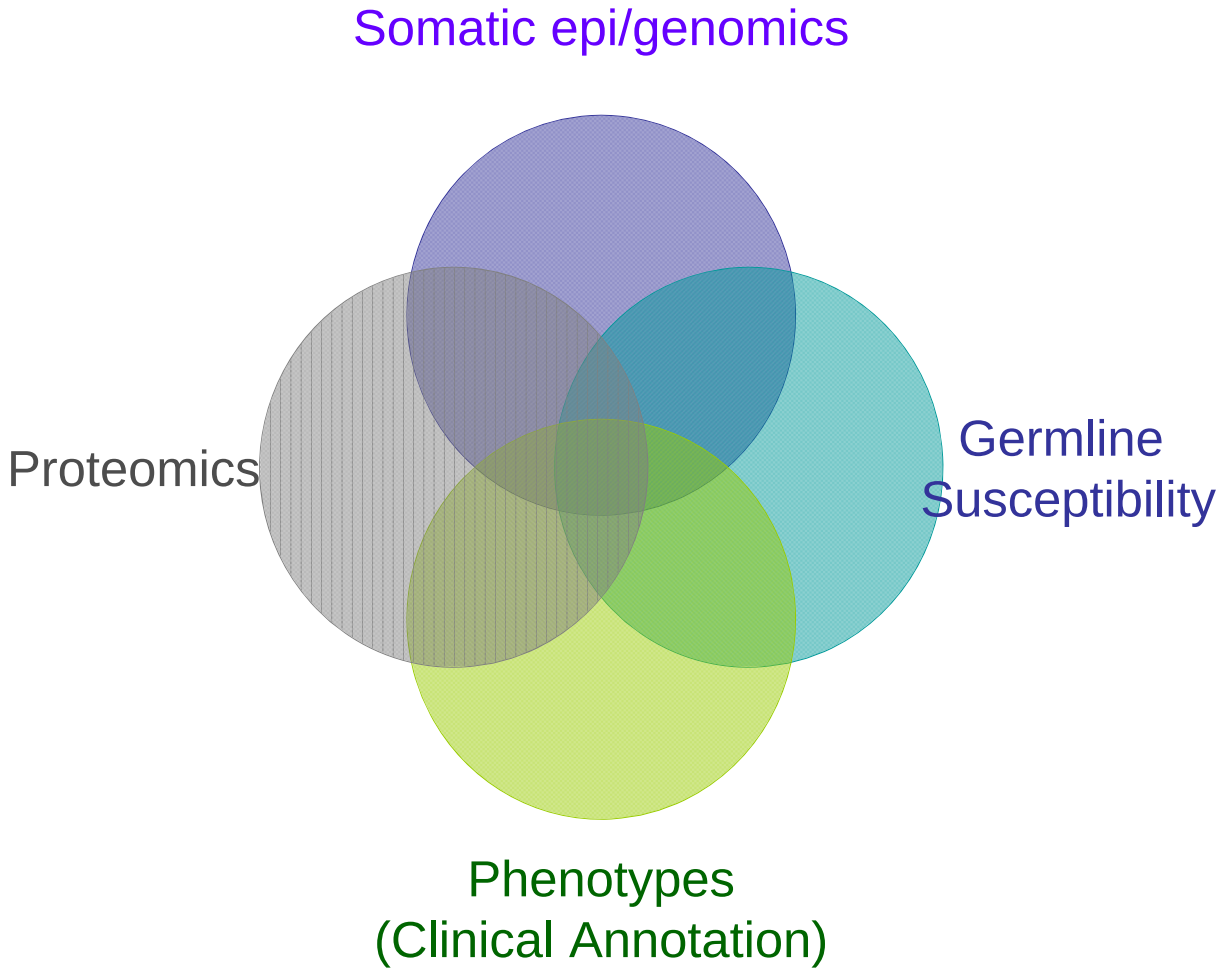
- Need to understand how somatic events manifest themselves in context of germline susceptibility…
- → GWAS integrated with TCGA

What about protein level information?



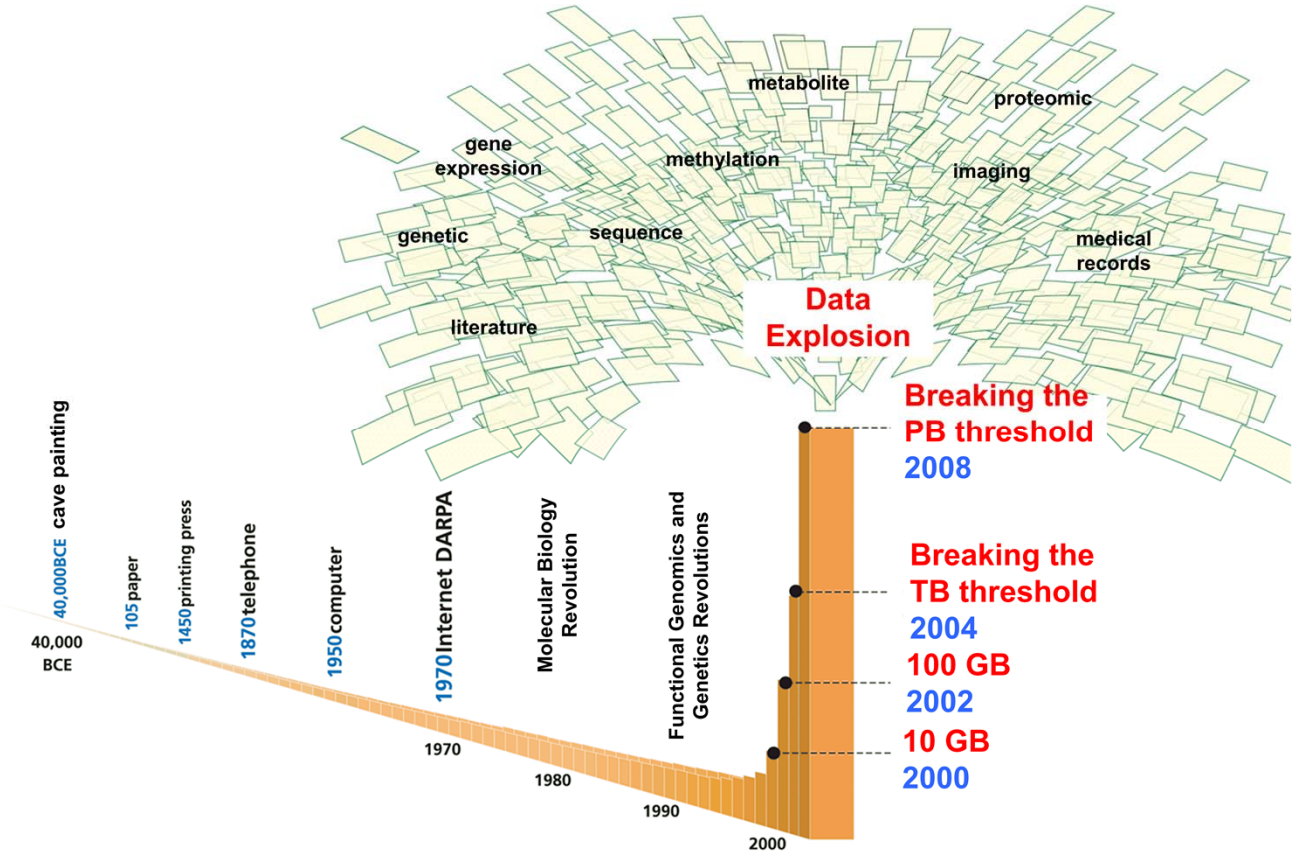
- Gap in proteomics is evident on many levels; needed are high resolution methods to deeply probe the proteome and understand how such data relates to genetic information…

Clinical annotation is key



- Transform the way human phenotype annotation –not just standard biospecimens banking, but electronic medical records, IT infrastructure ….Framingham like profiles…

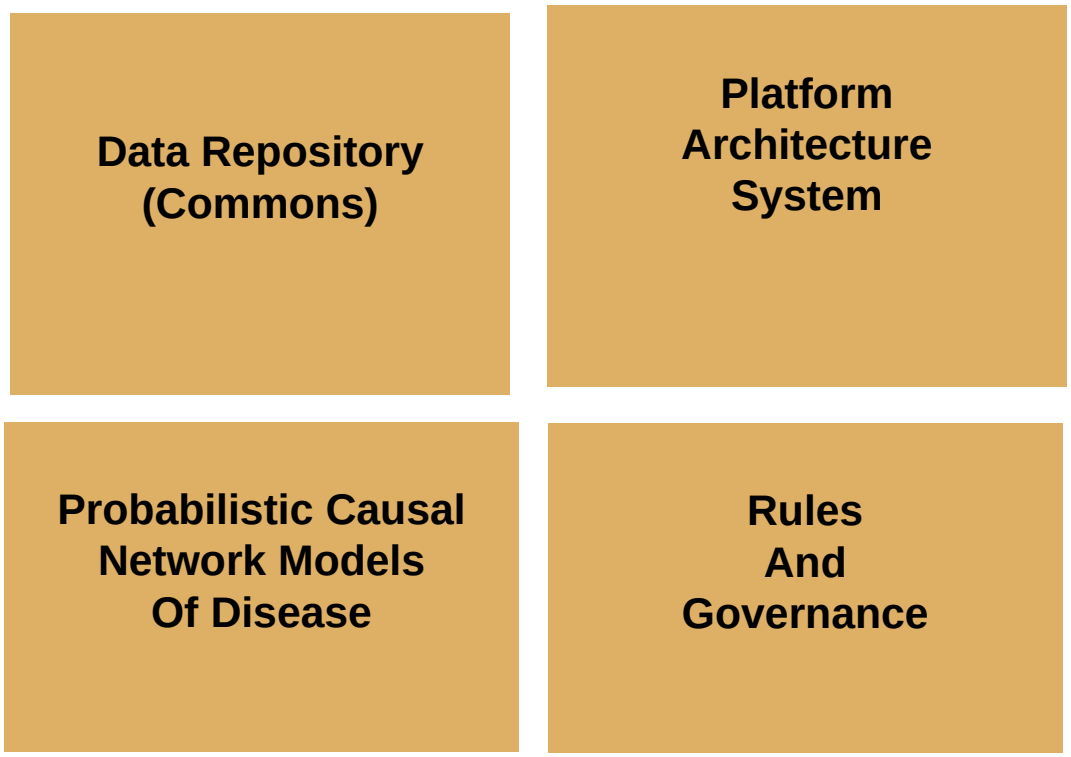
Explosion of Biological Genomic & Clinical Information



- **Computational methods for integrating massive molecular and clinical datasets obtained across sizable populations into predictive disease models can recapitulate complex biological systems**
- **Data should feed and refine a set of models that inform our understanding of disease causality as well as generate new mechanisms, targets, diagnostics and knowledge.**

Stephen Friend, M.D., Ph.D., Fred Hutchinson Cancer Research Center

Four Requirements to enable a Platform for Clinicians, Scientists and Patients



How to Leverage Existing NCI Programs: caBIG and TCGA?

Stephen Friend, M.D., Ph.D., Fred Hutchinson Cancer Research Center

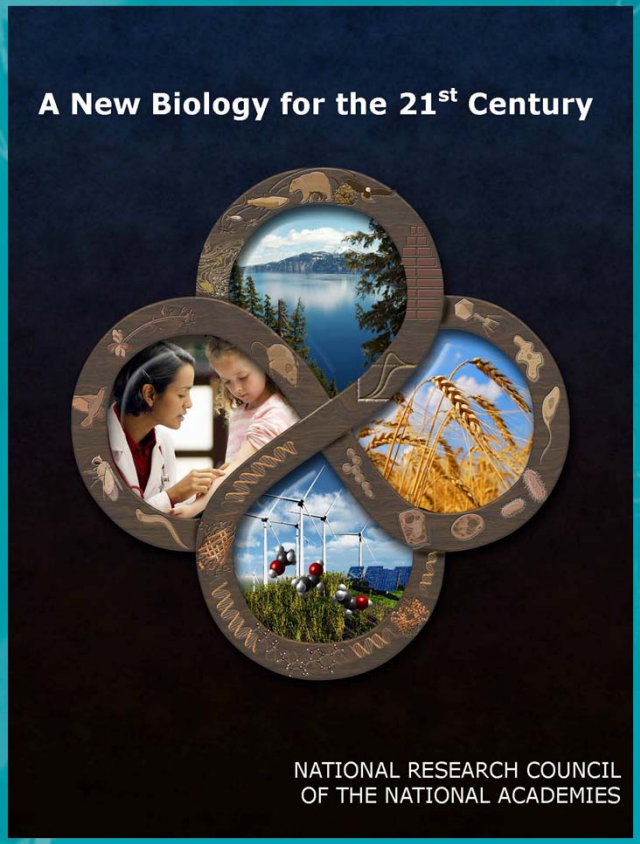
What is the New Biology?

The essence: integration

- re-integration of the many sub disciplines of biology

- working integration into biology of physics, chemistry, engineering, mathematics and computation

Will create a research community able to tackle extremely complex biological and societal problems



THE NATIONAL ACADEMIES

Biology is at a tipping point--poised to contribute to solving major societal problems

Relatively small investment in inspiring and crucial challenges will lead to development of cross-cutting technologies and sciences that will leverage the value of all biological research.

RECOMMENDATION:
Launch a National New Biology Initiative

a multi-agency, multi-year, multi-disciplinary initiative to capitalize on the extraordinary advances recently made in biology and address four major societal challenges.

THE CHALLENGES

- Food: Adapt any food crop to any growing condition
- Environment: Diagnose and repair ecosystem damage
- Energy: Expand sustainable alternatives to fossil fuels
- Health: Achieve individualized surveillance and care

The Science of Personalized Cancer Medicine

1) **Predicting your risk of getting cancer:**

- Genome wide association studies (GWAS) offered great promise for finding “all” clinically important cancer risk alleles.
- But all the newly discovered markers have modest hazard ratios and are therefore not clinically “actionable.”
- BRCA1 and 2 remain by far the most important predictive markers.

2) **Predicting the best treatment for your cancer:**

- Mutations, gene translocations, copy number alterations, etc. in the tumor (not germ line) define distinct diseases and new drug targets.
- Targeted cancer therapy works when used in the right patients.
- But we are still in the early days of knowing how to identify the right patients.

Charles L. Sawyers, M.D., Memorial Sloan-Kettering Cancer Center

Dr. Sawyers' Proposals for NCI

- Define all cancer drug targets within 10 years
  - Run the TCGA project to completion
  - Conduct a cancer synthetic lethal screen across several hundred cancer cell lines and xenografts
- Jump start the molecular diagnostics field
  - Establish an academic research community working on the science of molecular diagnostics (The Cancer Biomarker Project)
- Build a community network of molecular pathology centers now
  - Profile tumors from thousands of cancer patients
  - Establish registries of "pre-genotyped" patients available for clinical trials
  - Engage patients and advocates

Themes From EC Scientific Retreat

- Biospecimens, patient data, and patient-reported outcomes needed for evaluation, to inform healthcare reform
- The research reward culture needs to fully recognize the contributions of participants in team science
- Single-agent interventions will not work
- Need to utilize cancer centers, SPOREs and other programs to test new modalities

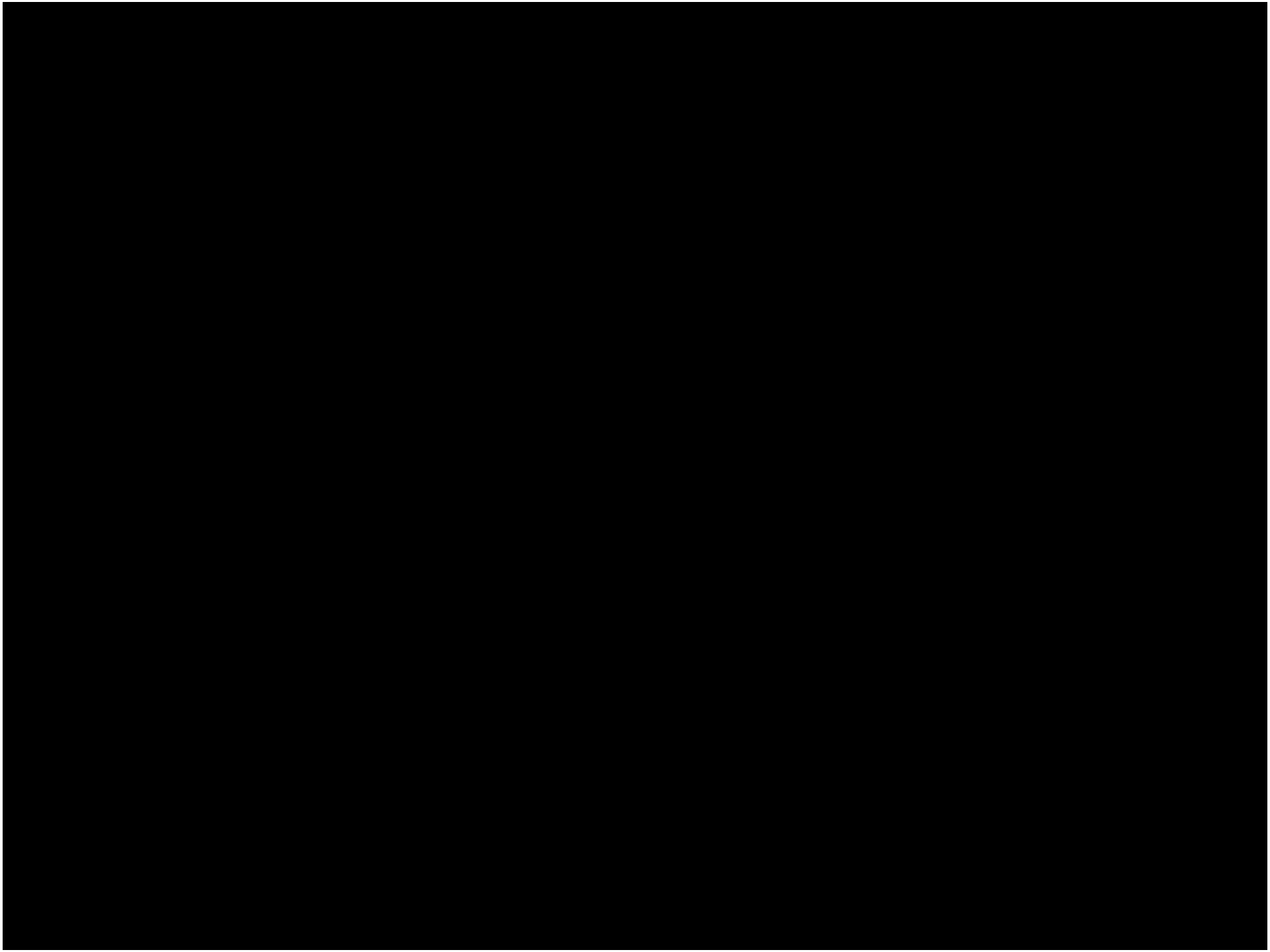
Messages From EC Scientific Retreat

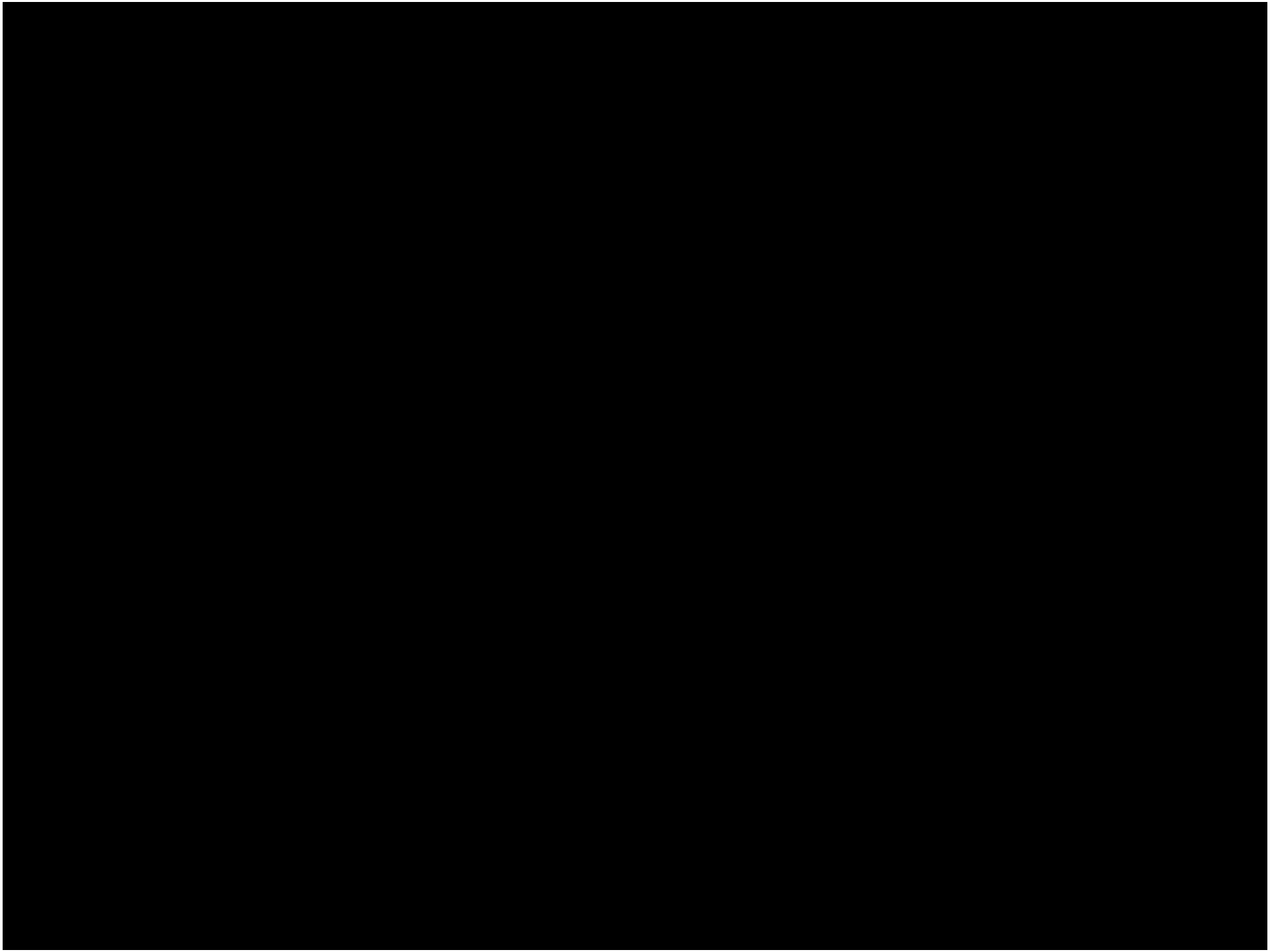
- New biology will be accomplished by team science – "a convergence of big and small science"
- New biology will be "data driven science"
- Establishing proteomics and function is essential
- Cancer is emergent complex system – network and pathway biology
- Translation will be facilitated by "PPP" and a reengineered clinical trials system - "virtual trials"

Messages From EC Scientific Retreat

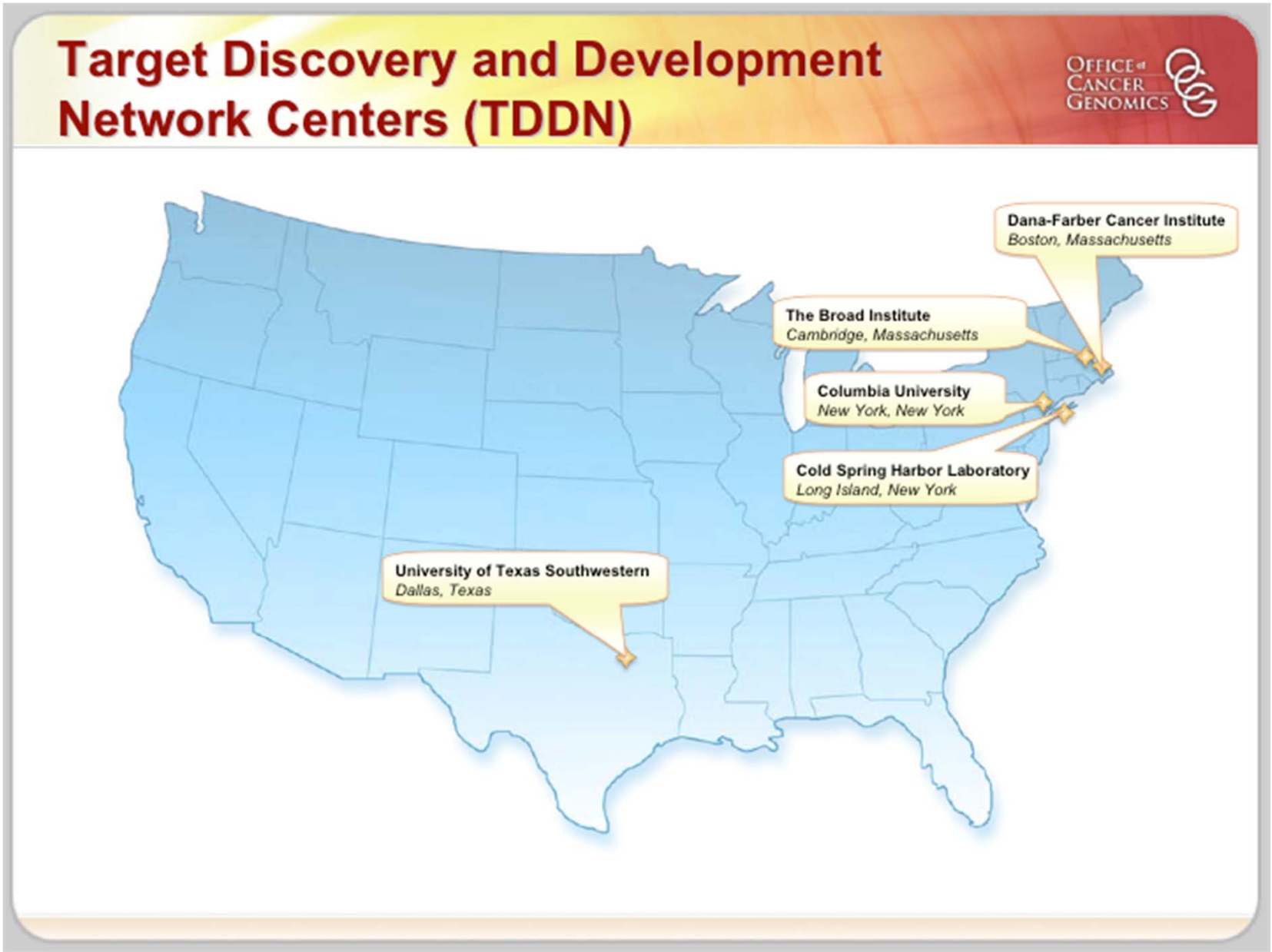
- The continuum of patient care begins before diagnosis. How can we create comprehensive cohorts to fully inform cancer care and healthcare in general?
- Effective translational science requires active coordination end to end. How will the science of tomorrow be fostered through a complement of investigator-initiated and more directed research? What is the future of team science?
- Cancer treatment going forward will not be single-agent interventions but recipes addressing specific genetic mutations and signaling pathways. How can our cancer research infrastructure more effectively test new approaches quickly and efficiently?


Patients & Families
www.cancer.gov

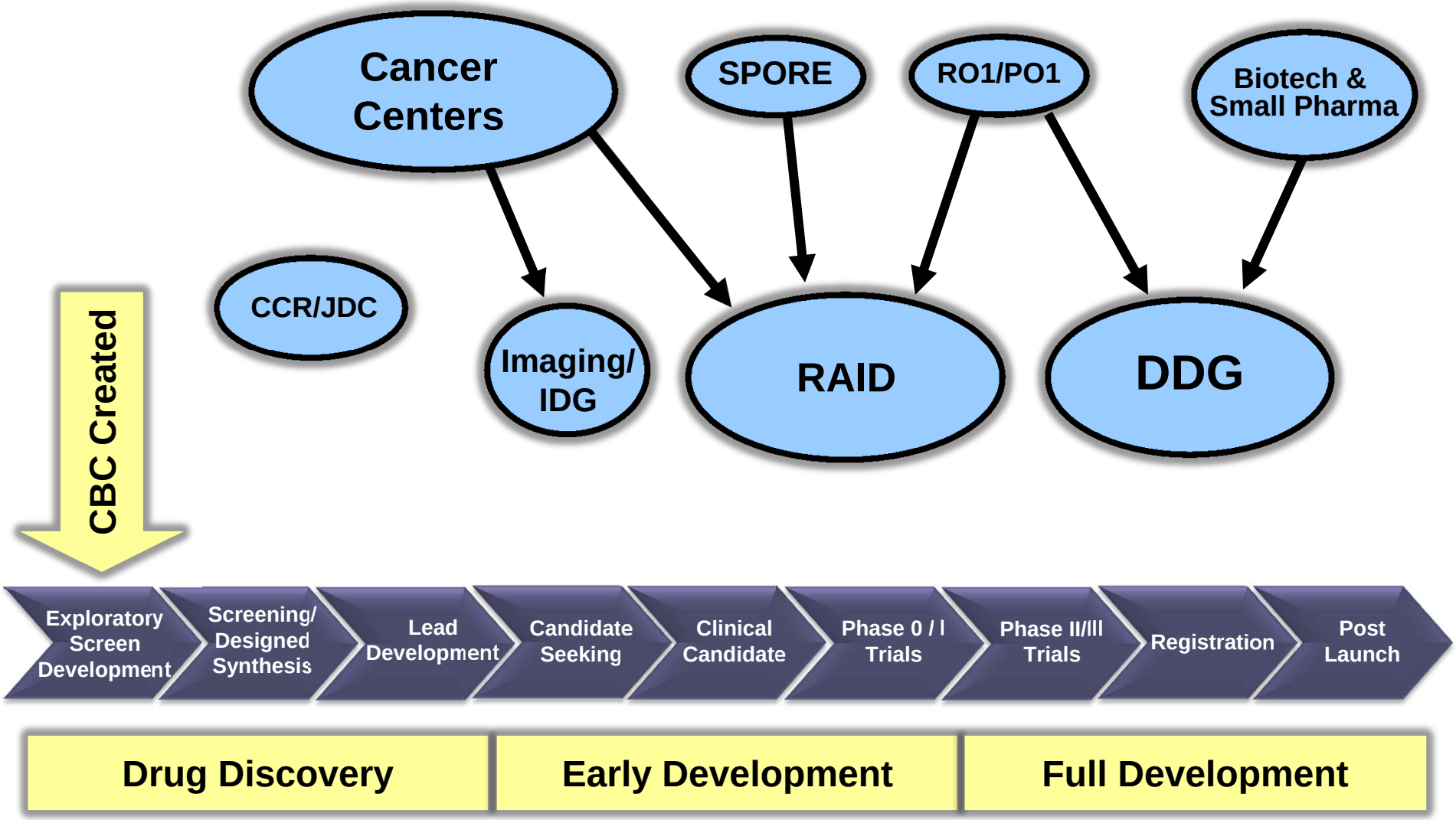




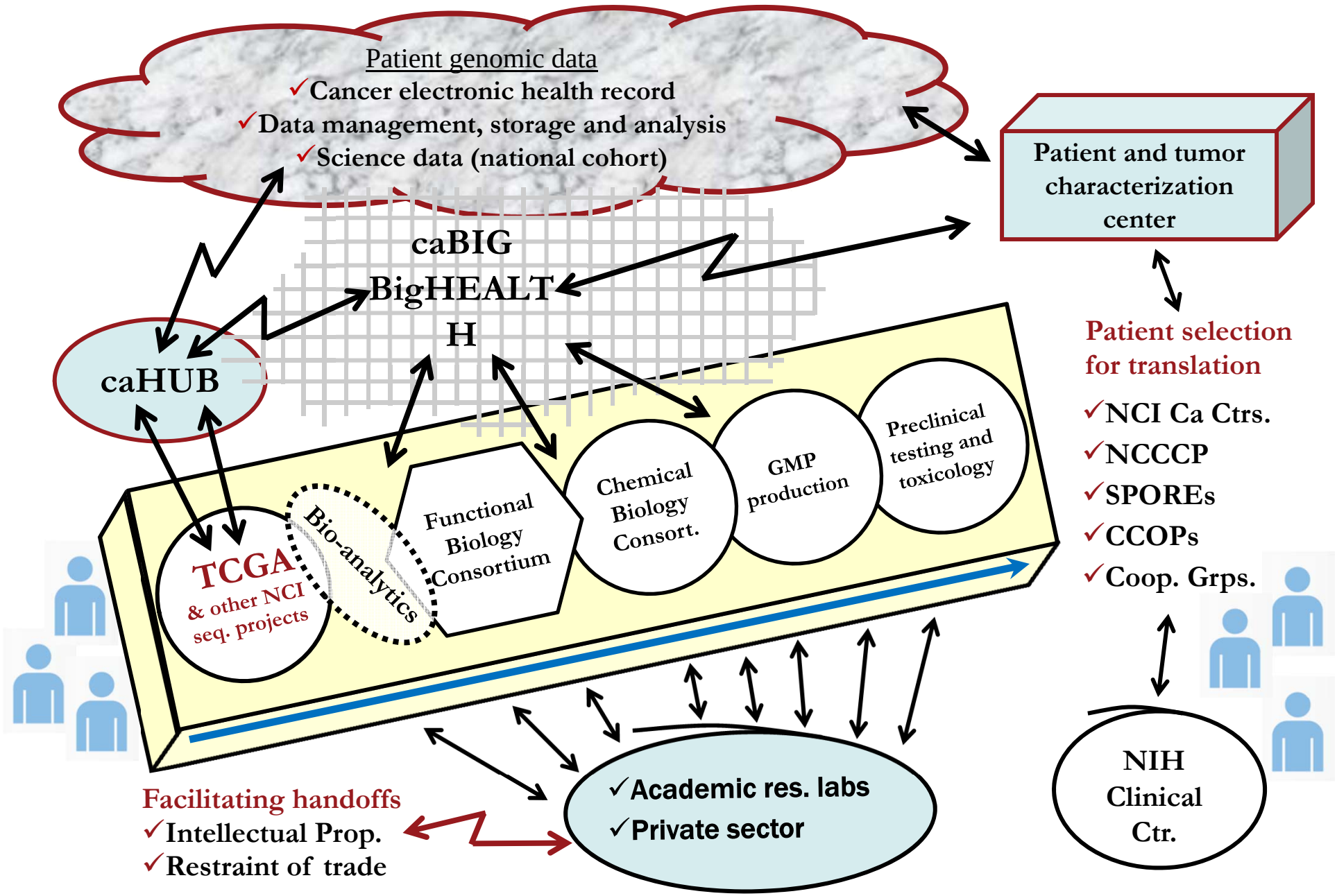
The NCI's Target Discovery and Development Network



The NCI Experimental Therapeutics (NExT) Pipeline



Transforming the Science of Translation



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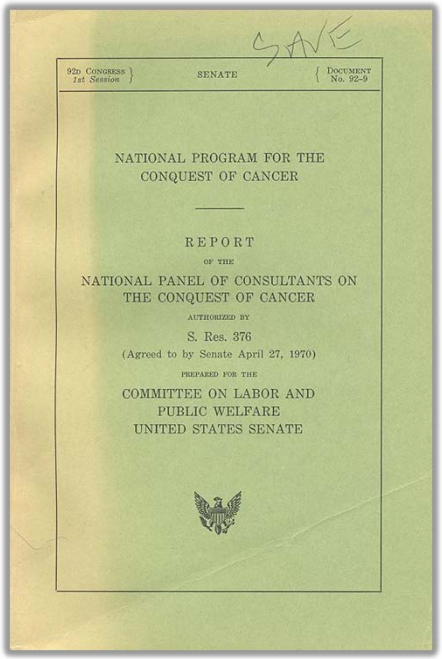
- Need to utilize cancer centers, SPOREs and other programs to test new modalities

The National Cancer Program

- The Director of the NCI shall coordinate all activities of the NIH relating to cancer with the National Cancer Program
- In carrying out the NCP the NCI Director shall:
  - With the advice of the NCAB, plan and develop an expanded, intensified and coordinated cancer research program


92d CONGRESS 1st Session } SENATE { DOCUMENT No. 92-9

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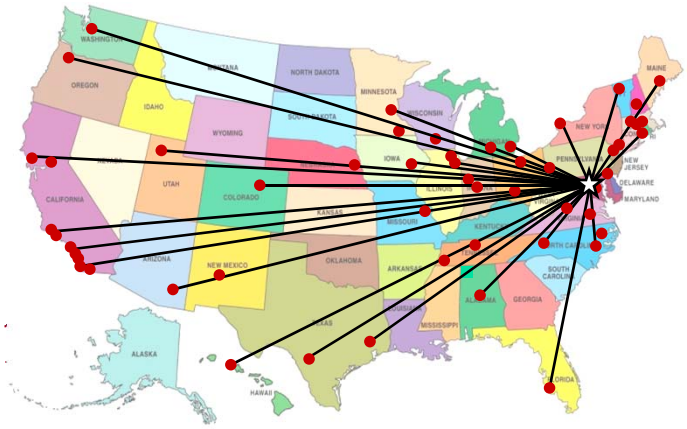
National Cancer Advisory Board

- Replaced prior National Advisory Cancer Council
- Members appointed by the President to advise and assist the Director with respect to the National Cancer Program
- May hold such hearings and act at such times as the Board deems advisable to review programs and activities of the National Cancer Program

Cancer Centers Program

The Act provides for the establishment of fifteen new centers for clinical research, training and demonstration o advanced diagnostic and treatment methods relating to cancer.



A Proposal for the NCI

(at the risk of shrinking creative R01 sponsored science)

Goal 1: define all cancer drug targets within 10 years

1) Run the TCGA project to completion (defined loosely):

   - over 5-10 years (no need to rush)
   - capitalize on the rapidly falling cost of sequencing
   - then end the TCGA

2) Conduct a cancer synthetic lethal screen across several hundred cancer cell lines and xenografts

   - broad representation of all cancers
   - shared platforms to allow comparative data analysis (pooled screening, common shRNA library)
   - immediate release of screening hits (~ sequencing)*****

*guarantees that all new cancer targets are in the public domain

Charles L. Sawyers, M.D., Memorial Sloan-Kettering Cancer Center

A Proposal for the NCI

(at the risk of shrinking creative R01 sponsored science)

Goal 2: jump start the molecular diagnostics field

Establish an academic research community working on the science of molecular diagnostics (The Cancer Biomarker Project)

1) methods of tissue analysis
   - biopsies
   - blood-based tests (circulating tumor cells, serum markers)

2) mutation profiles
   - DNA-based, RNA-based
   - multiplexing strategies
   - optimizing sensitivity/specificity with varying tumor purity

3) informatics challenges
   - data storage
   - translating sequence data into a “clinical report”

Charles L. Sawyers, M.D., Memorial Sloan-Kettering Cancer Center

A Proposal for the NCI

(at the risk of shrinking creative R01 sponsored science)

Goal 3: Build a community network of molecular pathology centers now!

1) profile tumors from thousands of cancer patients

2) establish registries of “pre-genotyped” patients available for clinical trials (for clinical investigators, pharma)

3) engage patients and advocates

-addresses the short term need to annotate patients for current drug targets

-will establish a potential business model so that commercial molecular diagnostic entities can take over

-could/should be a public-private partnership

Charles L. Sawyers, M.D., Memorial Sloan-Kettering Cancer Center

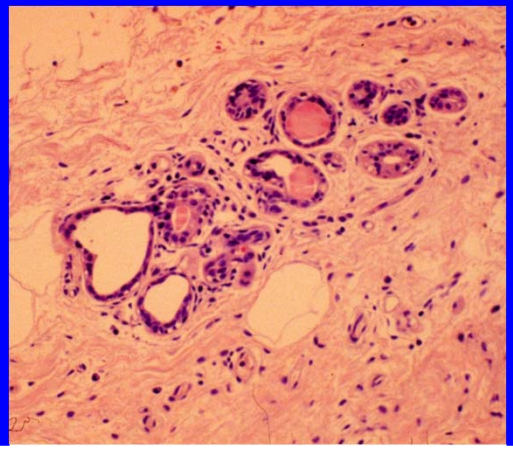
NCI FY 2008 and 2009 Competing RPGs

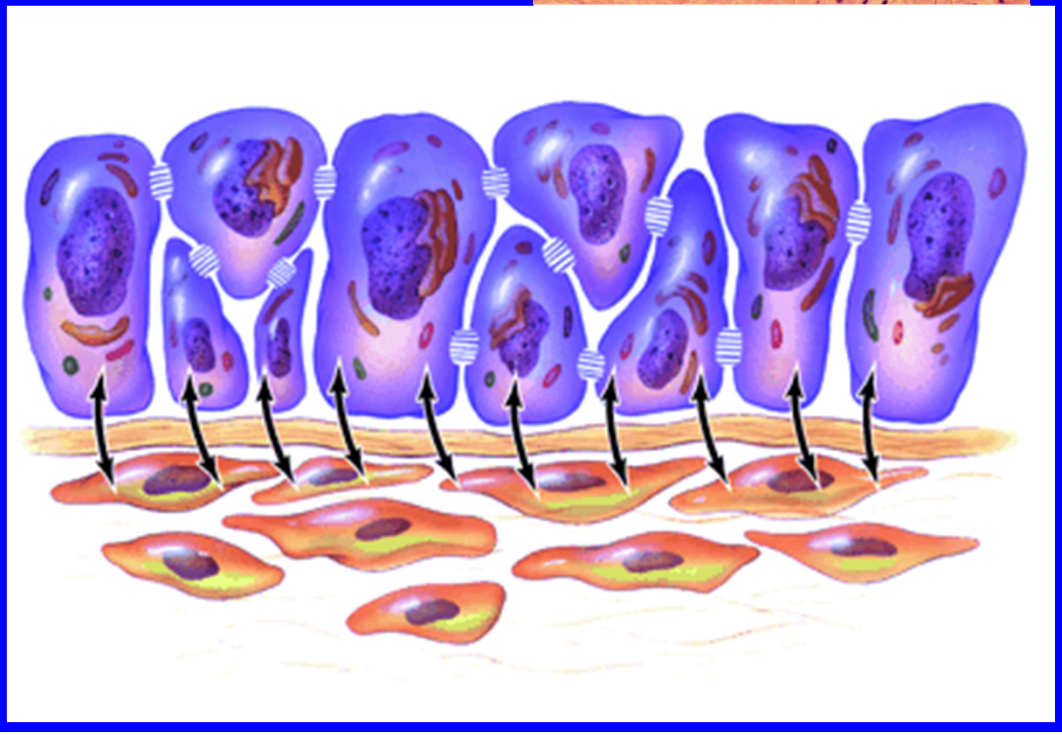
	FY 2008	FY 2009
Competing RPGs total	1,284 grants $456,644	1,235 grants $457,834
Competing RPG RFA portion	108 grants $50,726	89 grants $49,010

(dollars in thousands)

Tissue Architecture and Phenotype is Controlled by Stromal-Epithelial Interactions

Normal Mammary Gland





Thea D. Tlsty, Ph.D.,
University of California,
San Francisco

- Data on large sci projects

THE NATIONAL ACADEMIES

A moment of unique opportunity --

Current research has brought biology to an inflection point

- See both great complexity and paths to solution; data/knowledge/understanding gaps both growing and closing
- Integration of sub disciplines within biology; one biology, so advances not discipline-specific
- Cross-discipline integration: life science research by physical, computational, earth scientists, engineers
- Technological advances enable biologists to collect data unprecedented in quantity and quality
- Past investments providing value beyond expected

An opportunity for a New Biology with impact at an unprecedented scale

Why New Biology is best way to advance medical research and health

- **Biological**

– Reaching design-manipulation-prediction level difficult with only NIH budget and research

– One biology: advances in one discipline aid others

– Inflection point: new technologies (“all” and “one”) require extending and integrating biological research into fields supported by other agencies

– Genotype-phenotype gap: health determined by genotype, environment, nutrition, so health requires addressing food, environment, energy issues