Building the Right Team, Using the Right Resources, and Evaluating Progress

Jerry S.H. Lee, Ph.D.

Health Sciences Director

Office of the Director, National Cancer Institute (NCI)
National Institutes of Health (NIH)

HESI

Health and Environmental Sciences Institute Annual Meeting
Combining Interdisciplinary and Translational Expertise (CITE) Session

CITE

June 10, 2014

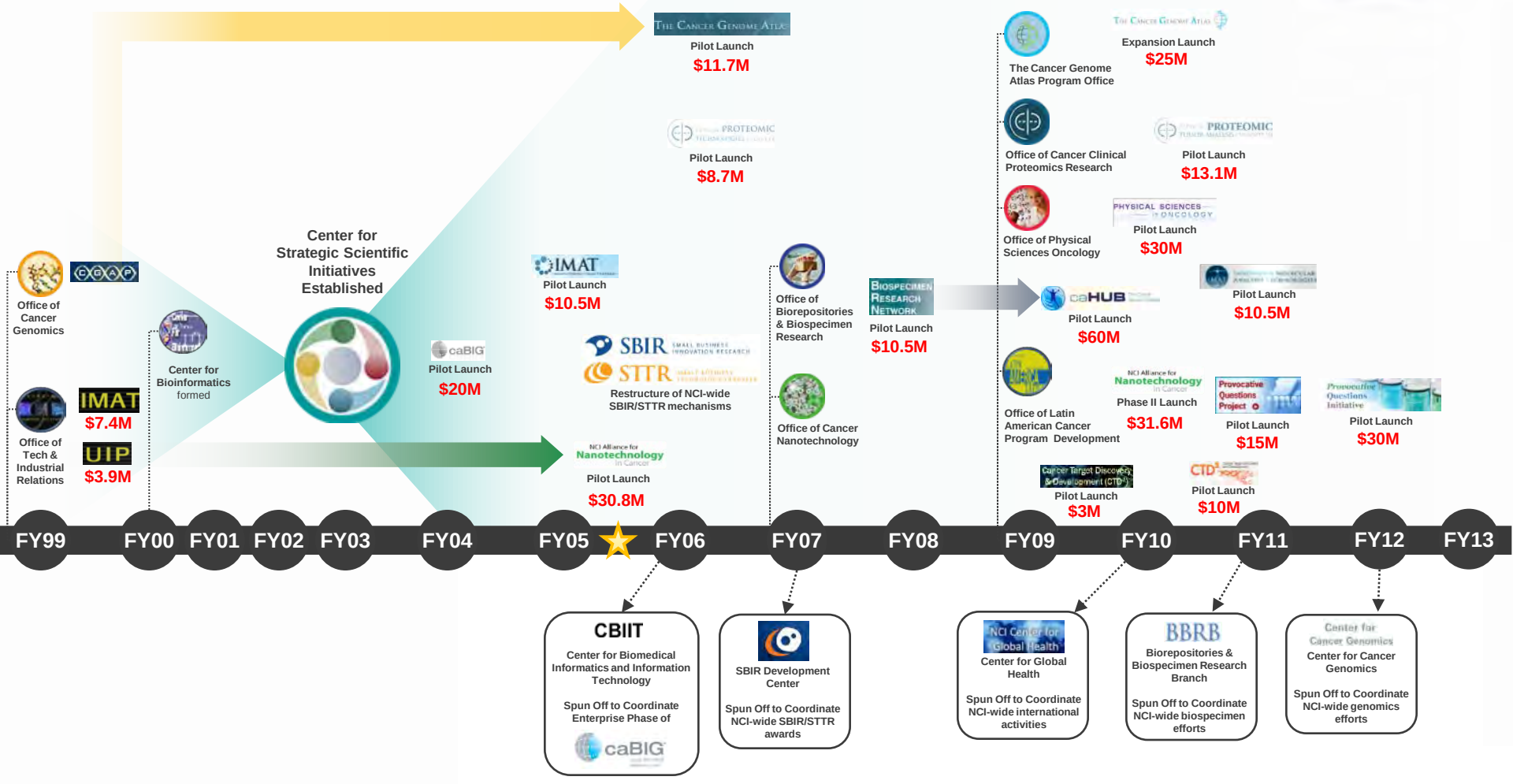
CLINICAL PROTEOMIC TUMOR ANALYSIS CONSORTIUM

NCI Alliance for Nanotechnology in Cancer

IMAT INNOVATIVE MOLECULAR ANALYSIS TECHNOLOGIES

Provocative Questions Initiative

NCI Center for Strategic Scientific Initiatives (FY99 – FY13)



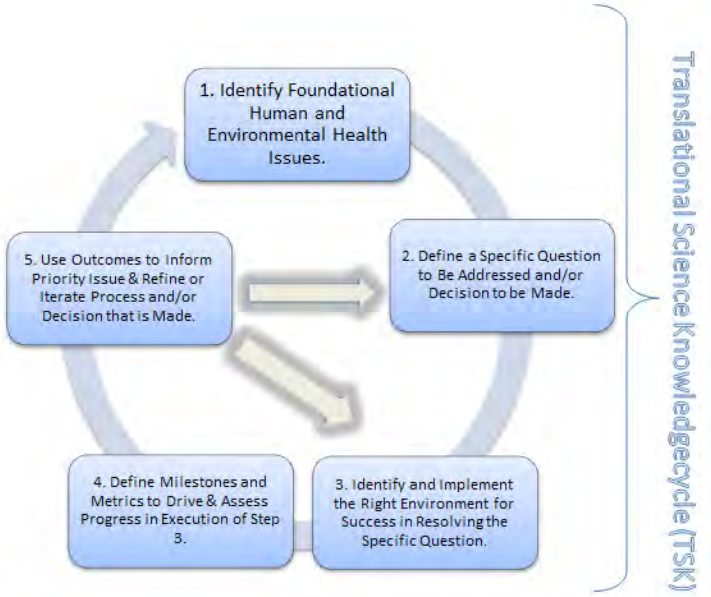
Data from NCI Factbooks (http://obf.cancer.gov/financial/factbook.htm)

HESI CITE Initiative:

Combining **I**nterdisciplinary and **T**ranslational **E**xpertise

CITE

COMBINING INTERDISCIPLINARY & TRANSLATIONAL EXPERTISE

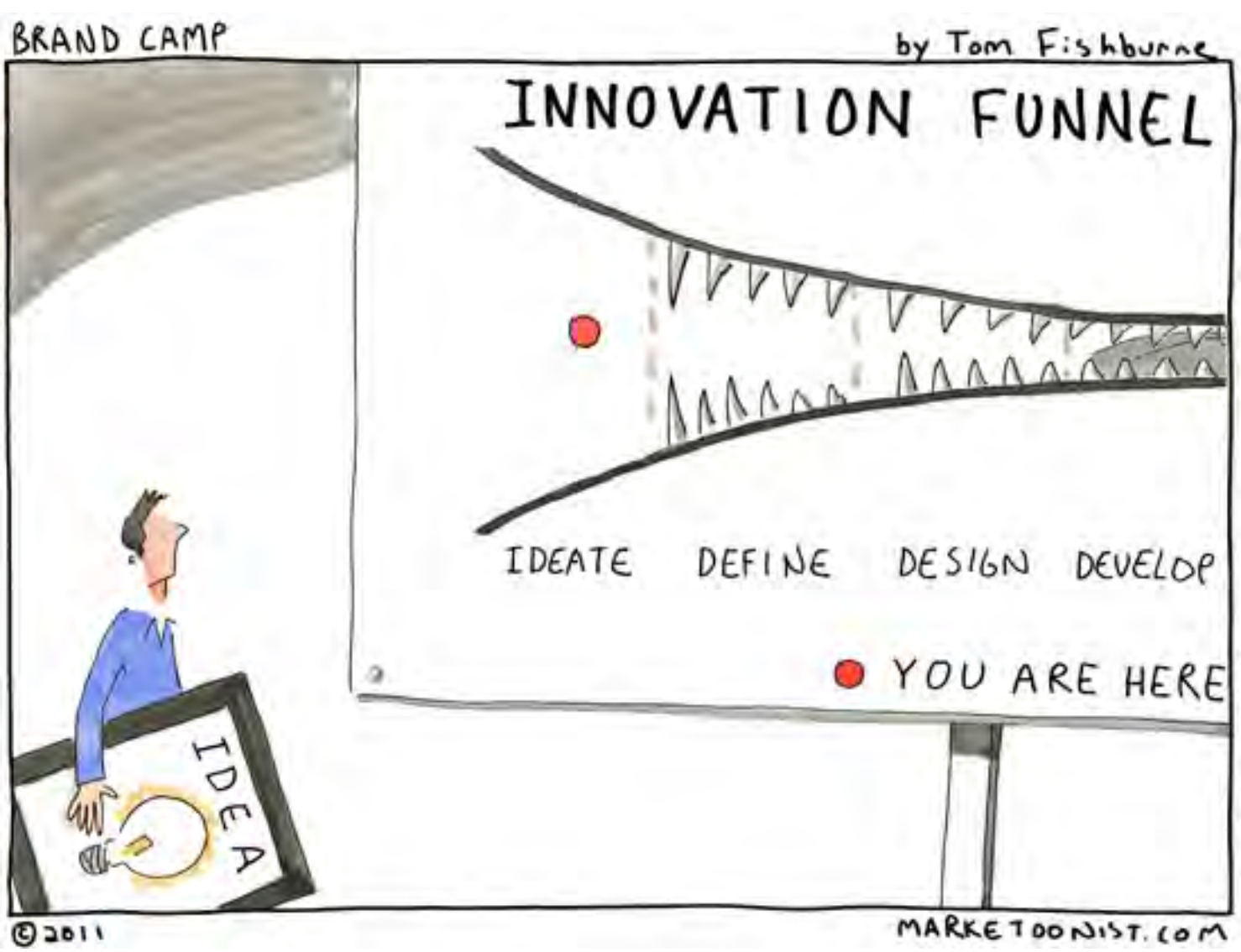


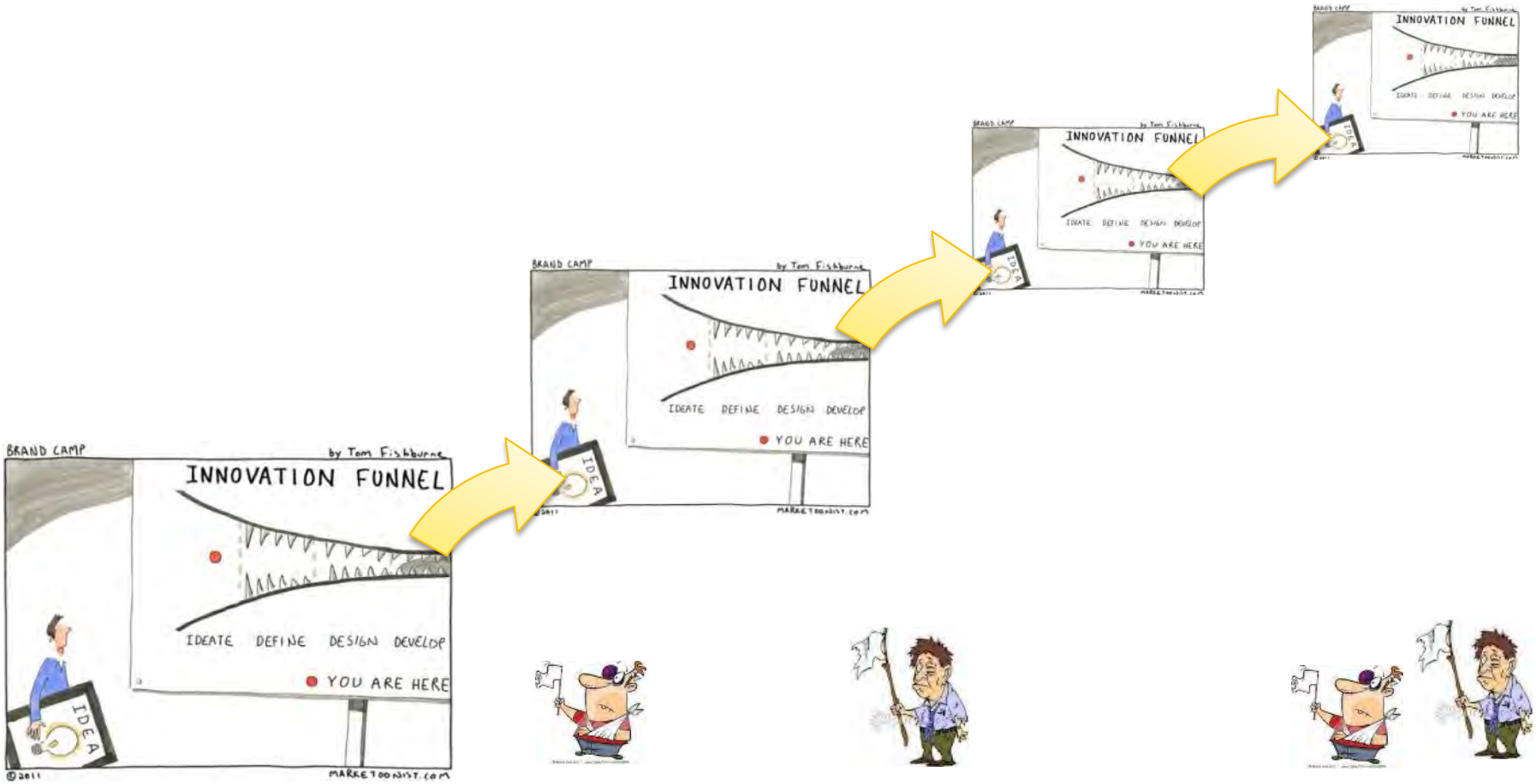
12 February 2014 EDITORIAL

Science Translational Medicine

From Silos to Multilingual Science

- Supporting research and thought leadership that **enhances** the **efficient movement of science** from **research** to **application** (December 2012 Workshop)
- February 2014 *Science Translational Medicine* Publication
- Ongoing Speaker Series
- Interdisciplinary Project Development


BRAND CAMP
by Tom Fishburne
INNOVATION FUNNEL
IDEATE
DEFINE
DESIGN
DEVELOP
YOU ARE HERE
IDEA
©2011
MARKETOONIST.COM



Basic Applied Translational Clinical Commercial/Industry

Support Convergence and Innovation At Many Scales

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

NCI Alliance for Nanotechnology in Cancer

Phase II

Cancer Target Discovery & Development (CTD²)

Early settlers

PHYSICAL SCIENCES in ONCOLOGY

Team Explorers

CLINICAL PROTEOMIC TECHNOLOGIES

Phase II

THE CANCER GENOME ATLAS

Phase II

Provocative Questions Initiative

IMAT

Discoverers/ Pioneers

Basic **Applied** **Translational** **Clinical** **Commercial/Industry**

National Institutes of Health (NIH): 27 Institutes and Centers

NHGRI
NIA
NIDA
NEI
NIAAA
CIT
FIC
CSR
NIBIB
NIGMS
NICHD
CC
NIAMS
NCCAM
NIAID
NCI
NHLBI
NINDS
NIDCD
NIMH
NINR
NLM
NIDDK
NIMHD
NIDCR
NIEHS
NCATS

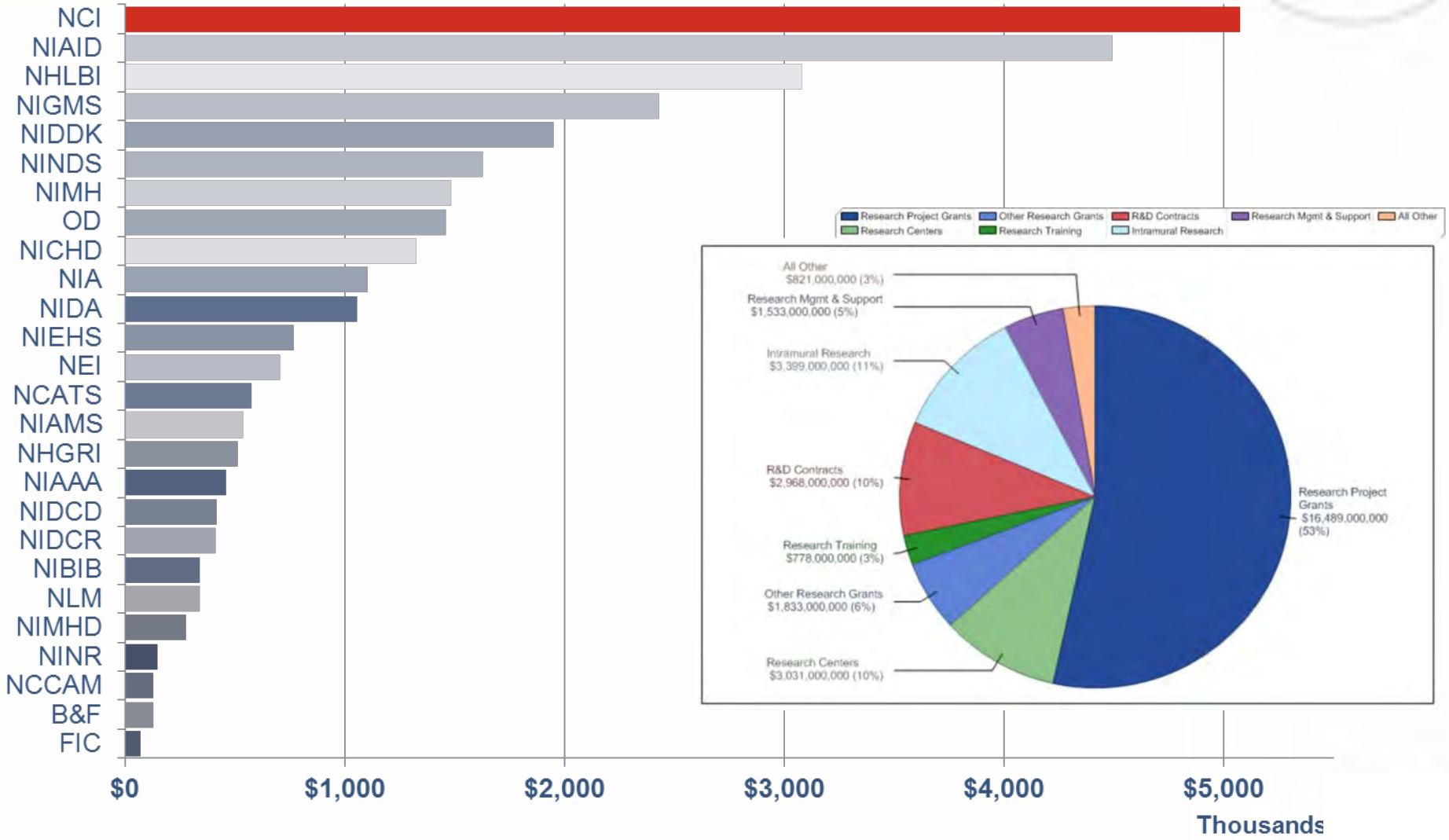
NIH Budget ~ $30.8 Billion (FY12)

- ***~82% for extramural support***
- ***~63,000 grants and contracts***

NCI Budget ~ $ 5.07 Billion (FY12)

- ***~ 76% for extramural support***
- ***~7,800 grants and contracts***

National Institutes of Health (NIH): 27 Institutes and Centers



NIH FY12 Appropriations Data Taken from http://www.nih.gov/about/almanac/appropriations/index.htm and http://report.nih.gov/nihdatabook/

NIH Research Portfolio Online Reporting Tools (RePORT)

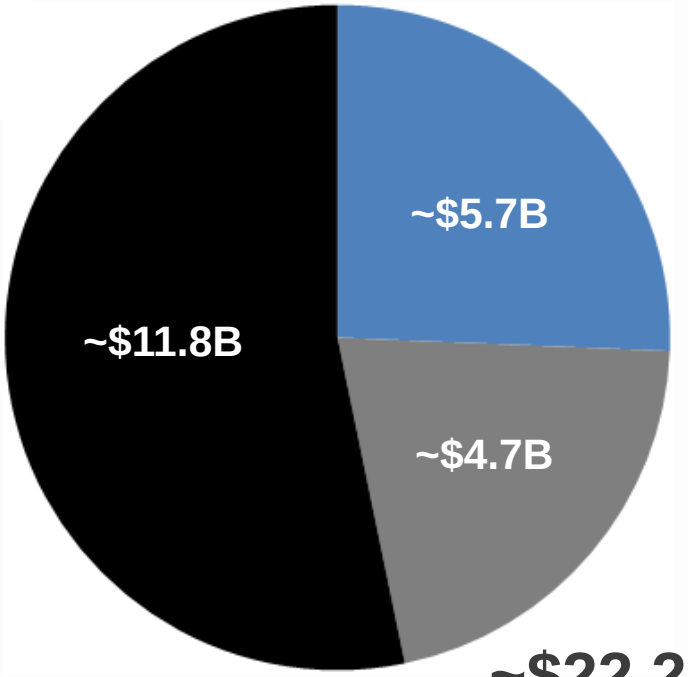
CENTER for STRATEGIC SCIENTIFIC INITIATIVES

RFA

PA*

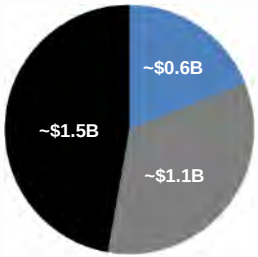
PA

NIH



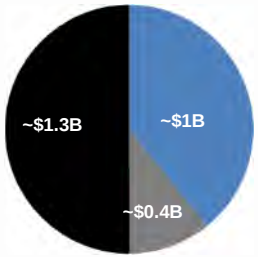
~$22.2B

NCI



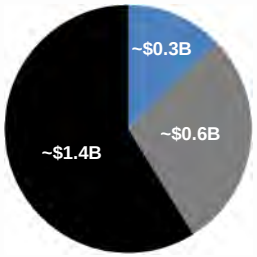
~$3.2B

NIAID



~$2.7B

NIGMS

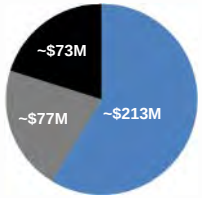


~$2.3B

NIBIB

~$288M

NHGRI



~$364M

FY12 grants data from http://projectreporter.nih.gov

National Cancer Institute Organization

Director
Harold Varmus, MD

National Cancer Institute

$5.07B
(FY12)

Deputy Director
Douglas Lowy, MD

Office of the Director

CSSI

~$132 M (~4%)

Center for Cancer Research	Division of Cancer Epidemiology and Genetics	Division of Cancer Treatment and Diagnosis	Division of Cancer Biology	Division of Cancer Control and Population Sciences	Division of Cancer Prevention	Division of Extramural Activities
~$858M (~17%)		***~$919M (~29%)***	***~$779M (~25%)***	***~$441M (~14%)***	***~$264M (~8%)***	**~$21M (~0.4%)**

Conducting – Intramural

Funding – Extramural

Red numbers: FY12 grants data only from http://fundedresearch.cancer.gov/nciportfolio; **Black numbers:** from FY12 http://obf.cancer.gov/financial/factbook.htm

NCI Center for Strategic Scientific Initiatives (CSSI): Concept Shop

Director
Douglas Lowy, MD

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

~$138.2 M (FY13)

Deputy Director
Jerry S.H. Lee, PhD

Mission

"…to create and uniquely implement exploratory programs focused on the development and integration of advanced technologies, **trans-disciplinary approaches, infrastructures, and standards**, to accelerate the **creation and broad deployment** of **data, knowledge, and tools** to empower the **entire cancer research continuum** in better understanding and leveraging knowledge of the cancer biology space **for patient benefit**…"

IMAT — Innovative Molecular Analysis Technologies
2003, 2007, 2011, 2013

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER
2005, 2010

PHYSICAL SCIENCES in ONCOLOGY
2008, 2013*

Provocative Questions Initiative
2011

NCI Alliance for Nanotechnology in Cancer
2004, 2008, 2014

THE CANCER GENOME ATLAS
2005, 2008

Cancer Target Discovery & Development (CTD²)
2010

*Red dates indicate approval(s) by NCI Board of Scientific Advisors

CSSI Programs and Evaluations (2004-2015)

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

CaNano Plan 1

NCI Alliance for Nanotechnology in Cancer

Phase I Launched
- U54
- R01
- F32/F33

Program Eval

Program Renewed

CaNano Plan 2

NCI Alliance for Nanotechnology in Cancer

Phase II Launched
- U54
- **U01**
- **K99/R00**
- **R25**

Program Eval

Program Renewed
- U54
- U01
- **T32**

IMAT

RFA Program Launched
- 3 R21
- 3 R33
- 3 R21/R33

Program Eval

Innovative Molecular Analysis Technologies

Program Renewed
- 3 R21 **(3 year)**
- **3** R33

Program Eval

Innovative Molecular Analysis Technologies

Program Renewed
- **2** R21 (3 year)
- **2** R33

Program Eval

Innovative Molecular Analysis Technologies

Program Renewed
- **2** R21 (3 year)
- **2** R33

Ongoing Eval

2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

Clinical Proteomic Technologies for Cancer

Phase I Launched
- U24
- R01
- R21/R33

Program Eval

Program Renewed

Clinical Proteomic Tumor Analysis Consortium

Phase II Launched
- U24
- **Linked with TCGA**

TRAQR

Prospective Electronic Program Eval

PHYSICAL SCIENCES in ONCOLOGY

Phase I Launched
- U54

TRAQR

Prospective Electronic Program Eval

Program Eval

PHYSICAL SCIENCES in ONCOLOGY

Program Renewed**
- U54
- **U01**

Provocative Questions Project

Phase I Launched
- R01
- R21

Pre-Review Applicant Eval

Program Eval

***Red Denotes Program Evals and Changes to Programs**

Then…(2002)

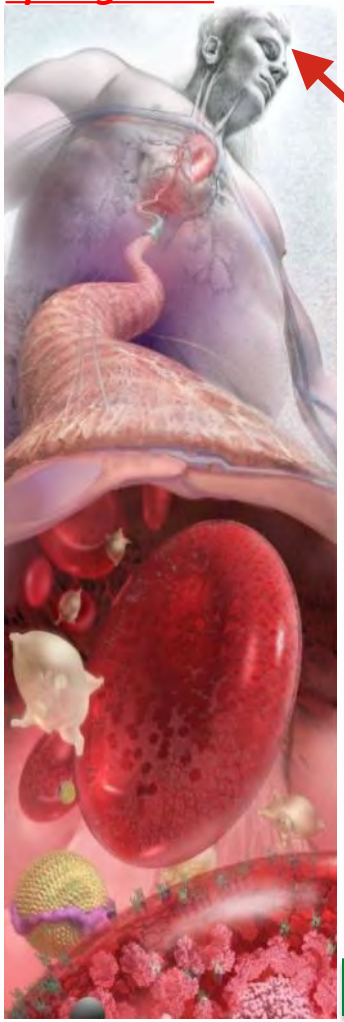
Drew Sheneman, The Star-Ledger, Newark, NJ

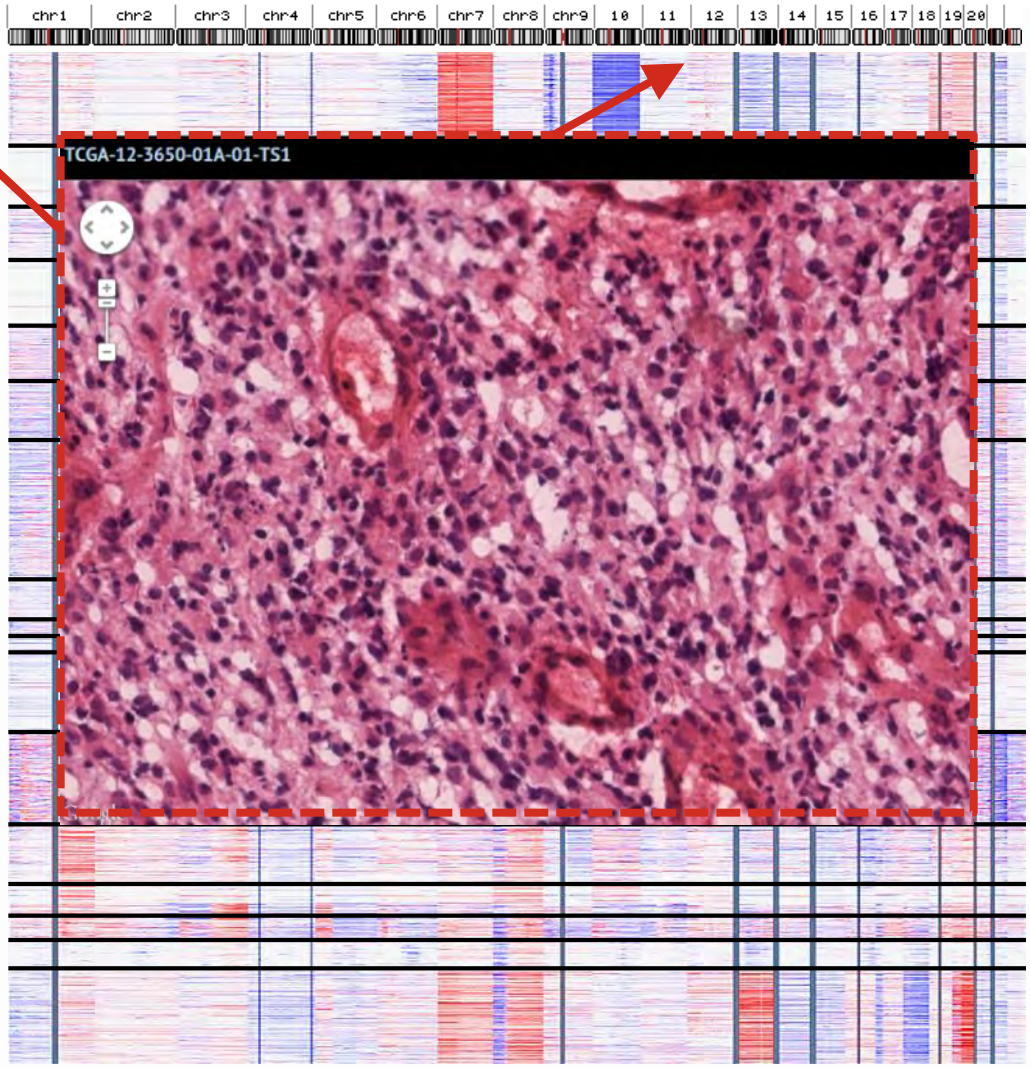
Genomic "Steam Table"

The Cancer Genome Atlas Data Portal — Understanding genomics to improve cancer care

Center for Strategic Scientific Initiatives

Spring 2013





Glioblastoma:	563
Brain lower grade glioma:	180
Head & neck:	306
Thyroid carc:	401
Lung adeno:	356
Lung squamous:	343
Breast carc:	866
Stomach adeno:	237
Liver hep. carc:	97
Kidney pap. cell carc:	103
Kidney clear cell carc:	493
Ovarian serous:	559
Uterine corpus end. carc:	492
Cervical carc:	102
Bladder carc:	135
Prostate adeno:	171
Colon/rectum adeno	
Total:	

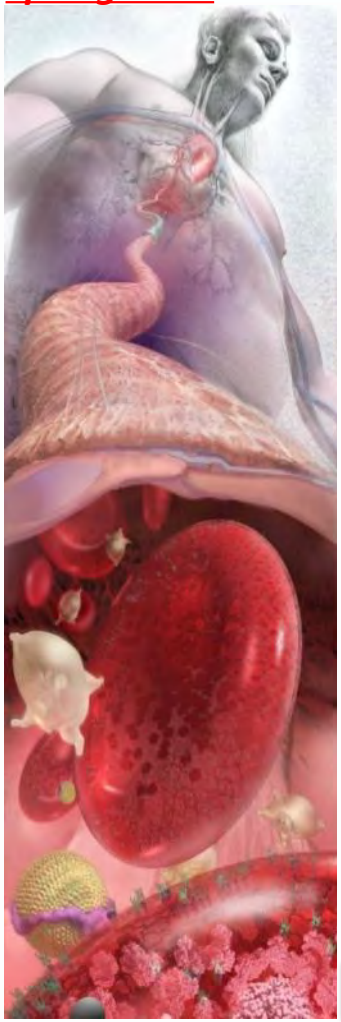
Source: UCSC Cancer Genomic Heatmaps (CopyNumber GISTIC2) [https://genome-cancer.ucsc.edu/] Compiled by Jerry S.H. Lee, PhD, March 2013

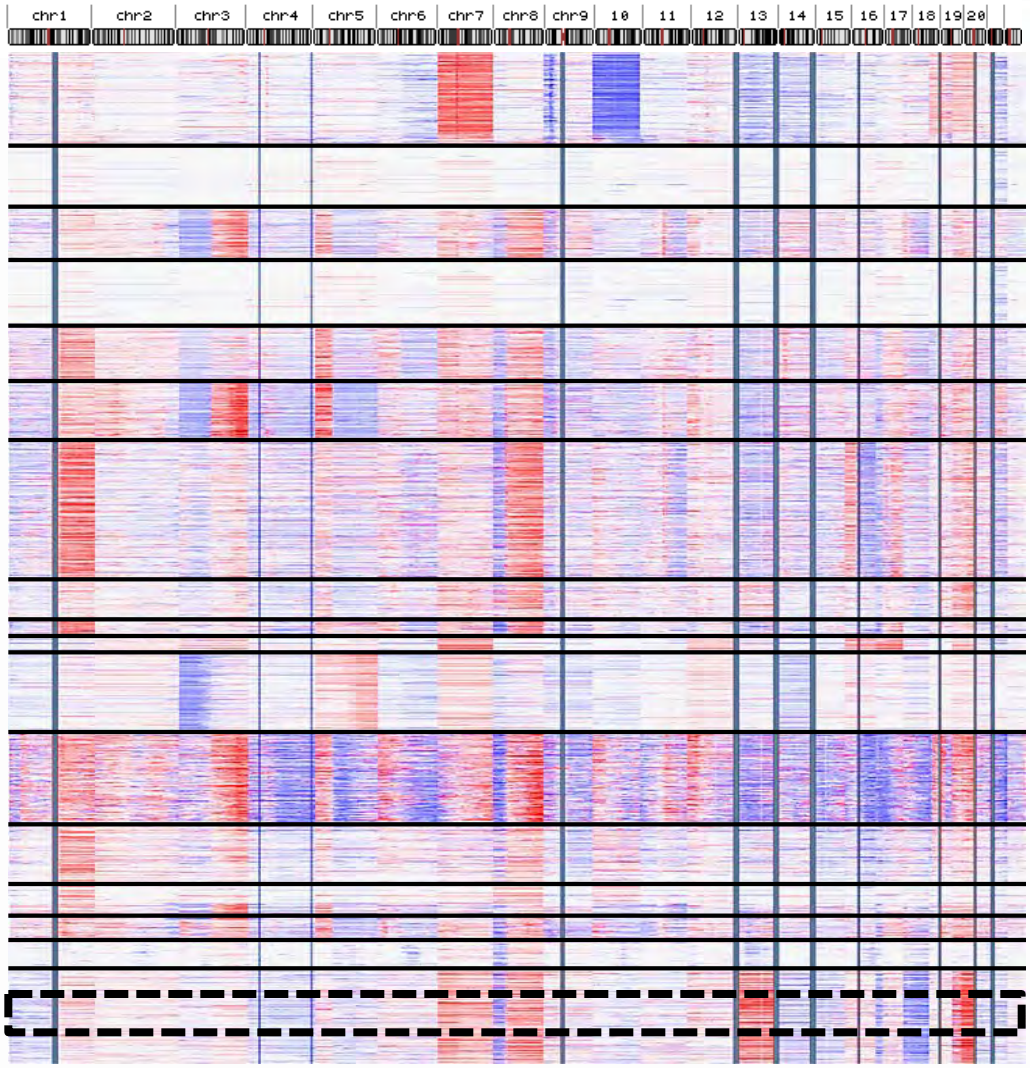
Genomic "Steam Table"

The Cancer Genome Atlas Data Portal — Understanding genomics to improve cancer care

Center for Strategic Scientific Initiatives

Spring 2013





Glioblastoma:	563
Brain lower grade glioma:	180
Head & neck:	306
Thyroid carc:	401
Lung adeno:	356
Lung squamous:	343
Breast carc:	866
Stomach adeno:	237
Liver hep. carc:	97
Kidney pap. cell carc:	103
Kidney clear cell carc:	493
Ovarian serous:	559
Uterine corpus end. carc:	492
Cervical carc:	102
Bladder carc:	135
Prostate adeno:	171
Colon/rectum adeno:	575
Total:	**5979**

Source: UCSC Cancer Genomic Heatmaps (CopyNumber GISTIC2) [https://genome-cancer.ucsc.edu/] Compiled by Jerry S.H. Lee, PhD, March 2013

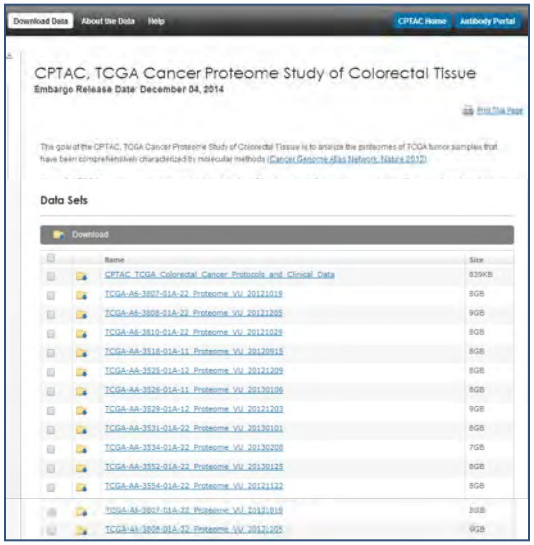
CPTAC Public Resources: http://proteomics.cancer.gov

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

LIVE

CPTAC Data Portal

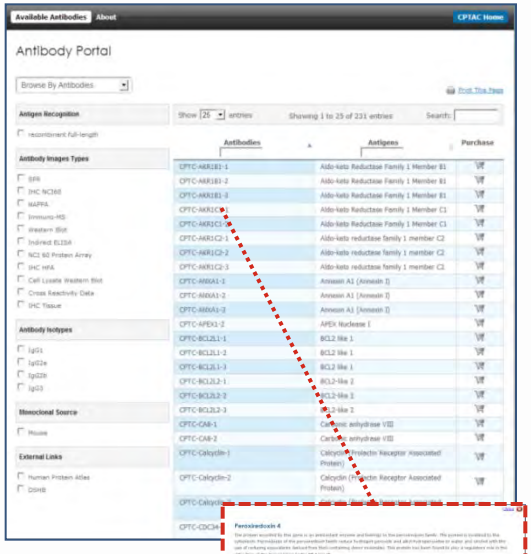
11,419 files (2.2 TB)

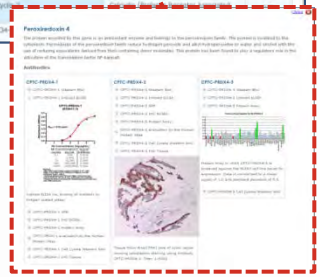


LIVE

NCI Antibody Portal

280 mAbs (~$35)

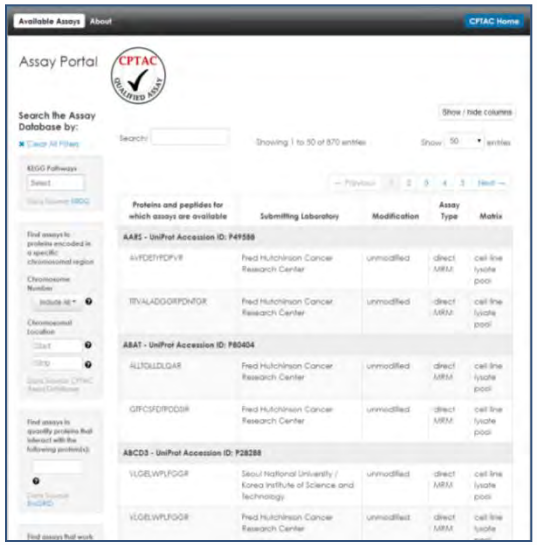




COMING SOON

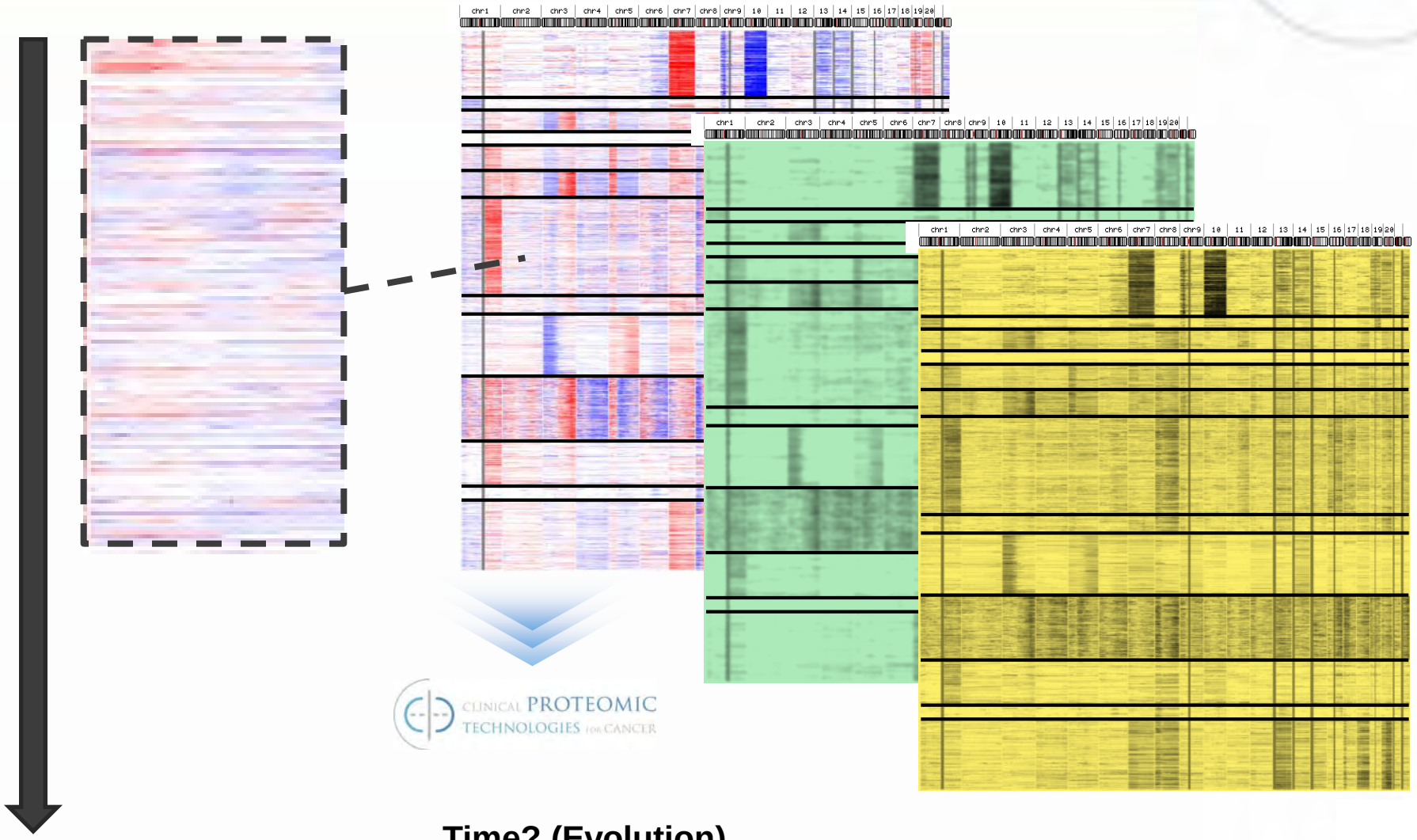
CPTAC Assay Portal

542 assays



Release Date	Disease	# of Samples	
9/4/2013	Colorectal	95	
2/20/2014	Breast	105	~8,000 proteins ~12,000 phospho-proteins
4/2014	Ovarian	TBD	

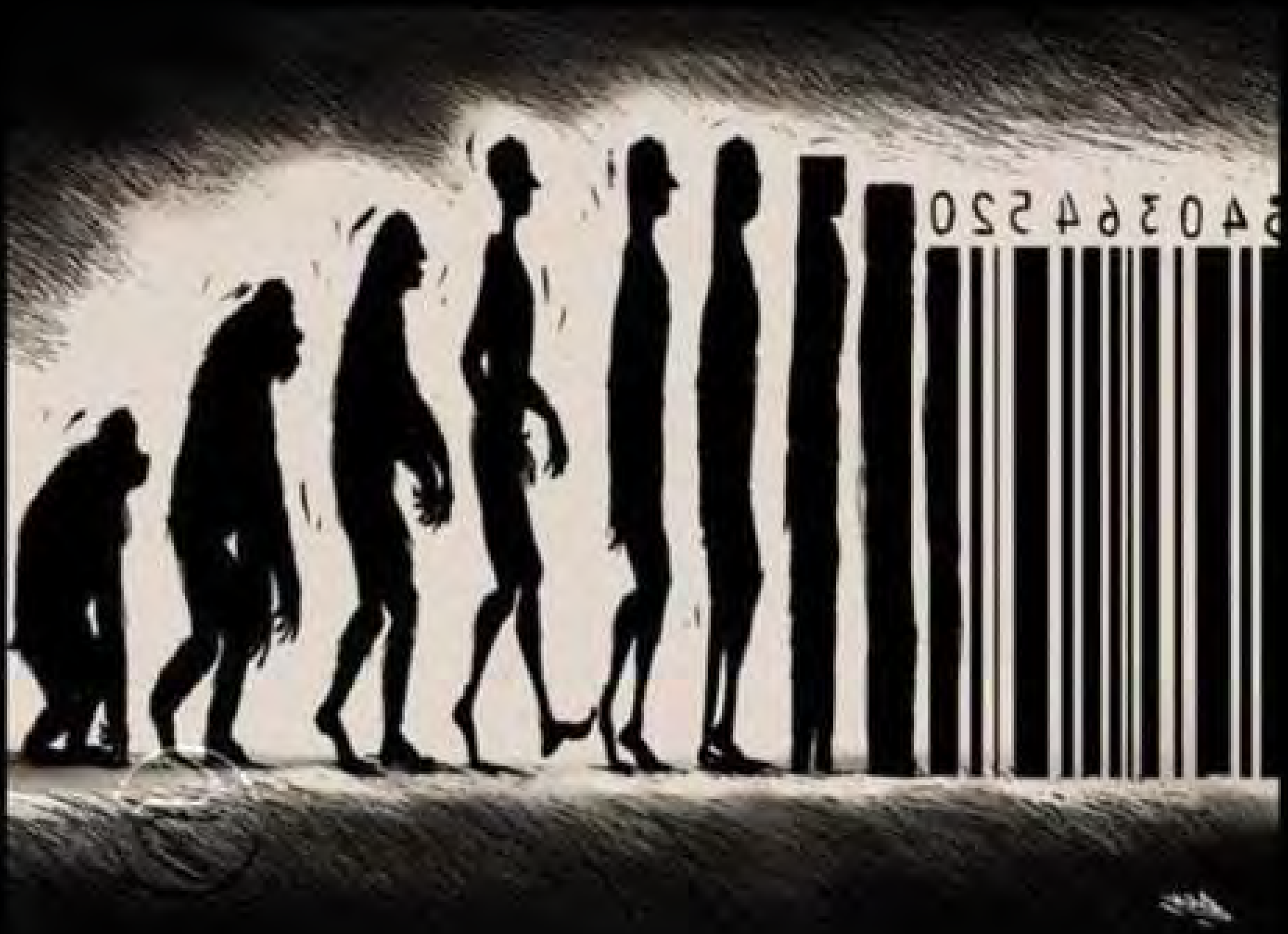
Where Do We Go From Here?
Is it JUST More Data?



CENTER for STRATEGIC SCIENTIFIC INITIATIVES

CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

Time? (Evolution)



Now…(2014): Moore's Law of Analysts?

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

~100

Comprehensive genomic characterization defines human glioblastoma genes and core pathways

The Cancer Genome Atlas Research Network*

~150

Integrated genomic analyses of ovarian carcinoma

The Cancer Genome Atlas Network*

~200

Comprehensive genomic characterization of squamous cell lung cancers

The Cancer Genome Atlas Network*

350+

Comprehensive molecular characterization of clear cell renal cell carcinoma

The Cancer Genome Atlas Research Network*

2007 2009 2011 2013 2015

Bringing In New Perspectives

PHYSICAL SCIENCES in ONCOLOGY

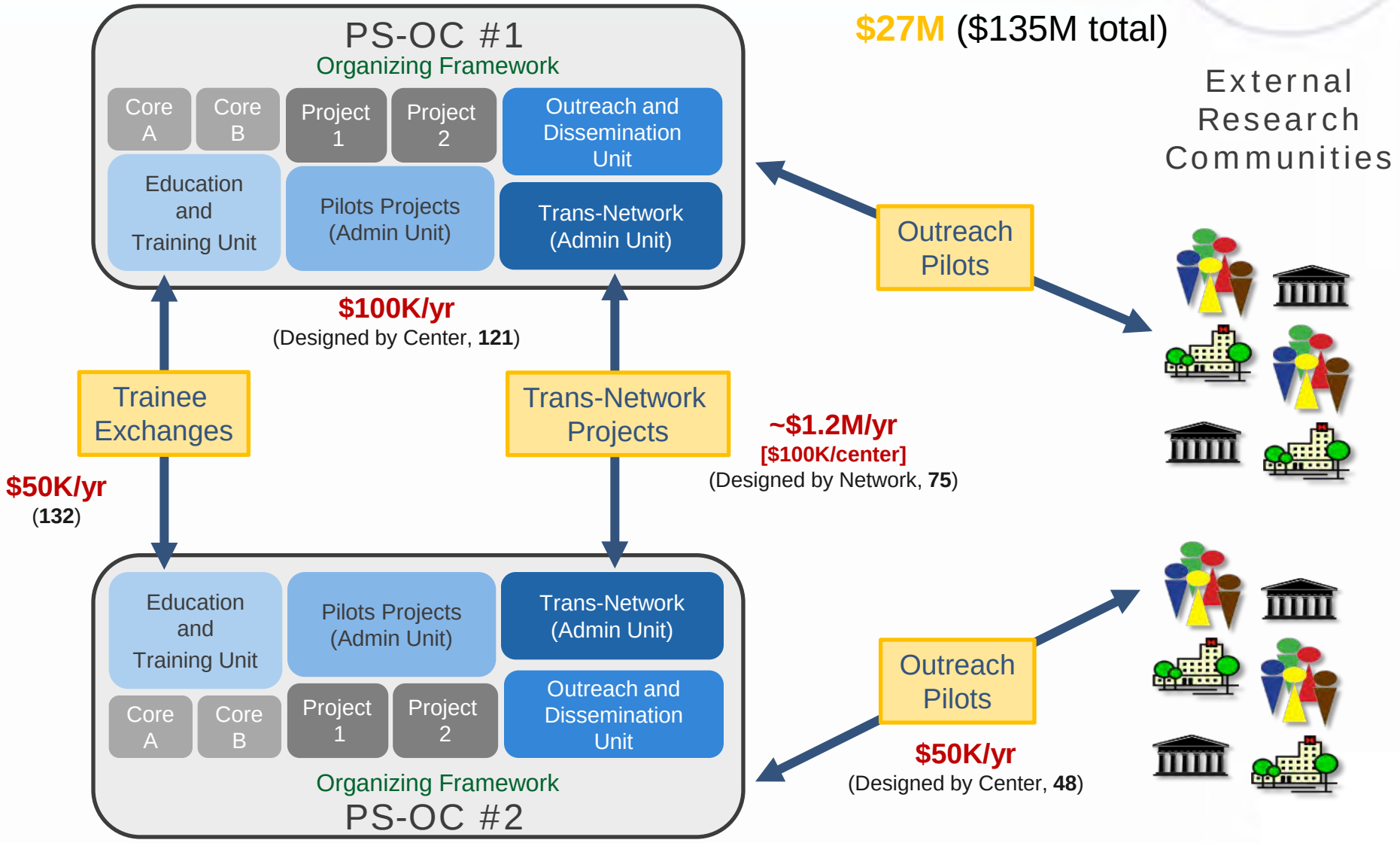
CENTER for STRATEGIC SCIENTIFIC INITIATIVES

- To generate ***new knowledge*** and catalyze ***new fields of study*** in cancer research by utilizing physical sciences/engineering principles to enable a better understanding of cancer and its behavior at all scales.
- Not looking for new tools to do "better" science, but new perspectives and approaches to do ***paradigm-shifting*** science that will lead to exponential progress against cancer.
- Build ***trans-disciplinary teams*** and infrastructure to better understand and control cancer through the convergence of physical sciences and cancer biology.

Physical Sciences-Oncology Centers (PS-OCs)

New – "Schools of Thought"

PS-OC Model: PI Driven Interactions Inside/Outside of Network/Center



Provocative Question (PQ) Project: Seeding Innovations for the Future

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

nature NATURE | COMMENT

Nature Jan 26, 2012

Science funding: Provocative questions in cancer research

Harold Varmus & Ed Harlow

- **Goal:**
  - Challenge the scientific community to creatively think about and answer **important, but non-obvious or understudied**, provocative questions (PQs) in cancer research
- **Implementation:**
  - PQs solicited through website and workshops
  - **Phase 1:** requested R01/R21 applications on 24 final PQs (**55 awards**)
  - **Phase 2:** new set of 24 PQs for R01/R21 apps (**93 awards**)
  - **Phase 3:** new set of 20 PQs

PQA4: For tumors that arise from a pre-malignant field, what properties of cells in this field can be used to design strategies to inhibit the development of future tumors?

PQC4: What in vivo imaging methods can be developed to portray the "cytotype" of a tumor?

PQD1: What molecular properties make some cancers curable with conventional chemotherapy?

PQB1: Why do second, independent cancers occur at higher rates in patients who have survived a primary cancer than in a cancer-naïve population?

PQE4: What are the best methods to identify and stratify subgroups of patients with particular co-morbidities who will benefit from defined cancer therapies?

High Content Data Integration Working Group

David Chang (Kite) and **Jerry Lee** (NCI), Co-Chairs

Industry

Ian Taylor	(Pfizer)
Archie Tse	(Daiichi Sankyo)
Steve Elmore	(AbbVie)
Caretha Creasy	(GSK)
Keisuke Kuida	(Takeda)

Government

David Litwack	(FDA)
Zivana Tezak	(FDA)
Anne Plant	(NIST)
Henry Rodriguez	(NCI)
Larry Nagahara	(NCI)
Kim Jessup	(NCI)
Emily Greenspan	(NCI)

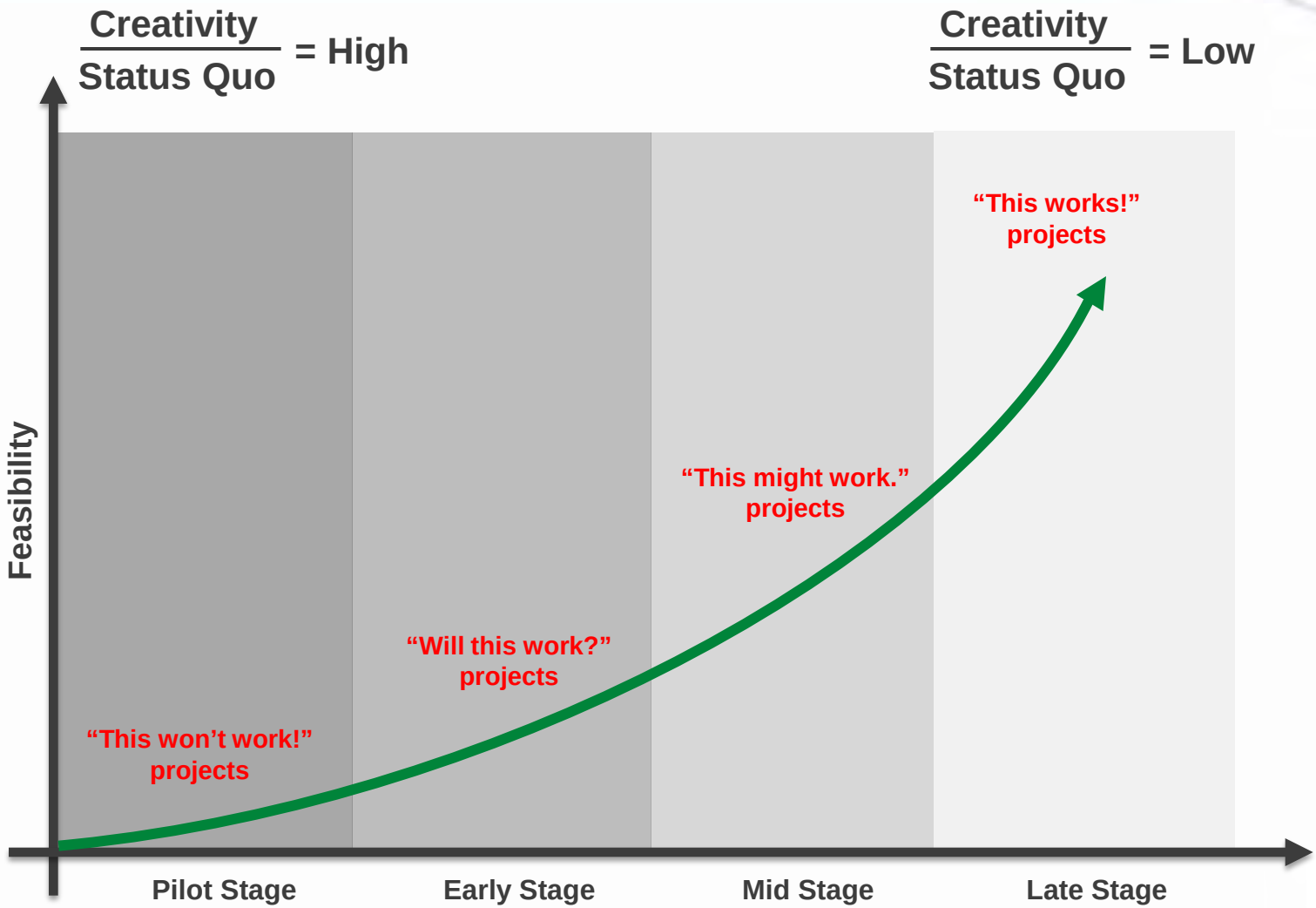
Academia

Jim Heath	(Cal Tech)
Garry Nolan	(Stanford)
David Rimm	(Yale)
Peter Kuhn	(USC)
D. Lansing Taylor	(U. Pittsburgh)
David Andrews	(Univ. Toronto)
Minetta Liu	(Mayo Clinic)
Scott Manalis	(MIT)
Deirdre Meldrum	(ASU)

Technical/Scientific Support

Caroline Sigman	(CCSA)
Susan Keating	(CCSA)

Lessons Learned Thus Far: Creativity vs. Feasibility



"Curve of Exponential Improvement"- Adapted from Carlson and Wilmot

CSSI Programs and Evaluations (2004-2015)

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

CaNano Plan 1

NCI Alliance for Nanotechnology in Cancer

Phase I Launched
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- R01
- F32/F33

Program Eval

Program Renewed

CaNano Plan 2

NCI Alliance for Nanotechnology in Cancer

Phase II Launched
- U54
- **U01**
- **K99/R00**
- **R25**

Program Eval

Program Renewed
- U54
- U01
- **T32**

IMAT

RFA Program Launched
- 3 R21
- 3 R33
- 3 R21/R33

Program Eval

Innovative Molecular Analysis Technologies

Program Renewed
- 3 R21 **(3 year)**
- **3** R33

Program Eval

Innovative Molecular Analysis Technologies

Program Renewed
- **2** R21 (3 year)
- **2** R33

Program Eval

Innovative Molecular Analysis Technologies

Program Renewed
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Ongoing Eval

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TRAQR

Prospective Electronic Program Eval

Physical Sciences in Oncology

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TRAQR

Prospective Electronic Program Eval

Program Eval

Physical Sciences in Oncology

Program Renewed**
- U54
- **U01**

Provocative Questions Project

Phase I Launched
- R01
- R21

Pre-Review Applicant Eval

Program Eval

***Red Denotes Program Evals and Changes to Programs**

CSSI Program Evaluations and Outcomes Highlights (as of 6/10/2014)

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

Provocative Questions Initiative

Phase I (May 2014)

- **~$30M** per year for 3 years
- **1,500+** applications in 2 years
- **~150** awards overall
- Enabled analysis and evaluation of applicants **pre-review**

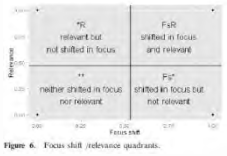
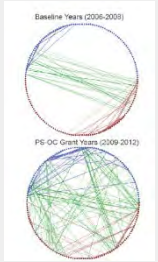


Figure 6. Focus shift /relevance quadrants.

PHYSICAL SCIENCES in ONCOLOGY

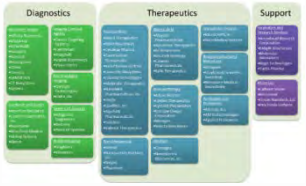
Phase II (Fall 2012)



- **$30M** per year for 5 years (over **$100M leveraged**)
- **600+** trainees
- **500** self-reported new collaborations
- **5** PS-OC advances tested in clinical settings
- **23** patent applications

NCI Alliance for Nanotechnology in Cancer

Phase II (March 2013)



- **$32.7M** per year for 5 years (over **$100M leveraged**)
- **70+** startup companies
- **17** clinical trials testing **8** Alliance therapeutics
- **5** diagnostic devices being tested under clinical protocol
- **39** patents awarded citing Phase I awards and over **100** patent applications filed during Phase II

CSSI Programs (FY99-FY14): Diverse Mechanisms

Center for Strategic Scientific Initiatives

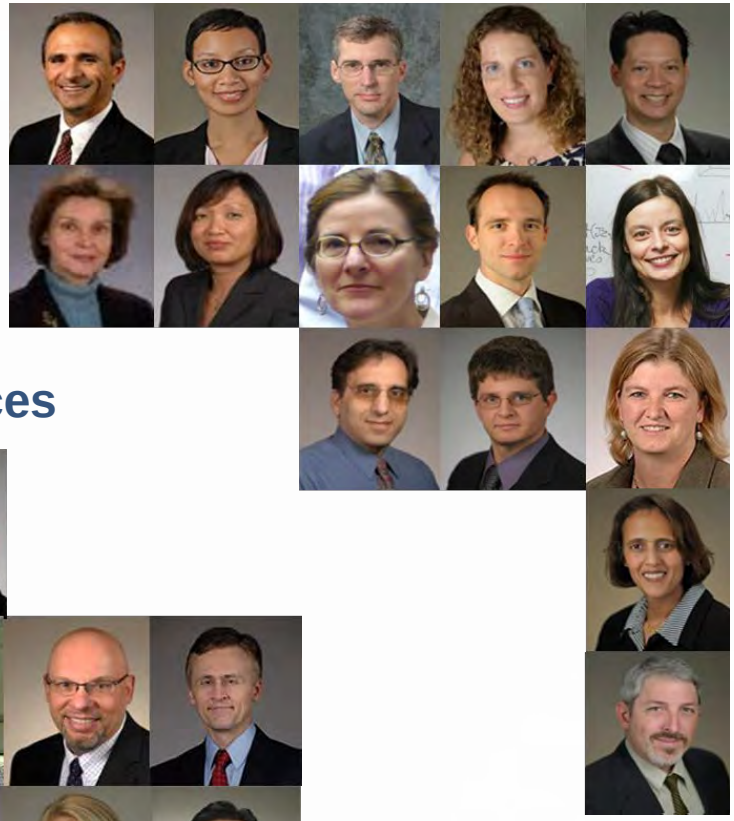
Program	Grants		Cooperative Agreements	Contracts	FFRDC		Interagency Collaborations (Co-funds/joint programs)
	Research	Training			Resource	R&D Subs	
Unconventional Innovations Program				✓			
Innovative Molecular Analysis Technologies	✓	✓					
NCI Alliance for Nanotechnology in Cancer	✓	✓	✓		✓	✓	✓ FDA NSF NIST
The Cancer Genome Atlas		✓	✓	✓		✓	
Clinical Proteomic Tumor Analysis Consortium	✓	✓	✓	✓	✓	✓	✓ FDA NIST
Biospecimen Research Network						✓	
CTD² Cancer Target Discovery and Development	✓		✓		✓		
Physical Sciences in Oncology	✓	✓	✓	✓		✓	✓ NSF
caHUB The Cancer Human Biobank					✓	✓	
Provocative Questions Initiative	✓		✓				

Acknowledgements/Thanks to the "Secret Ingredients"

Center for Strategic Scientific Initiatives

Clinical Sciences

Life Sciences



Physical Sciences

Learn More About Us…

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

http://cssi.cancer.gov

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HESI CITE Initiative:

Combining **I**nterdisciplinary and **T**ranslational **E**xpertise

CITE
COMBINING INTERDISCIPLINARY & TRANSLATIONAL EXPERTISE

Session Speakers

12:45 PM Resource Use

Spurring Efficient Innovation through CrowdSourcing - the Harvard Catalyst Model,

Eva Guinan, MD, Harvard Medical School

1:20 PM Evaluating Impact of NIH Clinical and Translational Science Awards Program

Deborah DiazGranados, PhD, Virginia Commonwealth University

1:55 PM HESI's Role in Translational Science via CITE

Dr. Brian Berridge, DVM, PhD, GlaxoSmithKline, HESI Trustee