U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

## NCI Director's Update

**Dr. John E. Niederhuber** Director, National Cancer Institute

National Cancer Advisory Board September 15, 2009

## NCI – Sept. 2009



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

## Final Quarter FY2009

Appropriated budget: \$4,968,973 (2.9% increase)

Number of grants awarded for FY2009 (as of Sept. 11)

6,239

7,010

7,103

Estimated final number of grants >7,075 to be awarded in FY009

Number of grants awarded in FY2008

Number of grants awarded in FY2007

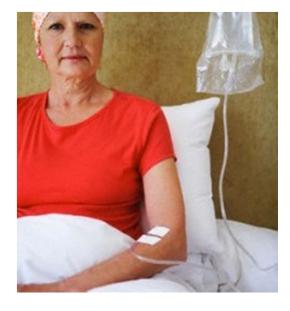
Dollars in thousands

## ARRA \$ to NIH

- \$7.4 billion: Institutes and Centers
  \$1.26 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

# 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 pe 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	\$493,837,000	39%		

academic community 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"

- 1,151 items have been submitted
- 1,069 items have been approved
- Awaiting approval of 82 items

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-	_	_						NAL INSTITUTES OF HEAL						-
L	Planned ARRA Funding Announcements													
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							A17 A174 1818	NATIONAL INSTITUTE						_
								Planned ARRA Funding						
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				Cuttore	Each C seads to care	ate a simple some single and a date	In Million Manual In Communi	untion (Office) on later them	10 am each Monday, If supplishing onlines for some	and the report when ready. Any project listed on this table must be fully				
				ready for i	release with no chang	es (already worked up). The PI and	Grant Number are for internal NH use	only. Please include all gra	nts (RPGs, Centers, etc.) and contracts to be funded	with ARRA (only excludes IR or RMS).				
	acific:			<b>Final actu</b>	al figures will be repor	rted through Recovery.gov and on I	be NH RePORTER Web site.							
1	WA.													
		40.04												Т
L		(pacific	Grant No.	ю.	Congressional		Institution	Location (City/State)	Project Title	Summary/Public Health Relevance	Total FY 2009 Obligation	Type Award	Anticipated	4
_		RFA									Congestion			4
L			05CA111340-03W1	NO	MF15	KATZ, STEVEN J	UNIVERSITY OF MICHIGAN AT ANN	ANN ARBOR, M	Quality of Cancer Care Evaluation and Interventions	A population-based study to evaluate online communication and service	\$ 108,000	Admin Supplement	9/10/09	T
-		I		1	1	1	ARBOR	1	1	bole in improving the quality of early detection initiatives for women with treast center.				1
1	- H	-	IOICA136043-01A1	NO	VAIOS	LEE, RUEYMIN RAY	VIRGINIA COMMONWEALTH	RICHMOND, VA	Development of Vescular Disrupting Agents	This proposal will investigate the mechanism(s) of stilbune-induced tumor	\$ 270,775	Grant	9/1/09	1
1				1	1	1	UNIVERSITY			blood few suppression with the goal of developing chemothempeutic strategies to enhance concer treatment.				1
L	- H	-	121CA128718-01A2	NO	CA63	MESSMER, DAVORKA	UNVERSITY OF CALIFORNA SAN	LA JOLLA CA	Real true quantitative multiplex analysis of call-call	This project will develop a new betweekers in allow the monitoring of the	\$ 147,967	Onert	91909	$^{+}$
⊢-	_						DEGO		interactions	complex communication process between gencer cells and cells of their				
<u> </u>		-	121CA132075-01A1	NCI	NC-04	RID-IN, ROBERT	NORTH CAROLINA STATE	RALEIGH, NC	Epigenetic profiling by near-field UV-Reman	environment in real time Study that combines nanofluidics and imaging technologies to identify	1 201404	Grant	91909	+
1							UNIVERSITY RALEIGH		scattering in nanocharmela	epigenetic alterations to aid cancer researchers in identifying subtle changes				
_		-	COLORI SANGACIONI	80	CARD	GERSET, RUTHA	TORREY PINES INST FOR	SAN DEGO, CA	Reputation and Function of thep	In the chromosomes of cancer patients. This study develops diagnostic tools for identifying thempy responsive	\$ 513,200	Revision	91009	+
							MOLECULAR STUDIES		144REAmpleomation   Complex in Center	Amore and refinition Paragatic radinana.				
-	-r		01CA114650-05W1	NO	MD-07	BAQUET, CLAUDIA ROSE	UNIVERSITY OF MARYLAND BALTMORE	BALTIMORE, MD	The Maryland Regional Community Network Program To Eliza	Funding will support acceleration of cencer and health departies research through robust multikingle site and multidecipinary research that will also	\$ 99,554	Admin Supplement	91309	T
				1	1					provide a foundation for training.				1
-	— <b>Г</b>		01CA12467042W1	NO	016-15	RINGEL, MATTHEW D	OHIO STATE UNIVERSITY	COLUMBUS, OH	Genetic and Signaling Pathways in Epithelial Thyroid Canvar	This study will improve our understanding of the genetics, mechanisms, and	\$ 409,865	Admin Supplement	91909	T
ŧ.	- H	-	0104007485-00001	NO	01611	LU ZHENGRONG	CASE WESTERN RESERVE	CLEVELAND, OH	Cancer Polymer chelds conjugates for degrands cencer	transpersent of thyroid cancer, a cancer with an increasing incidence rate. Study to evaluate the biodetribution of novel targeted nanoglobular MRI	1 376 104	Admin Supplement	91009	+
-	_						UNIVERSITY		imaging	contrast agents; critical parameters required to select agents precirical and				
ŧ.	- H	_	IDICAL TREATING	NO	81472	RESPECTIVES, YANA K	UNMERSITY OF ENOUS ISLAND	KINGSTON III	aHLP Nendechnology Pleform for Cencer Integing	clinical development. This supplement will evaluate novel ranotechnology construct - pHLIP (pH-	5 501 500	Admin Supplement	91009	+
-	_		and a second second						and Thempy	selective peptide) for selective delivery of imaging and therepeutic agents to				
ŧ.	- H	_	10C-0001546-00001	NCI	1X-07	DINNEY COUN P	UNVERSITY OF TEXAS MD	HOUSTON TX	Specialized Programs of Research Excellence	Lenons. The projected work is to establish new effective therapy with AD-IFN/Syn3	5 117 414	Admin Supplement	N2709	+
I—	_						ANDERSON CAN CTR	10	(SPOREs) in Geniloutnery Cencer	for patients with high-risk superficial bladder cancer that talls present				
L	- H	_	ARCALLING SOLVE	NC	MACO	COLONCARMONA ADAN	UNVERSITY OF MASSACHUSETTS	BOSTON MA	UMB/DFHCC Comprehensive Center Performinip	standard Terrates Funding to accelerate research and training activities providing resources to	1 154 000	Admin Supplement	91009	+
-	_			-			BOSTON		Program	hire up to nine undergraduate atudents and one postdoctoral fellow and				1
		_	INVESTIGATION OF TAXABLE	100	15.61	SRIVASTAVA, RAXESH K	UNIVERSITY OF TEXAS HETH CTR	THER TX	Chemoprevention of Pancreatic Cancer by EGCG	edificial resources for scientific activities. The study of combination of STAT3 inhibitor with EGCG or periodiabine	4 567 500	Admin Supplement	91009	+
17						A CONTRACTOR OF A CONTRACTOR OFTA CONTRACTOR O	ATTYLER		contraction of the second second	could open up a new therapeutic strategy for the treatment and/or prevention	- 207,000			
		_	000.4118740-0700	NO	14-01	BL HALLOUD	THOMAS JETTERSON UNIVERSITY	PHI ADEL PHIA PA	Experimental Modeling of Human Breast Cancer in	of human percenter cancer. Shufu of the mix of the contents in human breast cancer as mixed	1 141 710	Admin Supplement	91009	4
<b>Г</b>				NU					Mine	much, and reporters to arthurancer therapies.				
L			01CA03408-22W1	NO	10.487	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 inclute the identification of	\$ 716,400	Admin Supplement	91909	T
r	_									additional genes associated with disease risk leading to improved patient reanagement.				1
1			133CA126191-00W1	NCI	104-01	SMITH, RICHARD D	BATTELLE PACIFIC NORTHWEST	RICHLAND, WA	A Proteomics Platform for Quantitative, Ultra-High	The proposed study aims to develop a new analytical high-throughout	\$ 307,168	Admin Supplement	91309	T
-				1			LABORATORIES		Throughput, and Ultra-Genalitive	proteomics platform for cancer biomarker discovery, verification and relinition				
1	- F	-	101CA066169-00W1	NO	08404	BIGLAN, ANTHONY	OREGON RESEARCH INSTITUTE	EUGENE, OR	Rendomized Trial of a State Tobecco Prevention	Study to explore whether smoking prevention interventions that associate	\$ 148,642	Admin Supplement	91009	1
_				1			1		Program	with not using tobacco, increases social acceptance among young people, thereby deterting tobacco use.				
1	- H	-	101CA135110-02W1	NO	CT-03	DHOCAPKAR, MACHAV V	YALE UNIVERSITY	NEW HAVEN, CT	immunity to stem cell antigens in preneoplastic	This grant supports development of a relatively nontoxic treatment that may	\$ 264,299	Admin Supplement	91909	1
<u> </u>				1			1		genmopetry	prevent or control the development of myeloms, an otherwise incurable deepee of older Americana.				
t	- H	-	Q9CA120390403W1	NO	AZ-07	ROMANOWSKI, MAREK J	UNIVERSITY OF ARIZONA	TUCSON, AZ	A near-infrared contrast agent for targeted imaging of	Degradable gold-coated plearnon resonant ranoparticles will be prepared for	\$ 108,000	Admin Supplement	91009	+
-	_	I		1	1	1	1	1	ownow?	controlled delivery in liposomes for diagnostic imaging and therapeutic intervention in overlan cancer				1
t i	- H	-	(25CA127524-82W1	NCI	10-14	SPRATT, HEIDI	UNIVERSITY OF TEXAS MEDICAL BR	GALVESTON, TX	Signarker Discovery for Hepatite C Progression	Development of an interactive, web-based database, containing high-	\$ 107,967	Admin Supplement	91309	+
⊢	_			1			GALVESTON		using Machine Learning Techniques	throughput molecular and clinical data, will support construction of a				
L	- H	-	08CA151007-02W1	NO	MO-03	KRUPNICK ALEXANDER SASHA	WASHINGTON UNIVERSITY	SANT LOUIS, MO	The Role of Non-Hemeloopietic Cells in Tumor	biomerian same for discressing of hepatitis C-virus/hepatocelular cardinoms. Study to befor understand mechanisms used by tumors to evade the	\$ 108,000	Admin Supplement	91909	+
1	_								Tolerance Induction	mmune system leading to the design of retional therapeutic strategies to limit				1
L_		_	01CA118625-04W1	NO	MALCO	HAGIS, KEVIN MICHAEL	MASSACHUSETTS GENERAL	BOSTON MA	Genetic and genomic analysis of Ras signaling in	tumor growth. Study of the K-RAS oncogene in high grade dysplaxis of early stage	< 101.670	Admin Supplement	91000	4
E			and the second	-		Contraction and the second	HOSPITAL		colorectal cancer progression	colorvotal cancer leading to identification of molecular targets for novel				1
_	_	_	00041000440040	100	15.47	GIORDANO, SHARON HERMES	UNVERSITY OF TEXAS NO	HOUSTON, TX	Advance Among Older Women with Breast Cancer	twopeutos against color cancer. Dudy to identify patients and predictors of adherence to adjuvant twopy	5 45.953	Admin Supplement	91009	+
			ALC: NOT A REAL PROPERTY		1000	and the second s	AND ERSON CAN CTR		And a strong once Promen wer prese cance	among older women with breast cancer.	• • • • • • • •	Contract of Distance		1
			07CA127498-02W1		200.05	LAL BOSE	COLUMNA UNVERSITY HEALTH	NEW YORK, NY	A plot study of state thempy and risk of malignant	Study to evaluate how use of an individual's penetic makeup could predict	1 85.402	Admin Supplement	91000	

As of 9/14/09

## Supplements

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

- Promote re-entry into biomedical & behavioral research careers
- Diversity programs
- Faculty startup and re-entry
- Cancer research training, career development and education
- Cohort studies
- Phase I/II therapeutic & imaging clinical trials
- General needs and small equipment needs for active grants
- Summer students
- SBIR/STTR workforce enhal
- NCI Alliance for Nanotechnc
- Cancer Genome Characteriz
- Centers new faculty appoint Cancer Center Partnerships
- Activities to Promote Resea
- TARGET childhood cancer
- NCI Clinical Proteomic Tech

Equipment (admin.)	=	16.6%
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General support (admin.) = 15.0%

Payline for competitive supplements set at 23 (based on priority score)

## **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 Cancer Cloud
  - DCTD clinical assay development & molecular characterization centers
  - TCGA/TARGET

## 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)
- Pending availability of ARRA funds, NCI may select additional grants
- Comparative effectiveness research: NIH funded 15 NCI grants for \$13.2M
- Overall success rate 20% of 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 grants for \$48M
- Overall success rate 17% of 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 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

### The Power of Technology

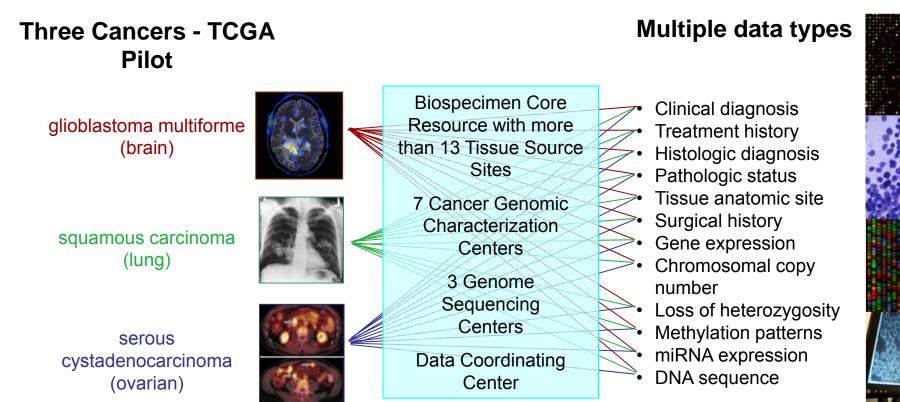
## Search for all gene defectsIsolate proteins



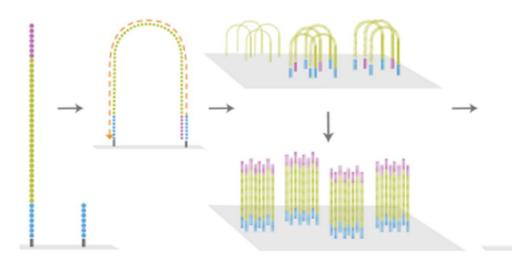




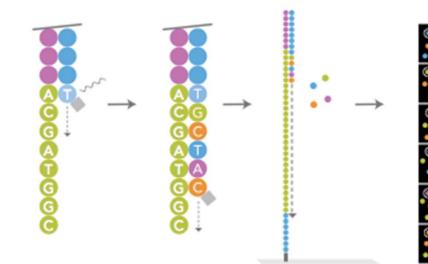
#### TCGA: Connecting multiple sources, experiments, and data types

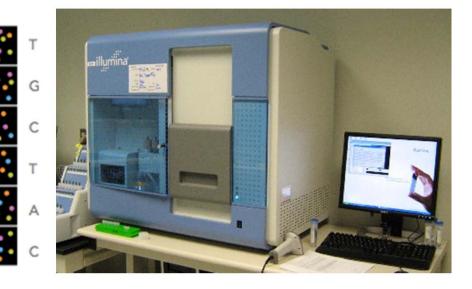


### "Next Gen" Sequencing Technology

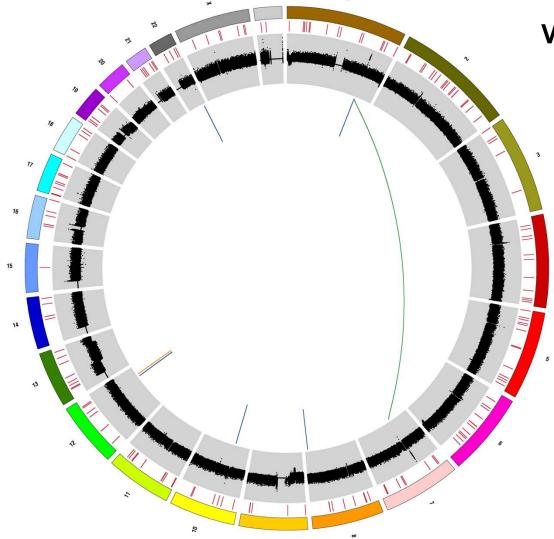


**"Solexa" (2006)** ~1 Gb/wk Illumina GA IIx (2009) 20-25 Gb/wk





### 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 31x / 30x 81%

ble Purity 90%

#### **Point Mutations**

Rate/Mb Total Coding 0.75 1786 9 MIS 5 STOP 1 INDEL ---

#### HIGHLIGHTS

HIGHLIGHTS

Ploidy

2.8

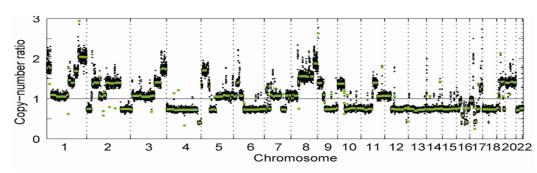
GENE	MUTATION	FUNCTION
TP53	Insertion	Tumor suppressor
EXOC6B	Missense	protein transport, exocytosis
ANKRD6	Missense	ankyrin
AHNAK	Missense	CNS development
C11orf52	Nonsense	?
GABRB3	Missense	GABA receptor

#### Lost BRCA1 germline indel

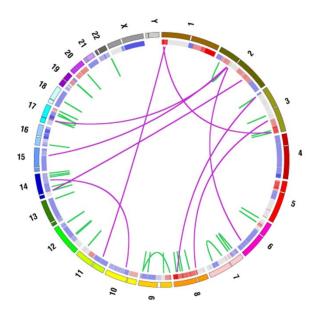
#### Chr. Aberrations

CNA Breaks	
TX-Inter	9
TX-Intra	15

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

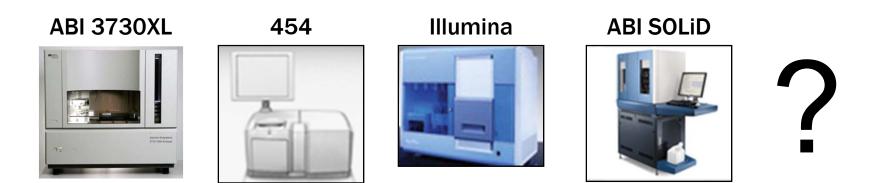


Courtesy of Gaddy Getz – Unpublished, Analysis in Process



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

### Cost of Sequencing



**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

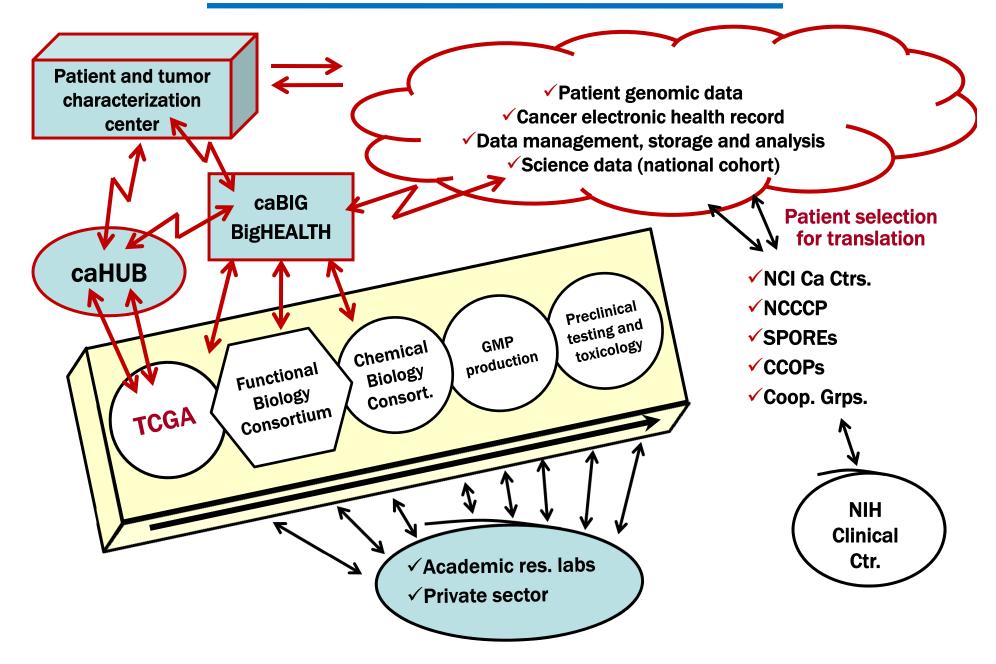
## TCGA and TARGET

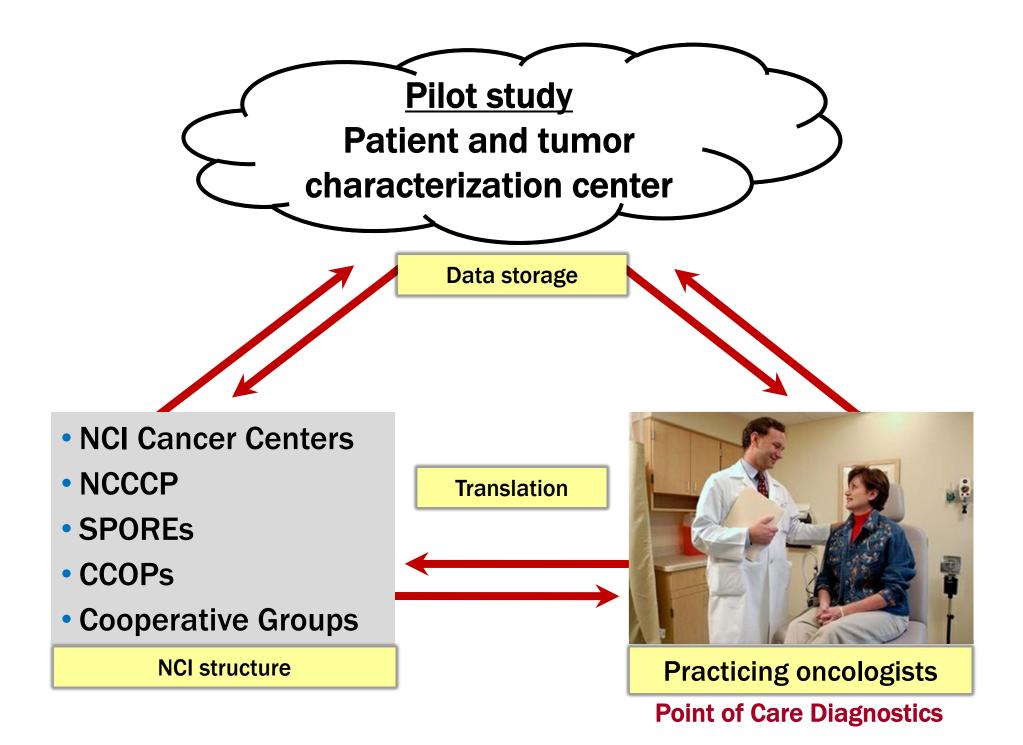
- NIH Signature Project (one of seven)
- Identification of relevant genetic alterations in cancer
- Involves >24 institutions and >100 scientists
- ARRA funding has allowed expansion up to 25 tumors
- Long-term goal of including all major cancer types and subtypes
- TARGET utilizes the TCGA approach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





Dr. Francis Collins' Five Themes as NIH Director

- Apply high-throughput technologies to understand fundamental biology and uncover causes of specific disease states
- Translation: develop diagnostics, preventive strategies, and therapeutics
- Put science to work for healthcare reform
- A greater focus on global health
- Reinvigorate and empower the biomedical research community

