
National Cancer Institute
NCI
Director's
Update
Dr. John E. Niederhuber
Director, National Cancer Institute
Board of Scientific Advisors
November 2, 2009
U.S. DEPARTMENT
OF HEALTH AND
HUMAN SERVICES
National Institutes
of Health

New BSA Chair

A “thank you” to Rich!

- **Internationally recognized and honored translational research physician-scientist**
- **Since 1995, chair of the Cancer and Leukemia Group B (CALGB)**
- **2008-2009 ASCO president**

Richard L. Schilsky, MD

Professor of Medicine

Section Chief, Hematology/Oncology

University of Chicago Medical Center

New BSA Members

Mr. Don Listwin

Joshua LaBaer, M.D., Ph.D.

Frank Torti, M.D., M.P.H.

Jeffrey Drebin, M.D., Ph.D.

Chi V. Dang, M.D., Ph.D.

NCI – Nov. 2009

- Closing out FY2009
- The American Recovery and Reinvestment Act
- Using ARRA dollars to fund vital science

NCI FY2009

FY2008 operating budget **$4.83 billion**

FY2009 appropriation **$4.96 billion**

Change, FY08 to FY09 +2.9%

Congratulations to NCI's budget office for closing the books on FY08 with a balance of $4,432.

ARRA $ to NIH

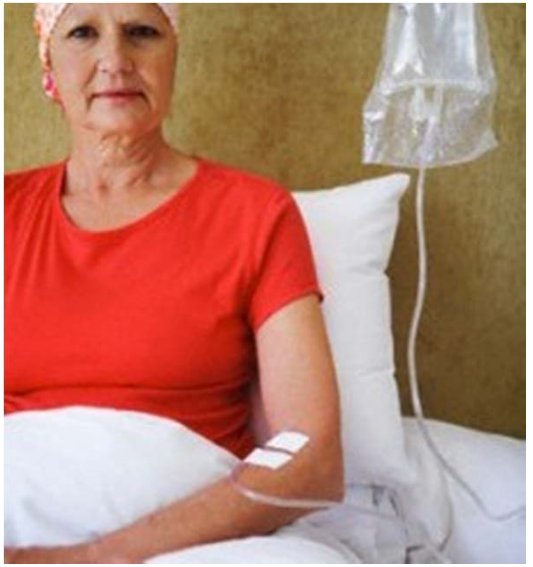
- $7.4 billion: **Institutes and Centers**
  - **$1.26 billion to NCI**
- $1 billion: **extramural construction**
- $300 million: **shared instrumentation**

} NCCR

- $500 million: **NIH construction**
- $400 million: **comparative effectiveness research ($400M HHS; $300M AHRQ)**
- $800 million: **NIH Office of the Director**

ARRA Funding: A Once in a Lifetime Opportunity

- **Careful and thoughtful planning by the NCI**
  - Strategic foresight: **minimizing the out-year (cliff) effect**
  - **Maximizing our ability to generate Congressional enthusiasm about investments in cancer research**



Payline – ARRA

- 16th percentile: 2009 RPG payline from appropriated funds
- 16th to 18th percentile: 4-year grants through stimulus, followed by appropriated do
- 18th to 25th p and 4-year grar years)

369 RPGs have been funded due to the extended payline under ARRA

ARRA at NCI

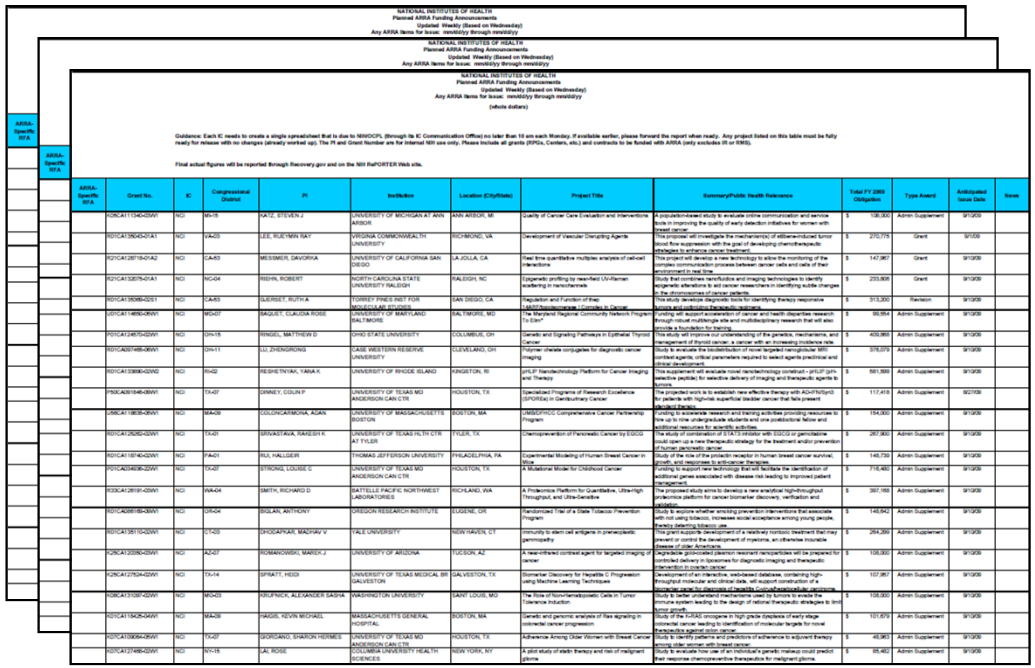
Total NCI ARRA	$1,256,517,000	% of Total
Grants	**$731,380,000**	**59%**
Supplements to existing awards	341,796,000	
New competing awards	389,584,000	
R&D contracts for the academic community	**$493,837,000**	**39%**
Intramural Equipment	**$6,300,000**	**0%**
Support	**$25,000,000**	**2%**

NIH Funded Cancer Grants

CER (27 awards)	$61,071,697
Summer (77 awards)	4,503,782
GO (matched 18 awards)	23,802,156
Challenge (18 awards)	17,700,000
Total (140 awards)	$106,077,635

“Blue Sheets”

1,700 items submitted



NATIONAL INSTITUTES OF HEALTH
Planned ARRA Funding Announcements
Updated: Weekly (Based on Wednesday)
Any ARRA items for issue: mm/dd/yy through mm/dd/yy
(whole dollars)

Guidance: Each IC needs to create a single spreadsheet that is due to NIHOCPL (through its IC Communication Office) no later than 10 am each Monday, if available earlier, please forward the report when ready. Any project listed on this table must be fully ready for release with no changes (already worked up). The PI and Grant Number are for internal NIH use only. Please include all grants (RPGs, Centers, etc.) and contracts to be funded with ARRA (only excludes IR or RMS).

Final actual figures will be reported through Recovery.gov and on the NIH RePORTER Web site.

ARRA-Specific RFA	Grant No.	IC	Congressional District	PI	Institution	Location (City/State)	Project Title	Summary/Public Health Relevance	Total FY 2009 Obligation	Type Award	Anticipated Issue Date	Notes
	3CA111340-03W1	NCI	MI-15	KATZ, STEVEN J	UNIVERSITY OF MICHIGAN AT ANN ARBOR	ANN ARBOR, MI	Quality of Cancer Care Evaluation and Interventions	A population-based study to evaluate online communication and service tools in improving the quality of early detection initiatives for women with breast cancer.	$ 100,000	Admin Supplement	9/1/09	
	R01CA135043-01A1	NCI	VA-03	LEE, RUEYMIN RAY	VIRGINIA COMMONWEALTH UNIVERSITY	RICHMOND, VA	Development of Vascular Disrupting Agents	This program will investigate the mechanism(s) of stilbene-induced tumor blood flow suppression with the goal of developing chemotherapeutic strategies to enhance cancer treatment.	$ 270,775	Grant	9/1/09	
	R21CA135119-01A2	NCI	CA-53	MESSMER, DAVORKA	UNIVERSITY OF CALIFORNIA SAN DIEGO	LA JOLLA, CA	Real time quantitative multiplex analysis of cell-cell interactions	This project will develop a new technology to allow the monitoring of the complex communication process between cancer cells and cells of their microenvironment.	$ 147,967	Grant	9/1/09	
	R21CA132075-01A1	NCI	NC-04	RISPIN, ROBERT	NORTH CAROLINA STATE UNIVERSITY RALEIGH	RALEIGH, NC	Epigenetic profiling by resn-field UV-Raman scattering in nanochannels	Study that combines nanofluidics and imaging technologies to identify epigenetic alterations to aid cancer researchers in identifying subtle changes in the chromosomes of cancer patients.	$ 233,906	Grant	9/1/09	
	R01CA135089-02S1	NCI	CA-53	GJERSET, RUTH A	TORREY PINES INST FOR MOLECULAR STUDIES	SAN DIEGO, CA	Regulation and Function of the TAF9/Stress Granule Complex in Cancer	This study develops diagnostic tools for identifying therapy responsive cancers and subsets of cancers in clinical specimens.	$ 313,200	Revision	9/1/09	
	U01CA114800-06W1	NCI	MD-07	SAQUET, CLAUDIA ROSE	UNIVERSITY OF MARYLAND BALTIMORE	BALTIMORE, MD	The Maryland Regional Community Network Program To Elim*	To build capacity for research of cancer and health disparities research through robust multifaceted site and multidisciplinary research that will also provide a long-term legacy.	$ 89,954	Admin Supplement	9/1/09	
	R01CA124570-02W1	NCI	OH-15	RINGEL, MATTHEW D	OHIO STATE UNIVERSITY	COLUMBUS, OH	Genetic and Signaling Pathways in Epithelial Thyroid Cancer	This study will determine the molecular underpinning of the genetics, mechanisms, and management of thyroid cancer, a cancer with an increasing incidence rate.	$ 409,966	Admin Supplement	9/1/09	
	R01CA097489-06W1	NCI	OH-11	LU, ZHENGRONG	CASE WESTERN RESERVE UNIVERSITY	CLEVELAND, OH	Polymer chelate conjugates for diagnostic cancer imaging	Study to evaluate the biodistribution of novel targeted nanoglobular MRI contrast agents; critical parameters required to select agents preclinical and clinical development.	$ 378,079	Admin Supplement	9/1/09	
	R01CA133690-02W2	NCI	RI-02	RESHETNYAK, YANA K	UNIVERSITY OF RHODE ISLAND	KINGSTON, RI	pHLIP Nanotechnology Platform for Cancer Imaging and Therapy	This supplement will evaluate novel nanotechnology construct - pHLIP (pH-selective peptide) for selective delivery of imaging and therapeutic agents to tumors.	$ 561,599	Admin Supplement	9/1/09	
	P50CA097189-06W1	NCI	TX-07	DINNEY, COLIN P	UNIVERSITY OF TEXAS MD ANDERSON CAN CTR	HOUSTON, TX	Specialized Programs of Research Excellence (SPORSes) in Genitourinary Cancer	The projected work is to establish new effective therapy with AD-hTERTpro2 for patients with high-risk superficial bladder cancer that fails present standard therapy.	$ 117,418	Admin Supplement	9/27/09	
	U56CA119838-06W1	NCI	MA-09	COLDITZ/MONA, ADAN	UNIVERSITY OF MASSACHUSETTS BOSTON	BOSTON, MA	UMB/DFHCC Comprehensive Cancer Partnership Program	Funding to accelerate research and training activities providing resources to link up to nine undergraduate students and one postdoctoral fellow and additional resources for scientific activities.	$ 154,000	Admin Supplement	9/1/09	
	R01CA125262-02W1	NCI	TX-01	SRIVASTAVA, RAKESH K	UNIVERSITY OF TEXAS HLTH CTR AT TYLER	TYLER, TX	Chemoprevention of Pancreatic Cancer by EGCG	The study of combination of STAT3 inhibitor with EGCG or gemcitabine could open up a new therapeutic strategy for the treatment and/or prevention of human pancreatic cancer.	$ 267,900	Admin Supplement	9/1/09	
	R01CA118740-02W1	NCI	PA-01	RUI, HALLGER	THOMAS JEFFERSON UNIVERSITY	PHILADELPHIA, PA	Experimental Modeling of Human Breast Cancer in Mice	Study of the role of the prolactin receptor in human breast cancer survival, growth, and responses to anti-cancer therapies.	$ 149,739	Admin Supplement	9/1/09	
	P01CA094056-05W1	NCI	TX-07	STRONG, LOUISE C	UNIVERSITY OF TEXAS MD ANDERSON CAN CTR	HOUSTON, TX	A Mutational Model for Childhood Cancer	Funding to support new technology that will facilitate the identification of additional genes associated with disease risk leading to improved patient management.	$ 716,400	Admin Supplement	9/1/09	
	R33CA128191-03W1	NCI	WA-04	SMITH, RICHARD D	BATTELLE PACIFIC NORTHWEST LABORATORIES	RICHLAND, WA	A Proteomics Platform for Quantitative, Ultra-High Throughput, and Ultra-Sensitive	The proposed study aims to develop a new analytical high-throughput proteomics platform for cancer biomarker discovery, verification and validation.	$ 397,168	Admin Supplement	9/1/09	
	R01CA095154-05W1	NCI	OR-04	EGLAN, ANTHONY	OREGON RESEARCH INSTITUTE	EUGENE, OR	Randomized Trial of a State Tobacco Prevention Program	Study to explore whether smoking prevention interventions that associate with not using tobacco, increases social acceptance among young people, thereby deterring tobacco use.	$ 148,642	Admin Supplement	9/1/09	
	R01CA135110-02W1	NCI	CT-03	CHODAPKAR, MADHAV V	YALE UNIVERSITY	NEW HAVEN, CT	Immunity to stem cell antigens in premyeloablc gammopathy	This grant supports development of a reactivey nontoxic treatment that may prevent or control the development of myeloma, an otherwise incurable disease of older Americans.	$ 264,299	Admin Supplement	9/1/09	
	K25CA123250-03W1	NCI	AZ-07	ROMANOWSKI, MAREK J	UNIVERSITY OF ARIZONA	TUCSON, AZ	A new-refined contrast agent for targeted imaging of cancer	Paghacitic, gold-coated plasmon resonant nanoparticles will be prepared for controlled delivery in liposomes for diagnostic imaging and therapeutic intervention in ovarian cancer.	$ 105,000	Admin Supplement	9/1/09	
	K25CA127534-02W1	NCI	TX-14	SPRATT, HEIDI	UNIVERSITY OF TEXAS MEDICAL BR GALVESTON	GALVESTON, TX	Biomarker Discovery for Hepatitis C Progression using Machine Learning Techniques	Development of an interactive, web-based database, containing high-throughput molecular and clinical data, will support construction of a biomarker panel for diagnosis of hepatitis C-induced hepatocellular carcinoma.	$ 107,967	Admin Supplement	9/1/09	
	K25CA133167-02W1	NCI	MO-03	KRUPNICK, ALEXANDER SASHA	WASHINGTON UNIVERSITY	SAINT LOUIS, MO	The Role of Non-Hematopoietic Cells in Tumor Tolerance Induction	Study to better understand mechanisms used by tumors to evade the immune system leading to the design of rational therapeutic strategies to limit tumor growth.	$ 105,000	Admin Supplement	9/1/09	
	R01CA135425-04W1	NCI	MA-09	HAGIS, KEVIN MICHAEL	MASSACHUSETTS GENERAL HOSPITAL	BOSTON, MA	Genetic and genomic analysis of Ras signaling in colorectal cancer progression	Study of the K-RAS oncogene in high grade dysplasia of early stage colorectal cancer leading to identification of molecular targets for novel therapeutics against colon cancer.	$ 101,879	Admin Supplement	9/1/09	
	R01CA109364-06W1	NCI	TX-07	GIORDANO, SHARON HERMES	UNIVERSITY OF TEXAS MD ANDERSON CAN CTR	HOUSTON, TX	Adherence Among Older Women with Breast Cancer	Study to identify patterns and predictors of adherence to adjuvant therapy among older women with breast cancer.	$ 48,963	Admin Supplement	9/1/09	
	R01CA127486-02W1	NCI	NY-15	LAI, ROSE	COLUMBIA UNIVERSITY HEALTH SCIENCES	NEW YORK, NY	A pilot study of statin therapy and risk of malignant glioma	Study to evaluate how use of an individual's genetic makeup could predict their response chemopreventive therapeutics for malignant glioma.	$ 85,462	Admin Supplement	9/1/09	

ARRA required a unique review process for project funding.

Training and Faculty Support

Promote re-entry into biomedical & behavioral research careers	$3.0M
Diversity programs	$20.6M
Faculty startups	$76.2M
Supplements: $58.6M Competing: $17.6M	
Cancer research training, career development, and education	$11.3M

Dollars cited for two years of ARRA funding.

Supplements

Examples of programs/projects funded via administrative and competitive supplements (current estimate of ARRA funds: $342 million)

- **Cohort studies**
- **Phase I/II therapeutic & imaging clinical trials**
- **General needs and small equipment needs for active grants**
- **Summer students**
- **SBIR/STTR workforce enhancement**
- **NCI Alliance for Nanotechnology in Cancer**
- **Cancer Genome Characterization Centers**
- **Centers new faculty appointments via Cancer Centers and Minority Institution Cancer Center Partnerships**
- **Activities to Promote Research Collaborations (APRC)**
- **TARGET childhood cancer**
- **NCI Clinical Proteomic Technologies for Cancer**

R&D Contracts

- Examples of programs and projects **funded under contracts (current estimate of ARRA funds: $494M)**
  - **Cohort studies**
  - **Phase I/II therapeutic & imaging clinical trials**
  - **DCTD expansion of Chemical Biology Consortium & overall therapeutics program**
  - caBIG Knowledge Base
  - **DCTD clinical assay development & molecular characterization centers**
  - TCGA/TARGET/CaHUB

Contract Example: CBC

- Goal: accelerate new therapies
- Government-academic collaborations
- Subcontracting
  - Identified qualified pool of academic contractors
  - Solicitation went to ~30 bidders
  - 11 awards made
    - 8 academic labs
    - 3 commercial labs

Challenge Grants

- NIH opted to fund 18 cancer Challenge Grants ($17.7M) of the 37 NCI sent forward
- NCI selected an additional 41 high priority grants ($38M)
- Comparative effectiveness research: NIH funded 15 NCI grants for $13.2M
- Overall success rate = 20% of NCI cancer-relevant grants reviewed

GO Grants

- NIH matched NCI's funding of 18 cancer GO Grants ($24M)
- NCI funded 33 additional GO Grants ($64M)
  - AIDS: 21 awards, $21M
  - Functional biology: 5 awards, $24M
  - Translational: 5 awards, $16M
  - Viruses and cancer: 2 awards, $3M
- Comparative effectiveness research: NIH fully funded 12 NCI GO Grants on CER for $48M
- Overall success rate = 17% of GO grants reviewed

ACTNOW

- Accelerating Clinical Trials of Novel Oncologic Pathways
  - 37 early phase clinical trials of new treatment regimens
    - Awards contingent on IRB approval and opening to patient enrollment within 90 days; completion in 2 years

ARRA at NIH in FY10

- NCI does not have funds set aside for most NIH initiatives slated for FY10 ARRA funds
- There will be several opportunities for grantees to compete for FY10 NIH-funded ARRA opportunities
  - Check the NIH website for announcements
- Currently open: Building Community-linked Infrastructure to Enable Health Science Research
  - Closes 12/11/09; NIH funds available, $30M

ARRA at NCI in FY10

- NCI obligated or committed all available ARRA funds prior to Sept. 30, 2009
- Remaining balance (~$400M) will be used to cover FY09 ARRA commitments and a limited number of FY10 projects
  - NCI will not solicit competitive revisions or general administrative supplements in FY10
- Specific NCI opportunities:
  - Program specific administrative supplements
  - R&D contracts for the academic community

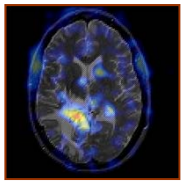
TCGA: Connecting multiple sources, experiments, and data types

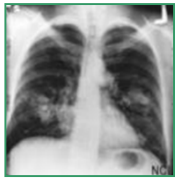
Three Cancers - TCGA Pilot

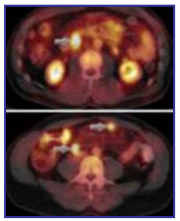
glioblastoma multiforme (brain)

squamous carcinoma (lung)

serous cystadenocarcinoma (ovarian)







Biospecimen Core Resource with more than 13 Tissue Source Sites

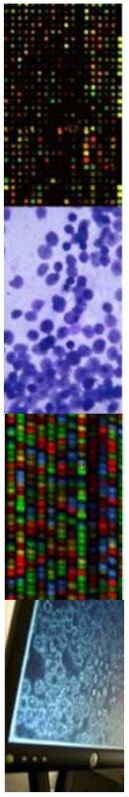
7 Cancer Genomic Characterization Centers

3 Genome Sequencing Centers

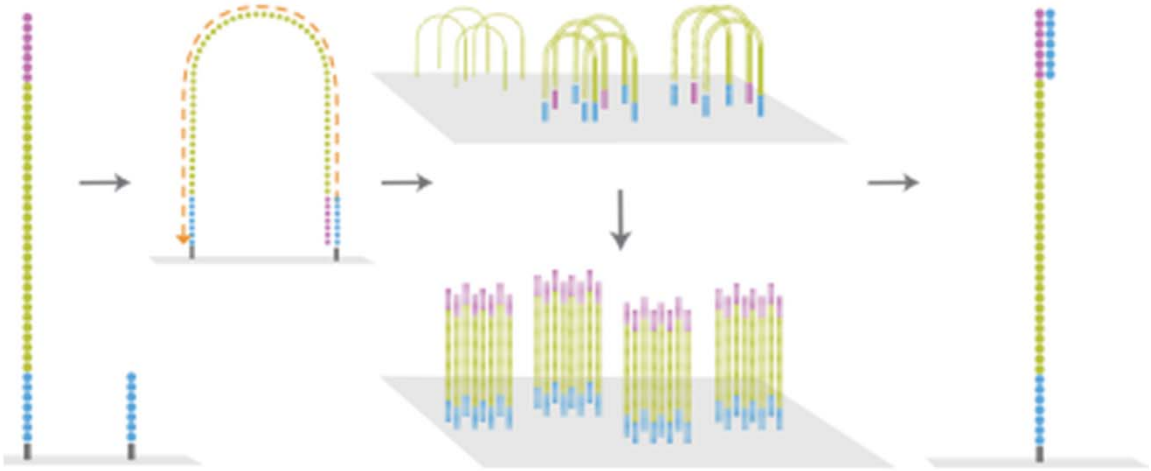
Data Coordinating Center

Multiple data types

- Clinical diagnosis
- Treatment history
- Histologic diagnosis
- Pathologic status
- Tissue anatomic site
- Surgical history
- Gene expression
- Chromosomal copy number
- Loss of heterozygosity
- Methylation patterns
- miRNA expression
- DNA sequence



“Next Gen” Sequencing Technology

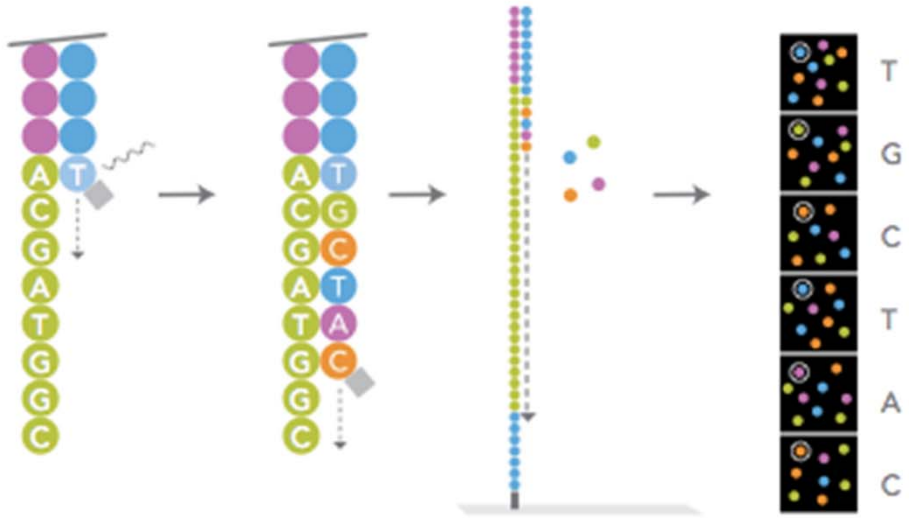


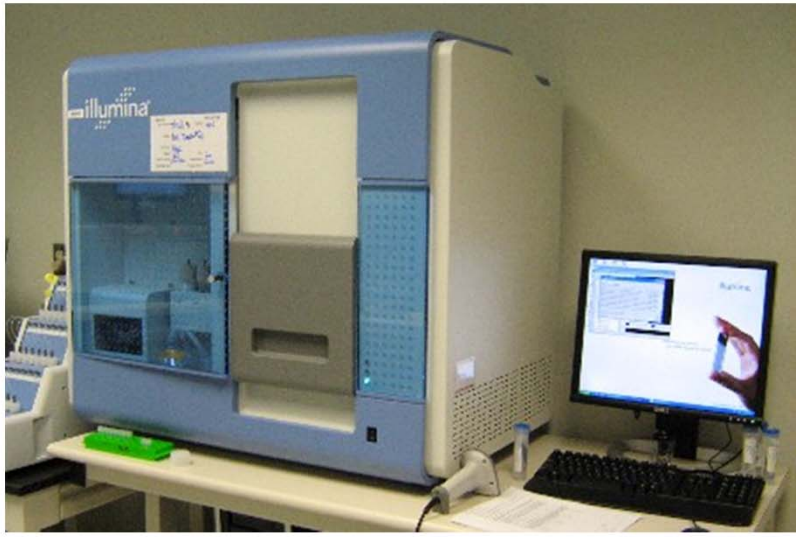
“Solexa” (2006)

~1 Gb/wk

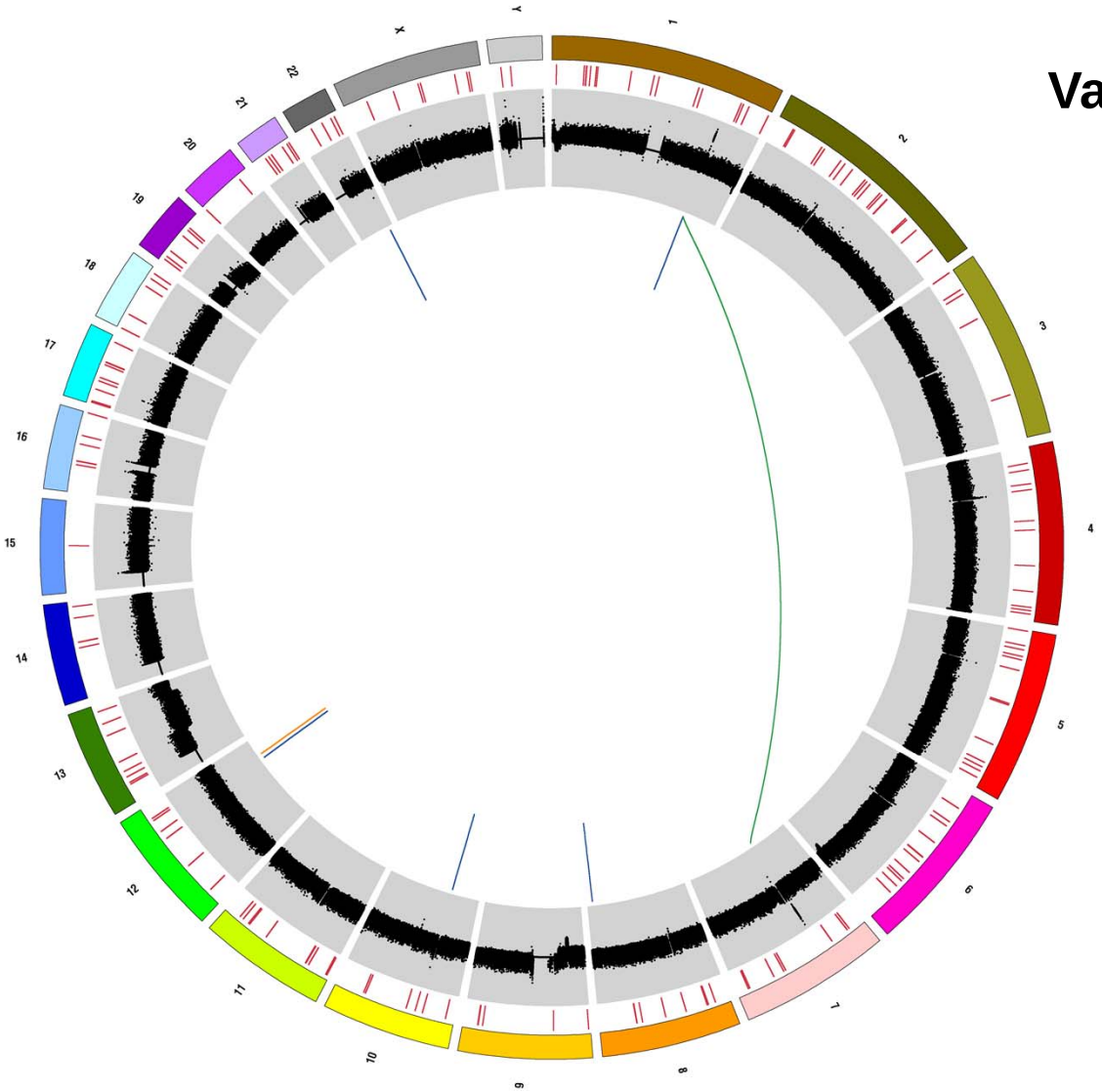
Illumina GA IIx (2009)

20-25 Gb/wk





Power of Whole Genome Sequence: "GBM1" Genome



Validated Somatic Changes:

- 185 mutations (40 Tier 1)
- 6 large indels
- 1 translocation

OVARIAN

Coverage(T/N)	Callable	Purity	Ploidy
31x / 30x	81%	90%	2.8

Name	TCGA-13-0751
Alias	OV-0751
Issued By	Broad Institute
Issue Date	July 8, 2009

Point Mutations

Rate/Mb	0.75
Total	1786
Coding	9

MIS	5
STOP	1
INDEL	---

HIGHLIGHTS

GENE	MUTATION	FUNCTION
TP53	Insertion	Tumor suppressor
EXOC6B	Missense	protein transport, exocytosis
ANKRD6	Missense	ankyrin
AHNAK	Missense	CNS development
C11orf52	Nonsense	?
GABRB3	Missense	GABA receptor

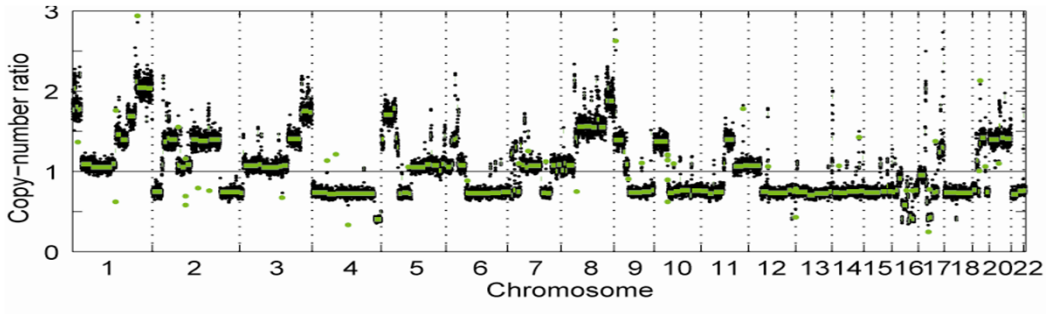
Lost BRCA1 germline indel

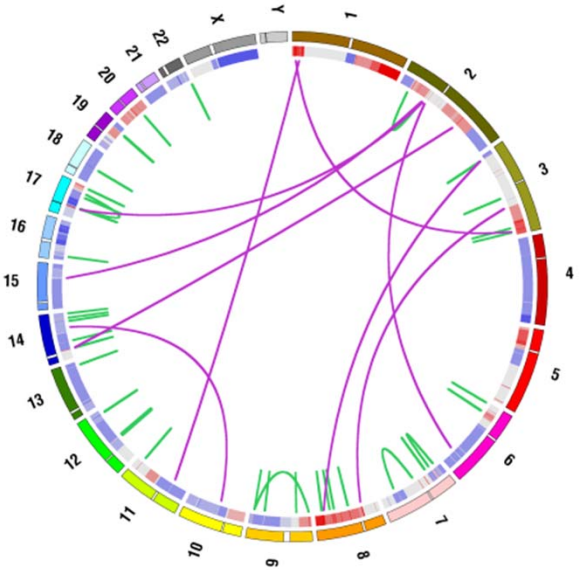
Chr. Aberrations

CNA Breaks	---
TX-Inter	9
TX-Intra	15

HIGHLIGHTS

NF1-EFCAB5 fusion gene probably inactivating validated by RNA-seq





Courtesy of Gaddy Getz – Unpublished, Analysis in Process

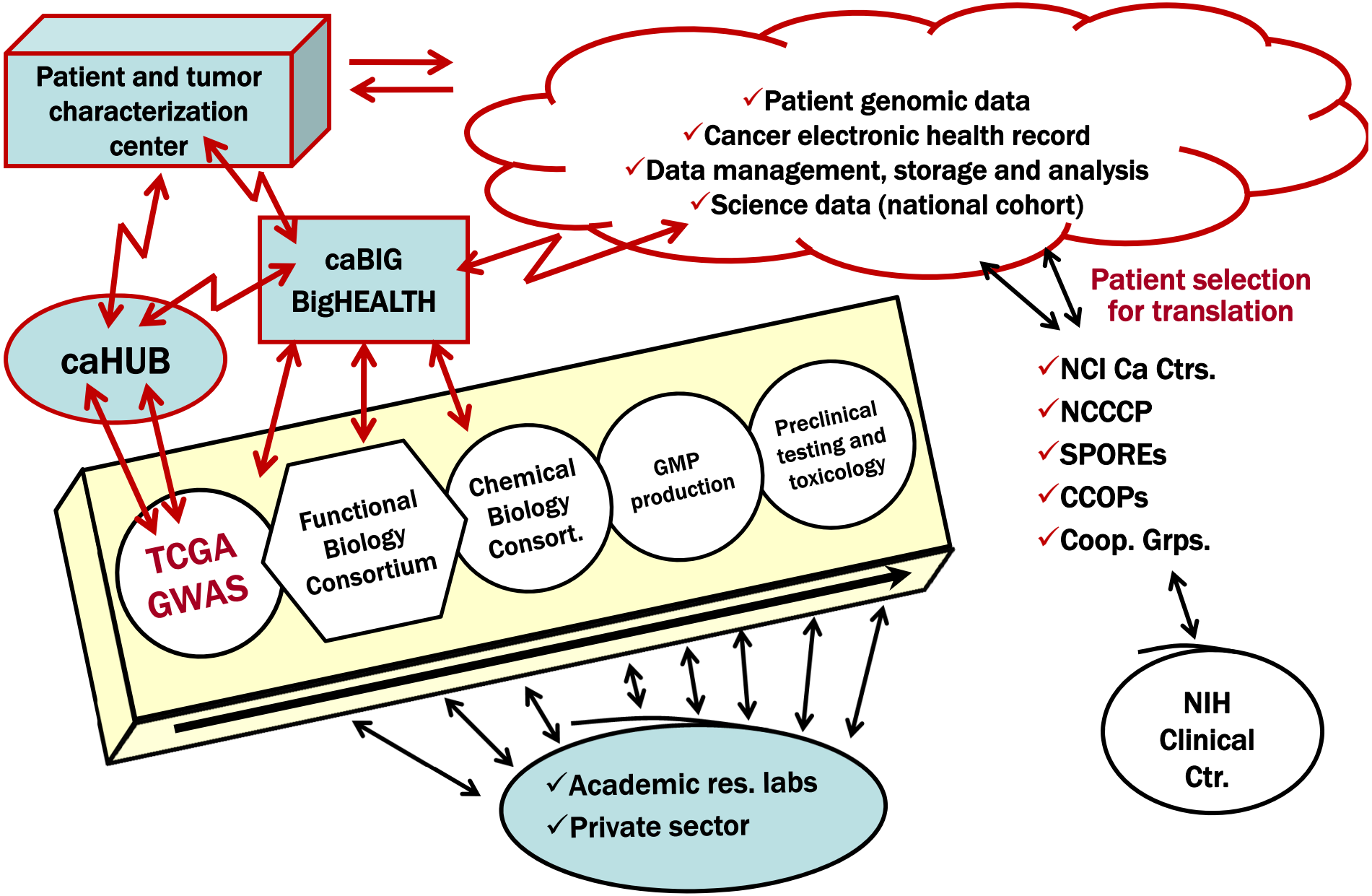
TCGA

- NIH Signature Project (one of seven)
- Identification of relevant genetic alterations in cancer
- Involves >24 institutions and >100 scientists
- ARRA funding has allowed expansion up to 25 tumors
- Long-term goal of including all major cancer types and subtypes
- TARGET utilizes the TCGA approach in childhood cancers

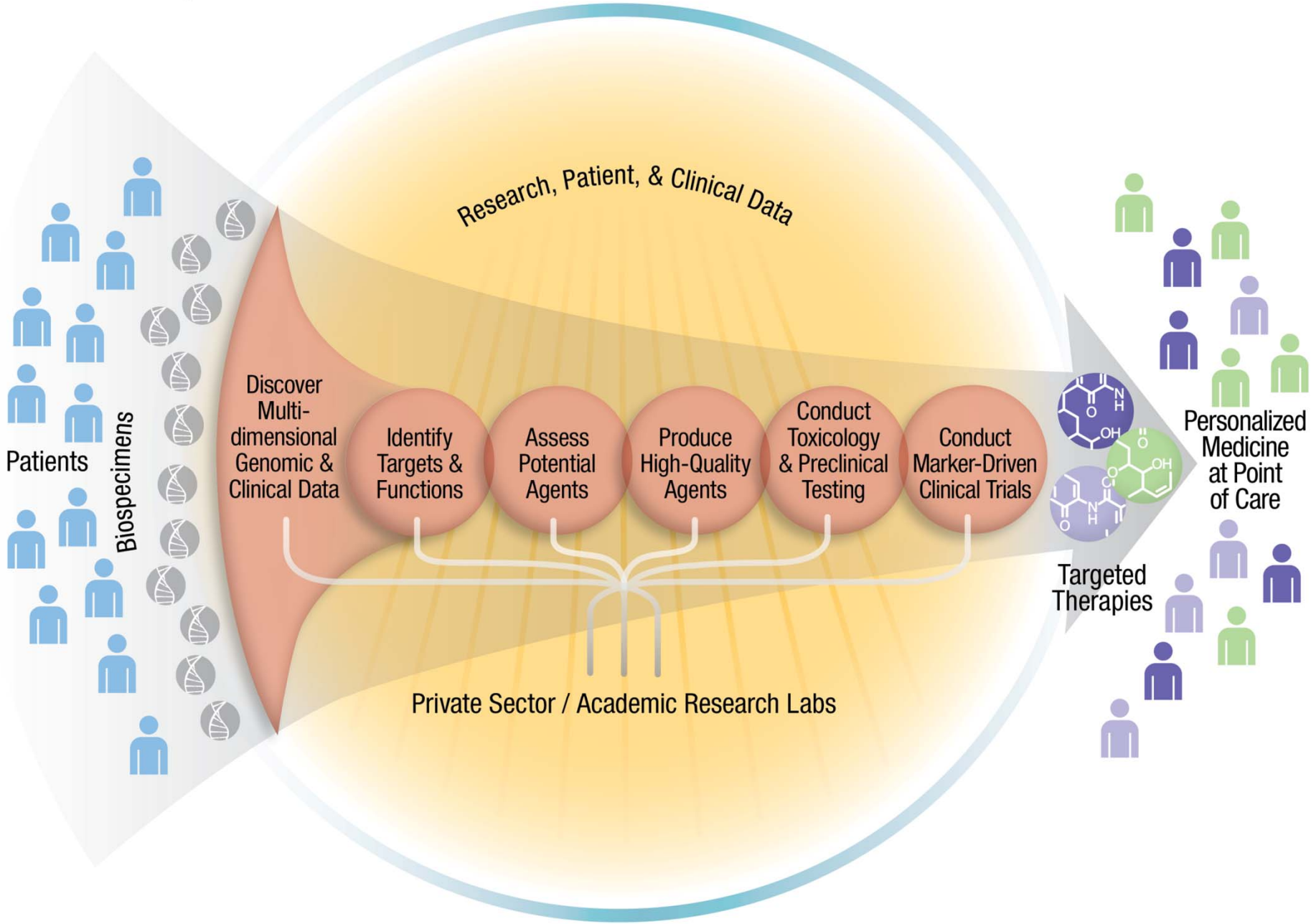
caHUB

- **A unique, centralized, public resource to** ensure the adequate and continuous supply of human biospecimens **and associated data**
- **caHUB Implementation**
  - **Tissue procurement (tumor and normal)**
  - **Pathology reference center/core biospecimen resource**
  - **Biospecimen R&D**
- **ARRA funds: $60M**

TCGA: Informing Science and Medicine



NCI Therapeutics Platform



Pilot study

Patient and tumor characterization center

Data storage

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

NCI structure

Translation

Practicing oncologists

Point of Care Diagnostics

Dr. Francis Collins' Five Themes as NIH Director

- **Apply high-throughput technologies to understand fundamental biology and uncover causes of specific disease states**
- **Translation: deve**
  strategies, and t
- **Put science to w**
- A greater focus
- **Reinvigorate and**
  research commu

The National Cancer Program has long been committed to making a difference in these areas.

How Do We Move Ahead?

- Obama administration supports science
- Emphasis not on what we've done or on capacity, but on seeing science impact patients and decrease cost
  - Economic impact is a key factor
- But there is tremendous pressure on the discretionary portion of the federal budget
  - Will support translate into new resources?


Patients & Families
www.cancer.gov

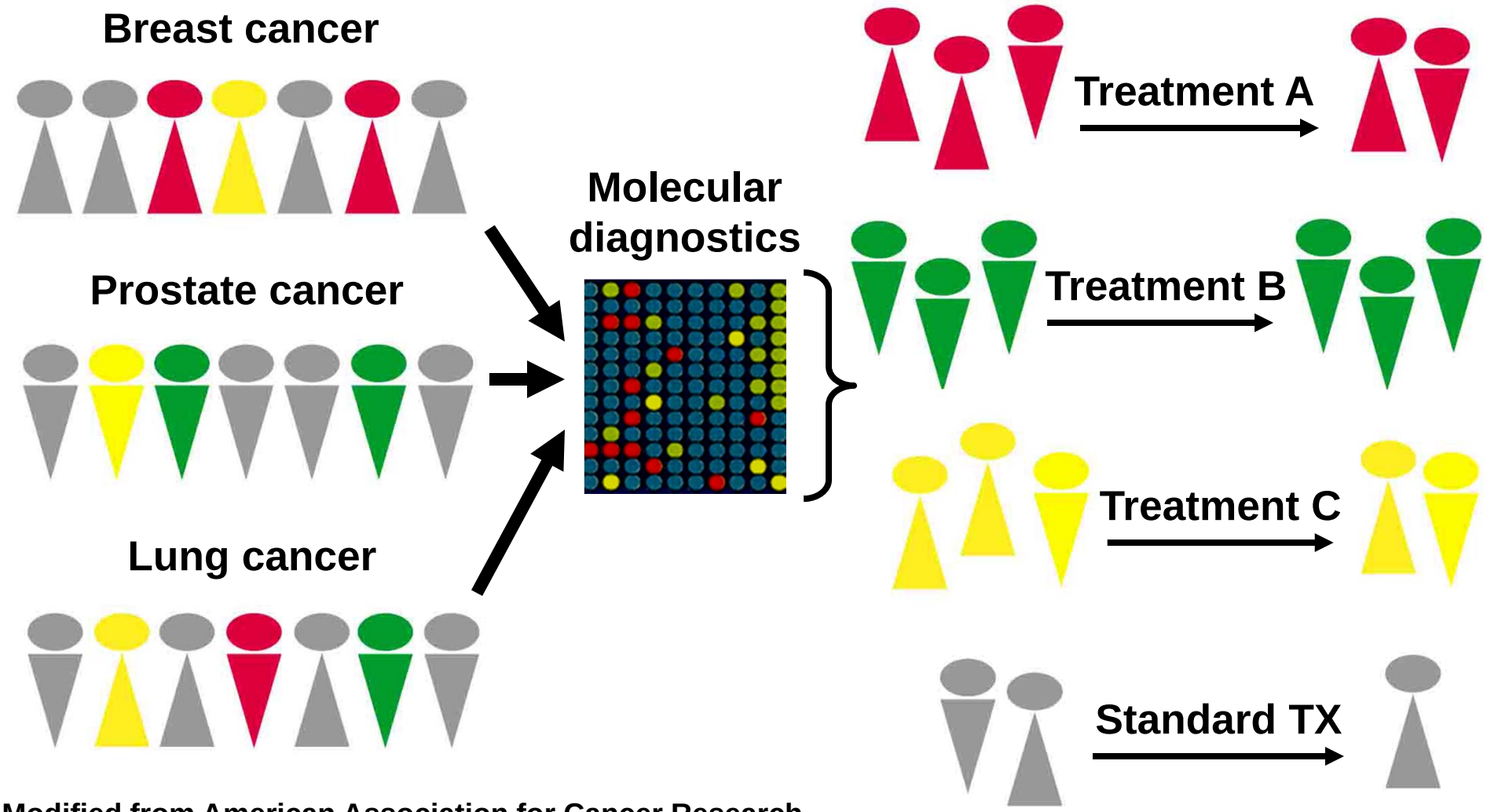
ARRA Funding for Cancer Research by Organ Site

Breast cancer	**76 grants**	**$14,735,425**
Prostate cancer	**54 grants**	**$ 7,415,299**
Colorectal cancer	**40 grants**	**$ 7,284,159**
Lung cancer	**35 grants**	**$ 6,045,434**
Pancreatic cancer	**17 grants**	**$ 2,969,897**
Ovarian cancer	**8 grants**	**$ 1,430,823**

As of July 2009

Individualized Medicine

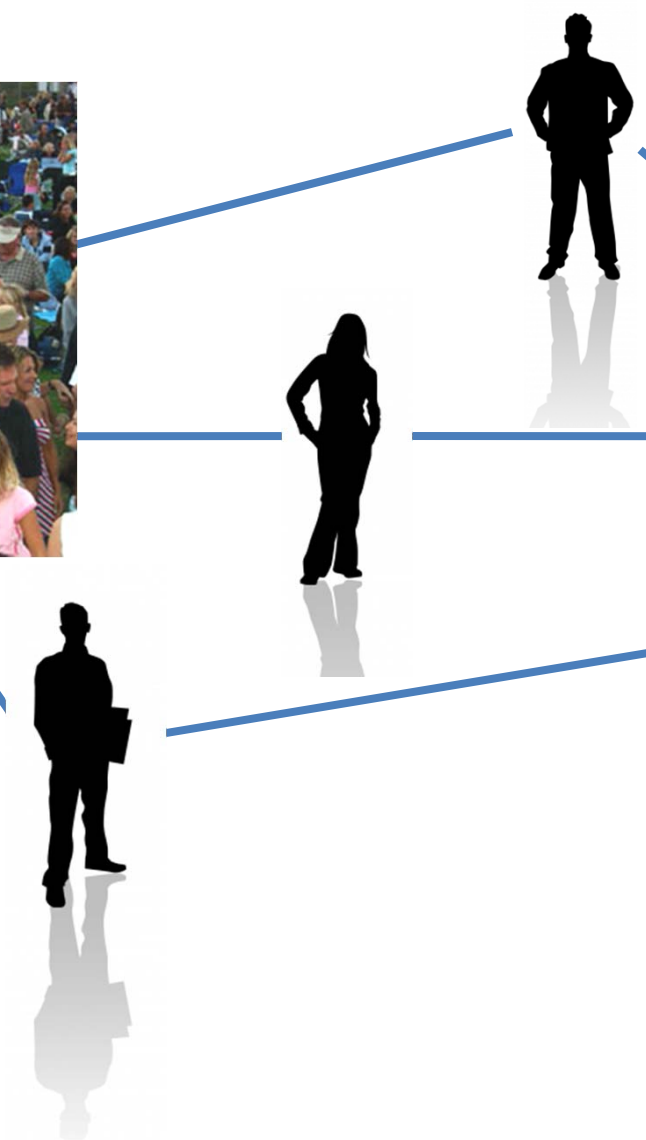
The hope for the future



Modified from American Association for Cancer Research

Treatment for the Individual

Science and technology

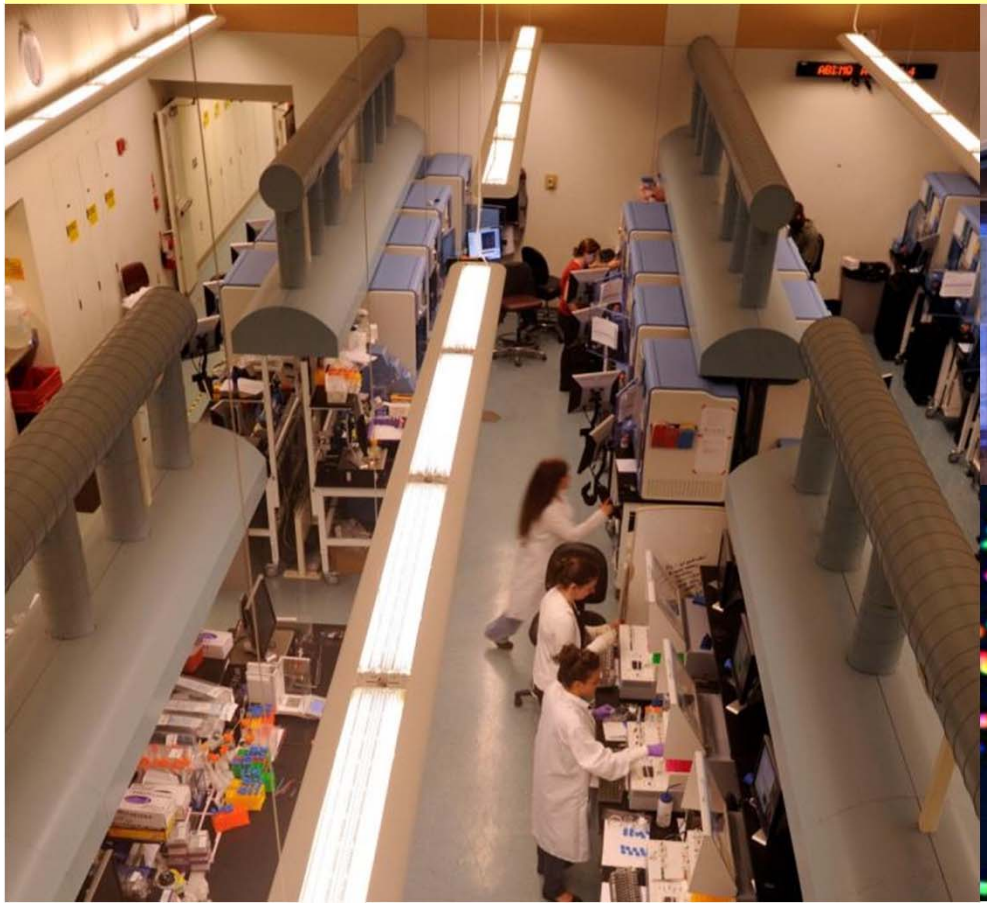


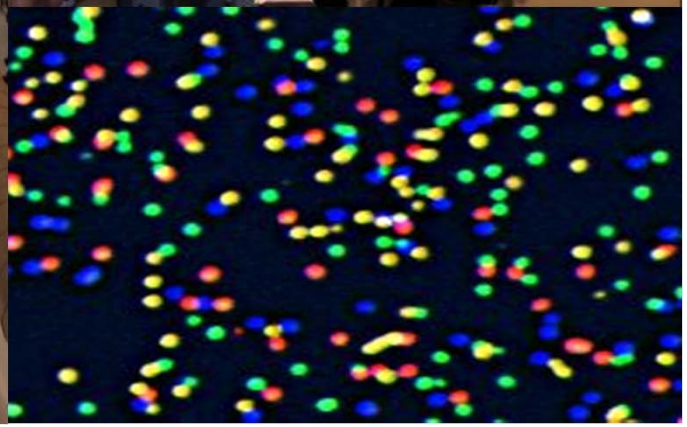
Phase 0/1

- ✓ IND30452
- ✓ Approved Drug A
- ✓ Approved Drug B
- ✓ Approved Drug C

The Power of Technology

- Search for all gene defects
- Isolate proteins





Cost of Sequencing

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

Courtesy of Eric Lander