



CENTER for
STRATEGIC
SCIENTIFIC INITIATIVES

NATIONAL CANCER INSTITUTE

Advancing Innovation and Convergence In Cancer Research

Jerry S.H. Lee, Ph.D.

Health Sciences Director

Deputy Director, Center for Strategic Scientific Initiatives
Office of the Director, National Cancer Institute (NCI)
National Institutes of Health (NIH)

May 15, 2013

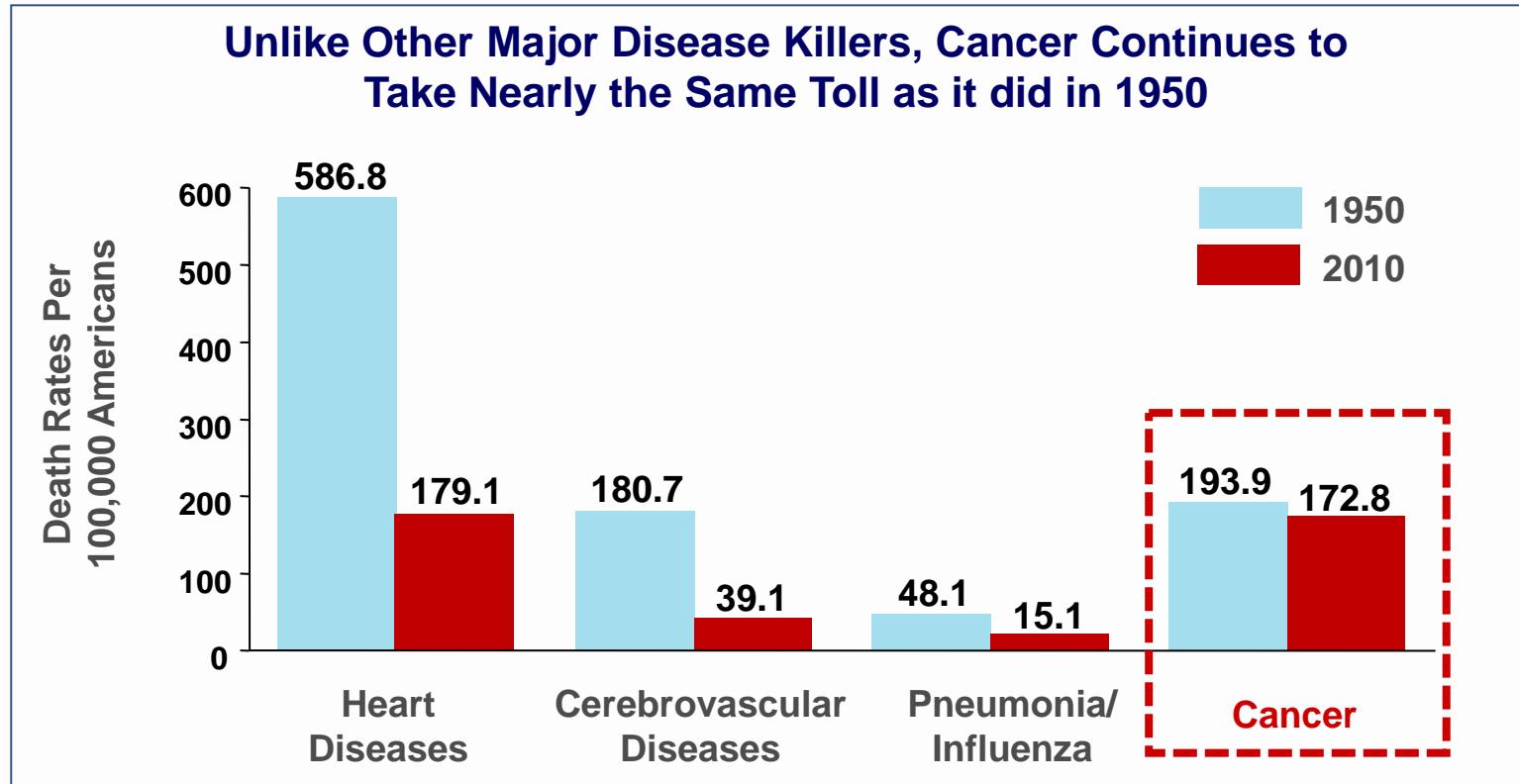


THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

In the U.S., Cancer Continues to Represent an Enormous Burden

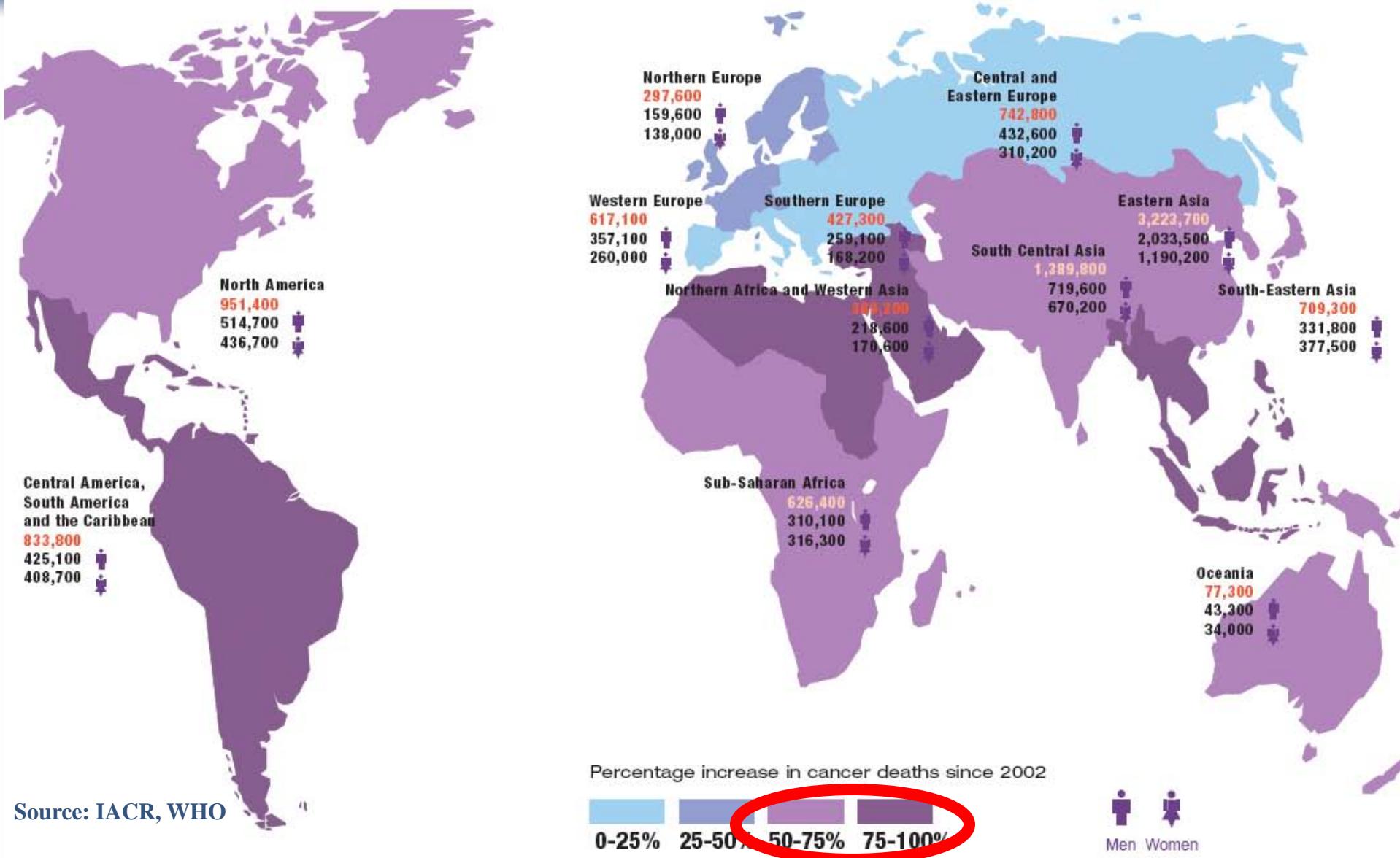


- **567,628** Americans died of cancer in 2009 (**580,350** projected for 2013)
- **1,660,290** Americans will be newly diagnosed with cancer in 2013 (projected)
- **\$124.6 billion** in 2010 for cancer healthcare costs

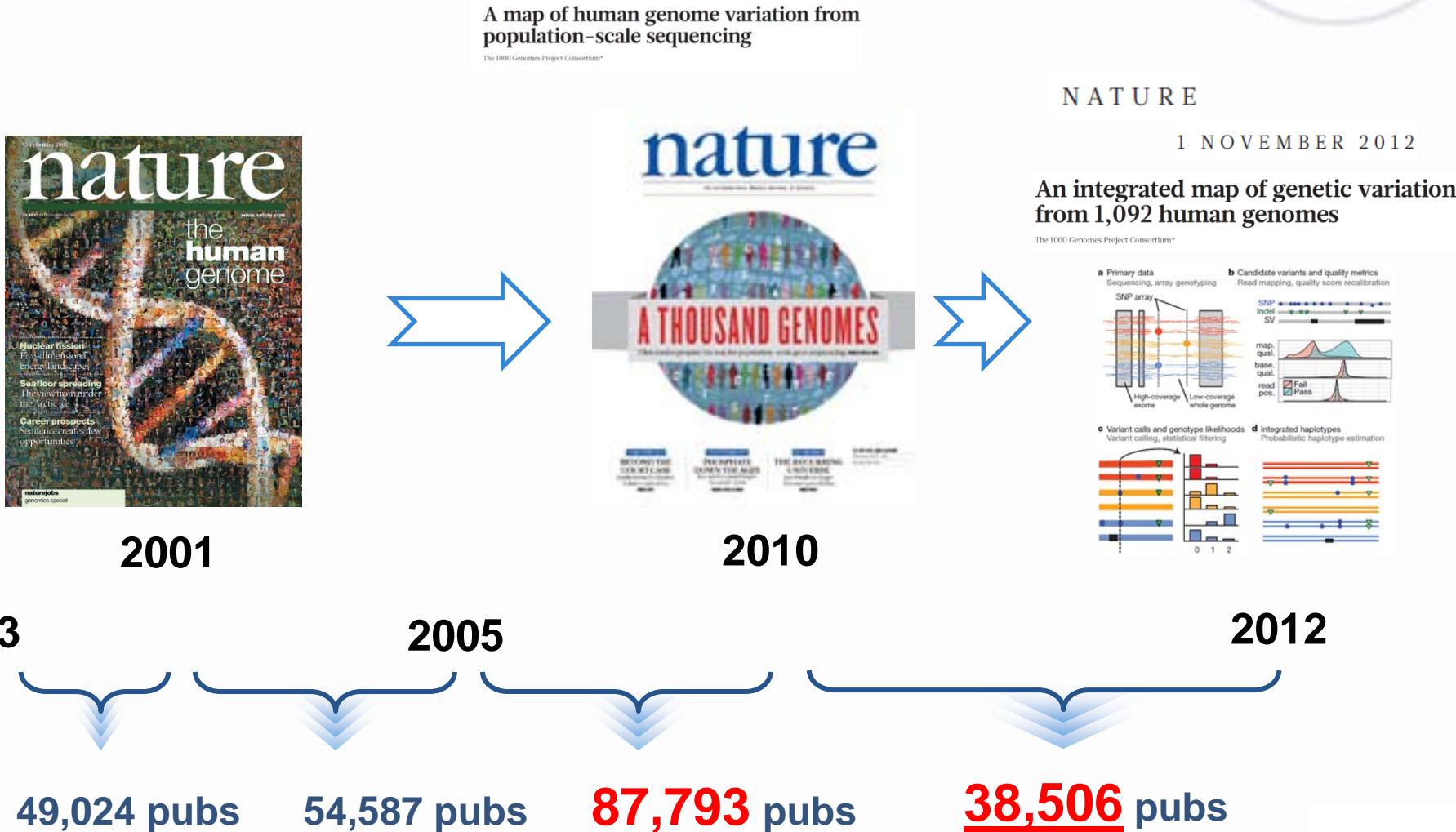


Source for 2013 projected deaths and diagnoses: Siegel et. al, Cancer Statistics, 2013
Source for 2010 age-adjusted death rate: National Center for Health Statistics, NCHS Public-use file for 2010 deaths.

Global Burden: By 2020, Cancer Mortality 10 M/yr (Incidence 16 M/yr)

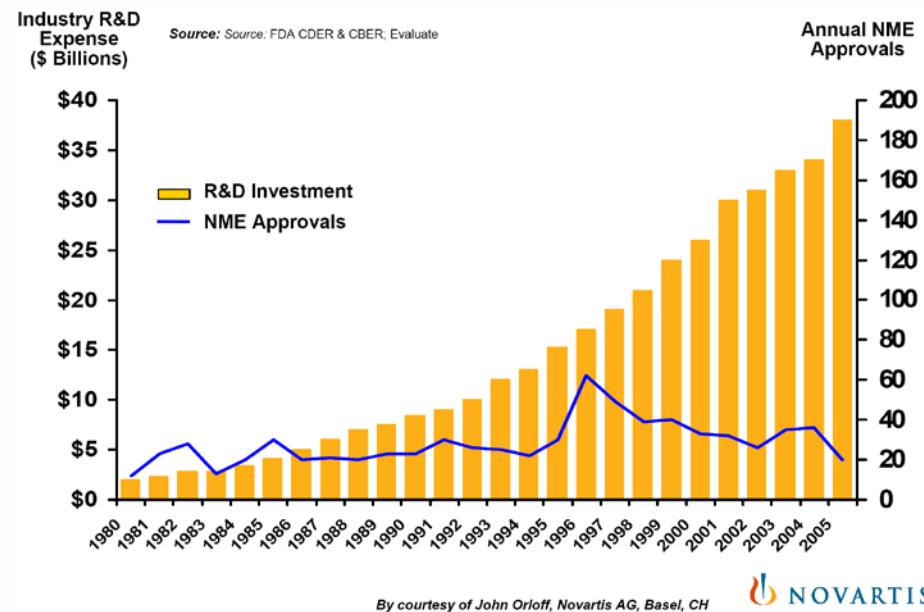


Unprecedented Amount of Scientific Knowledge: Omics(ssss)

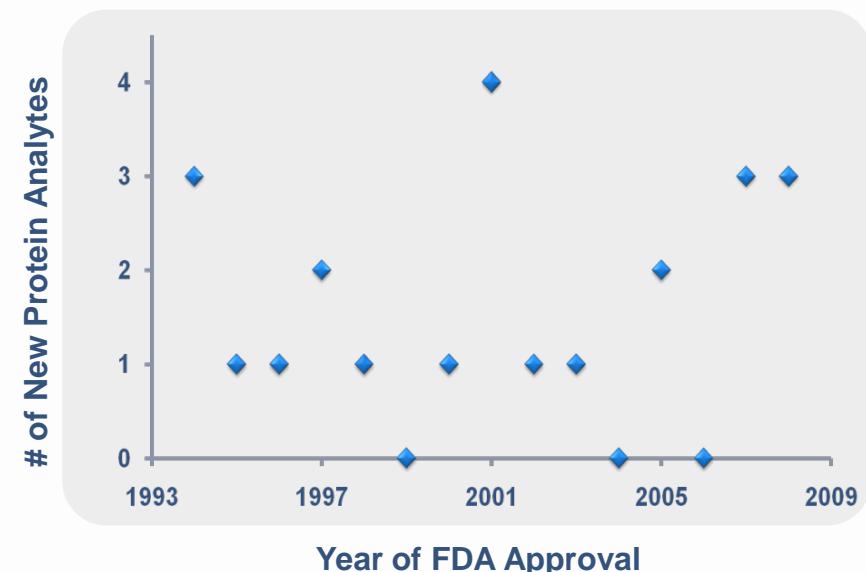


Is More Knowledge Yielding More Solutions for Patients?

Drug Discovery and Development



Diagnostic Biomarkers

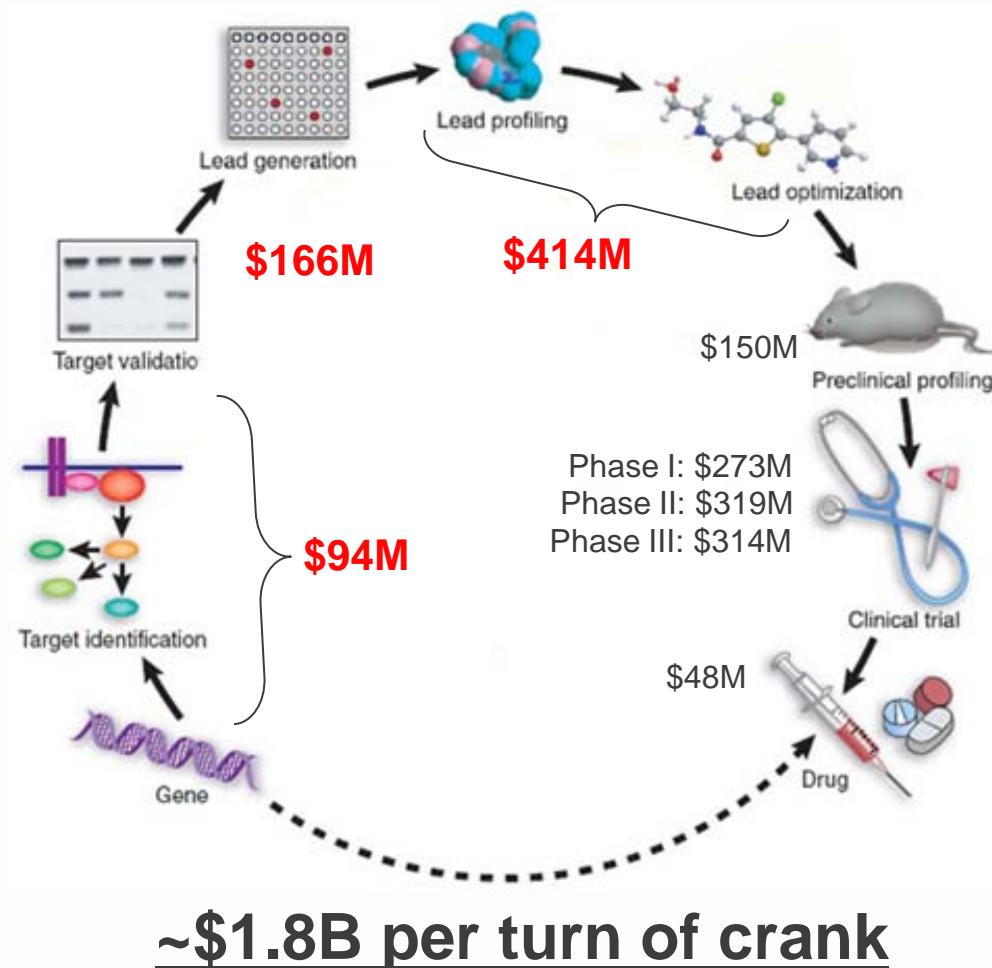


- 10 – 15 years at ~ \$1.8 billion*
- 2007: 19 NMEs [lowest since 1983]
- 2008: 21 NMEs [29% new-in-class]
- 2009: 24 NMEs [17% new-in-class]

- Averaging 1.5 FDA approvals per year†
- 1000's of samples
- Balancing complexity of biology against heterogeneity of patients

Maybe...but can it be more efficient?

Translation Pace: How To Break Out of Current Paradigm?



Key Needs (from community '02)

- Standards and protocols
- Real-time, public release of data
- Large, multi-disciplinary teams
- Pilot-friendly team environment to **share failures and successes**
- Team members with **trans-disciplinary training**

**The potential to transform
cancer drug discovery and
diagnostic development**

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



NHGRI



NIA



NIDA



NIH Campus – Bethesda, Maryland



NINDS



NIDCD



NIMH



NEI



NIAAA



CIT



NINR



NLM



NIDDK



FIC



CSR



NIBIB



NIGMS



NICHD



CC



NIMHD



NIDCR



NIEHS



NIAMS



NCCAM



NIAID



NCATS



NCI



NHLBI

NIH Budget ~ \$30.8 Billion (FY12)

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

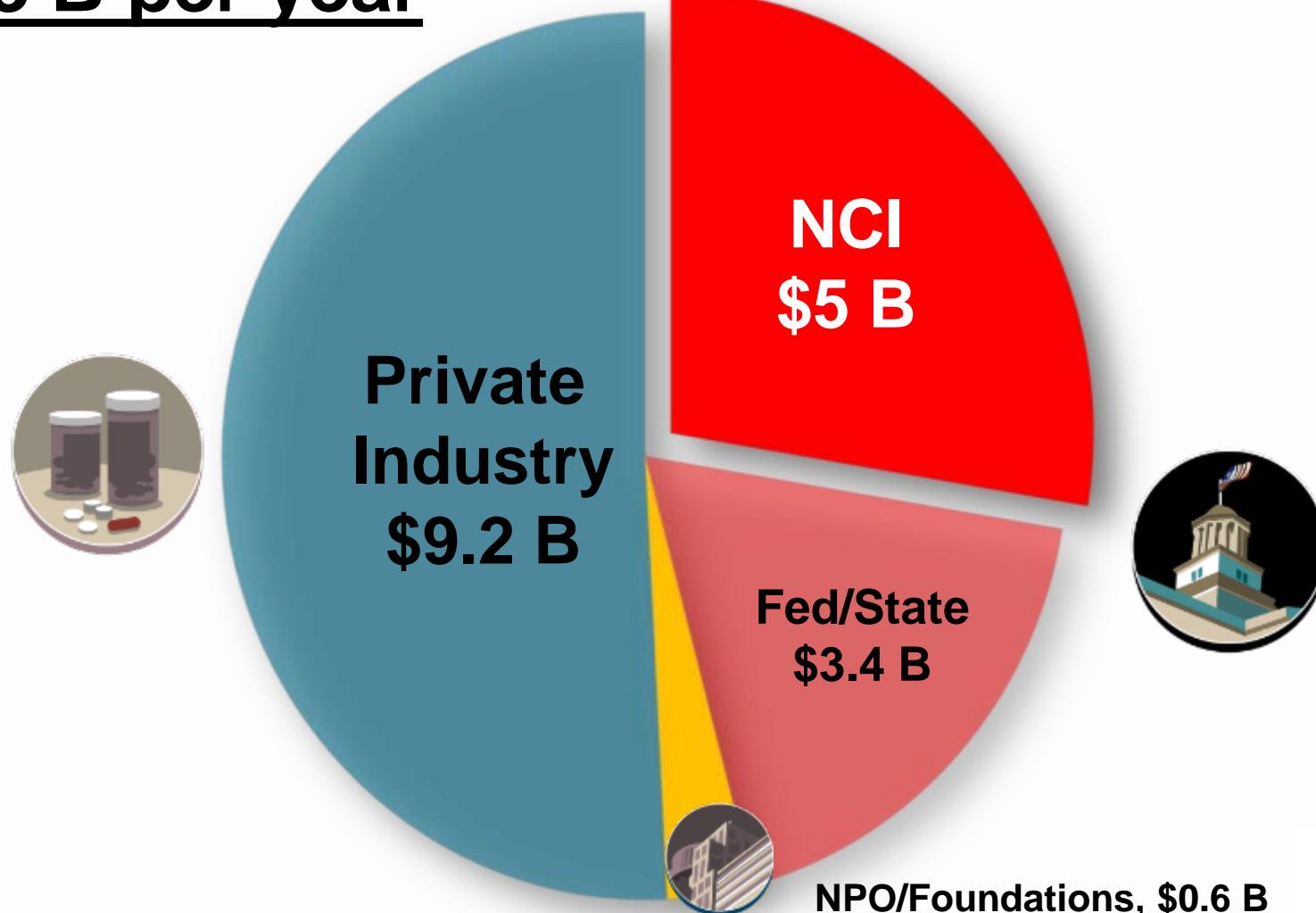
NCI Budget ~ \$ 5.07 Billion (FY12)

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

National Cancer Program: Stakeholders



~\$18 B per year



National Cancer Institute Organization



Director
Harold Varmus, MD

National Cancer Institute

\$5.07B
(FY12)

Office of the
Director

CSSI

~\$190 M (~4%)



Deputy Director
Douglas Lowy, MD

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

Conducting – Intramural

Funding – Extramural

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



Director
Douglas Lowy, MD



~\$190M (FY12)



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...”



2003, 2007, 2011



2005, 2010



2008



2011



2004, 2008



2005, 2008



2010

Support Convergence and Innovation At Many Scales



NCI Alliance for
Nanotechnology
in Cancer

Phase II

Cancer Target Discovery
& Development (CTD²)



Early
settlers

PHYSICAL SCIENCES
in ONCOLOGY

CLINICAL PROTEOMIC
TECHNOLOGIES FOR CANCER

Phase II



Team
Explorers

THE CANCER GENOME ATLAS

Phase II

Provocative
Questions
Initiative

IMAT
Innovative Molecular Analysis Technologies



**Discoverers/
Pioneers**

Basic

Applied

Translational

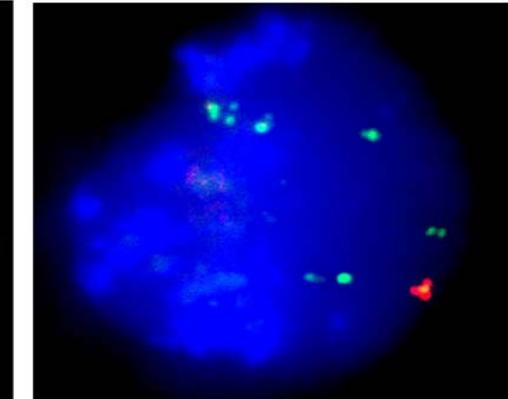
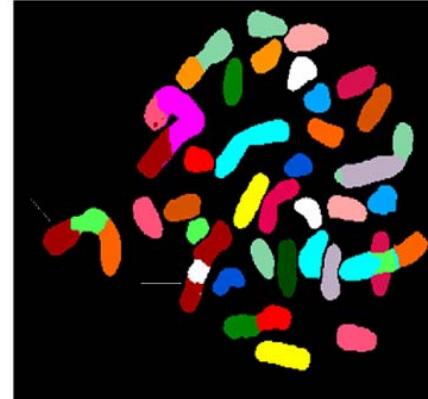
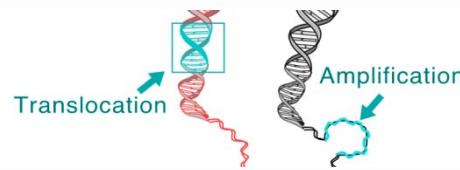
Clinical

Industry

First Step(back)- Cancer Genomics: Taking a Page from Engineers

Disease of Genomic Alterations

- Copy number
- Expression (regulation of)
- Regulation of translation
- Mutations
- Epigenome



- Systematic identification of all genomic changes
- Repeat (a lot) for individual cancer
- Repeat for many cancers
- Make it publically available

Pressure (kg/cm ²)	Temp (°C)	Saturated steam		Superheated steam	
		Vapour enthalpy (kcal/kg)	Specific volume (m ³ /kg)	Density (kg/m ³) at 250 °C	Specific volume (m ³ /kg) at 300 °C
1	99.1	638.8	1.725	0.580	2,454
2	119.6	646.2	0.902	1.109	1,223
3	132.9	650.6	0.617	1.621	0.812
4	142.9	653.7	0.471	2.123	0.607
5	151.1	656.0	0.382	2.618	0.484
6	158.1	657.0	0.321	3.115	0.400
7	164.2	659.5	0.278	3.597	0.343
8	169.6	660.8	0.245	4.082	0.299
9	174.5	661.9	0.219	4.566	0.265
10	179.1	662.9	0.198	5.051	0.238
12	187.1	664.5	0.166	6.024	0.196
14	194.1	665.7	0.143	6.993	0.167
16	200.4	666.7	0.126	7.937	0.145
18	206.1	667.4	0.112	8.929	0.128
20	211.4	668.0	0.101	9.901	0.114
22	216.2	668.4	0.092	10.870	0.103
24	220.7	668.7	0.085	11.765	0.093
26	225.0	669.0	0.078	12.821	0.085
28	229.0	669.1	0.073	13.699	0.078
30	232.7	669.2	0.068	14.706	0.072

Steam table (Reference)

TCGA: Connecting Multiple Standardized Sources, Experiments, and Data Types

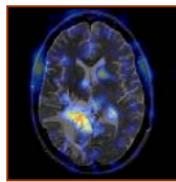


THE CANCER GENOME ATLAS

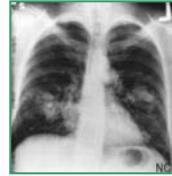


Three Cancers- Pilot

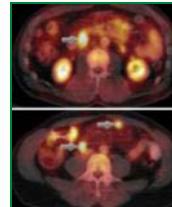
glioblastoma multiforme
(brain)



squamous carcinoma
(lung)



serous
cystadenocarcinoma
(ovarian)



Biospecimen Core Resource with more than 13 Tissue Source Sites

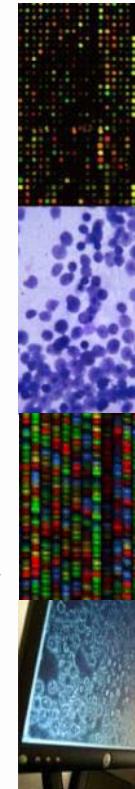
7 Cancer Genomic Characterization Centers

3 Genome Sequencing Centers

Data Coordinating Center

Multiple data types

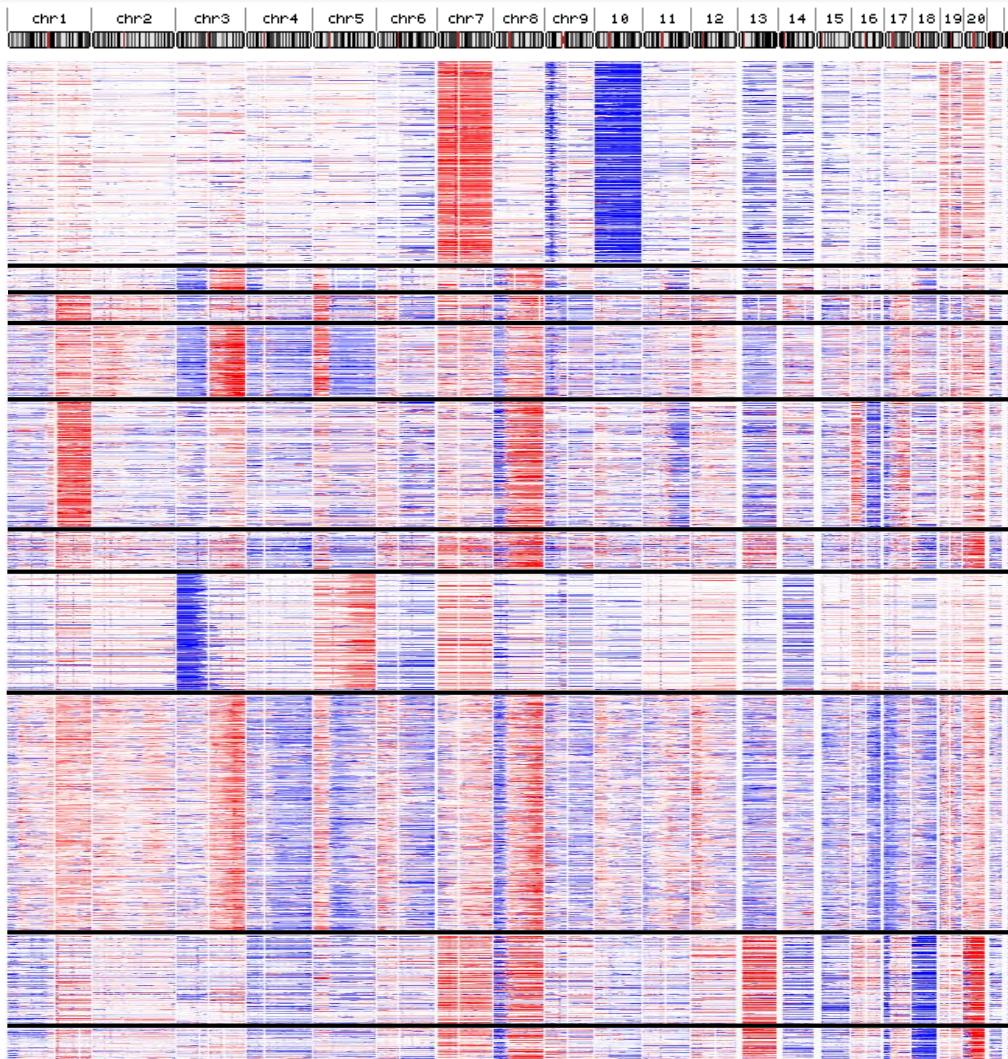
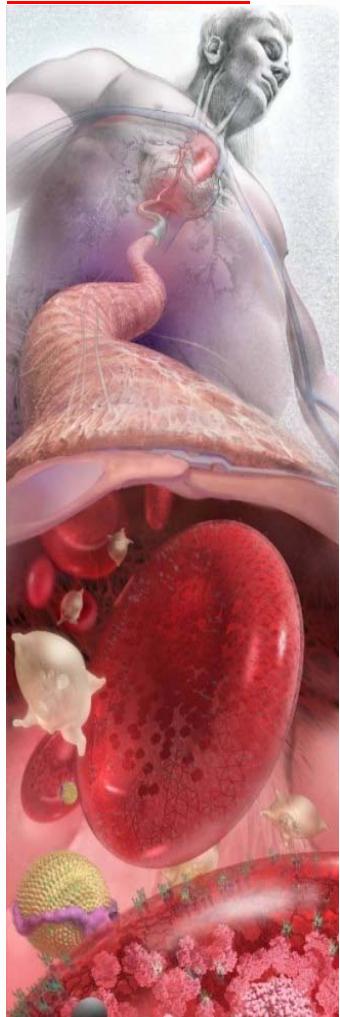
- Clinical diagnosis
- Treatment history
- Histologic diagnosis
- Pathologic status
- Tissue anatomic site
- Surgical history
- Gene expression
- Chromosomal copy number
- Loss of heterozygosity
- Methylation patterns
- miRNA expression
- DNA sequence



Genomic “Steam Table”



Summer 2011

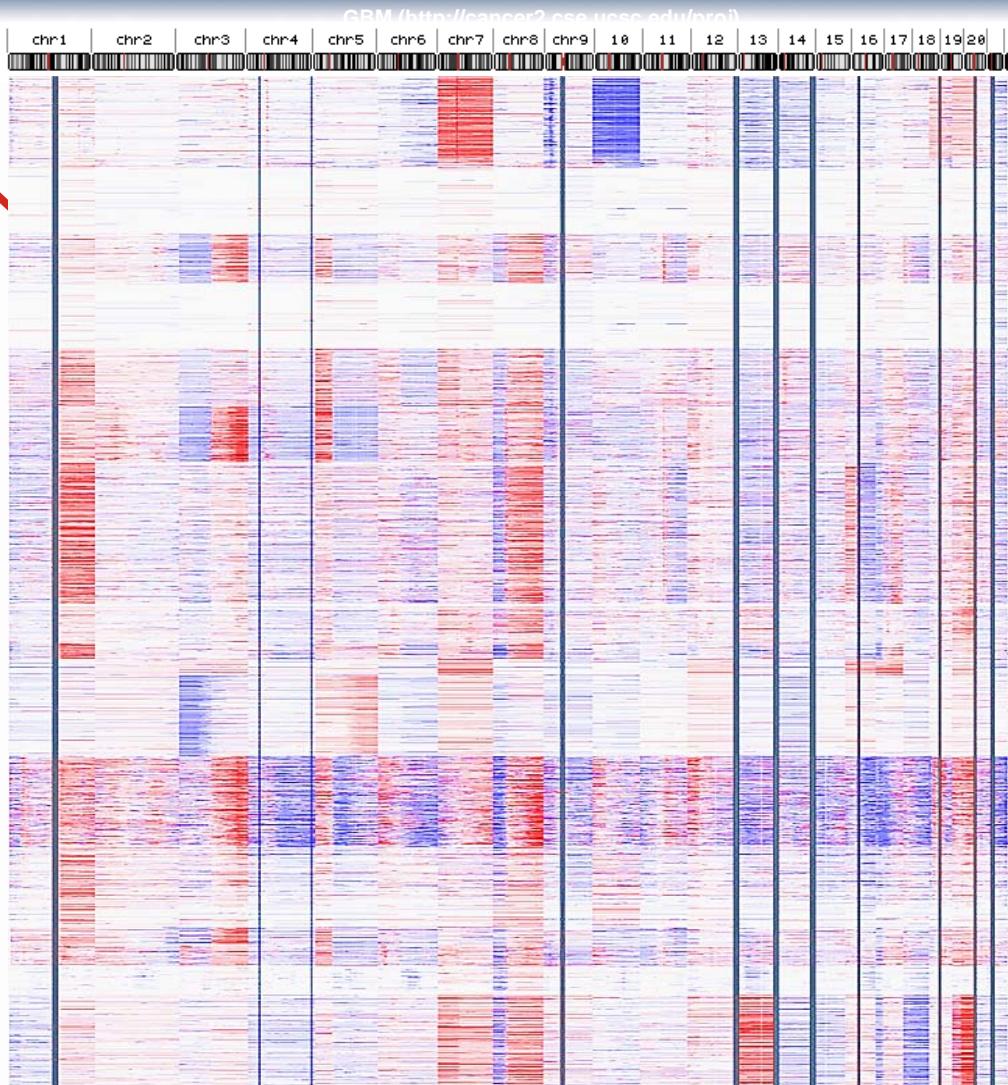
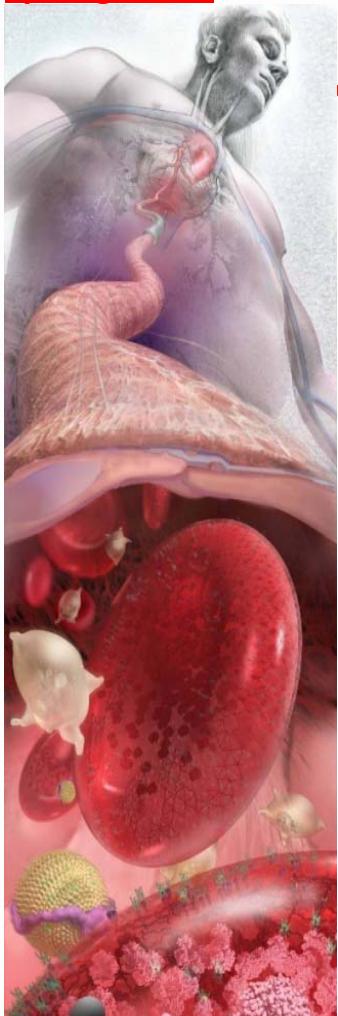


Glioblastoma:	470
Head & neck:	51
Lung adeno:	57
Lung squamous:	159
Breast carcinoma:	180
Stomach adeno:	84
Kidney clear carc:	260
Ovarian serous:	520
Colon adeno:	198
Rectum carcinoma:	
Total:	

Genomic “Steam Table”

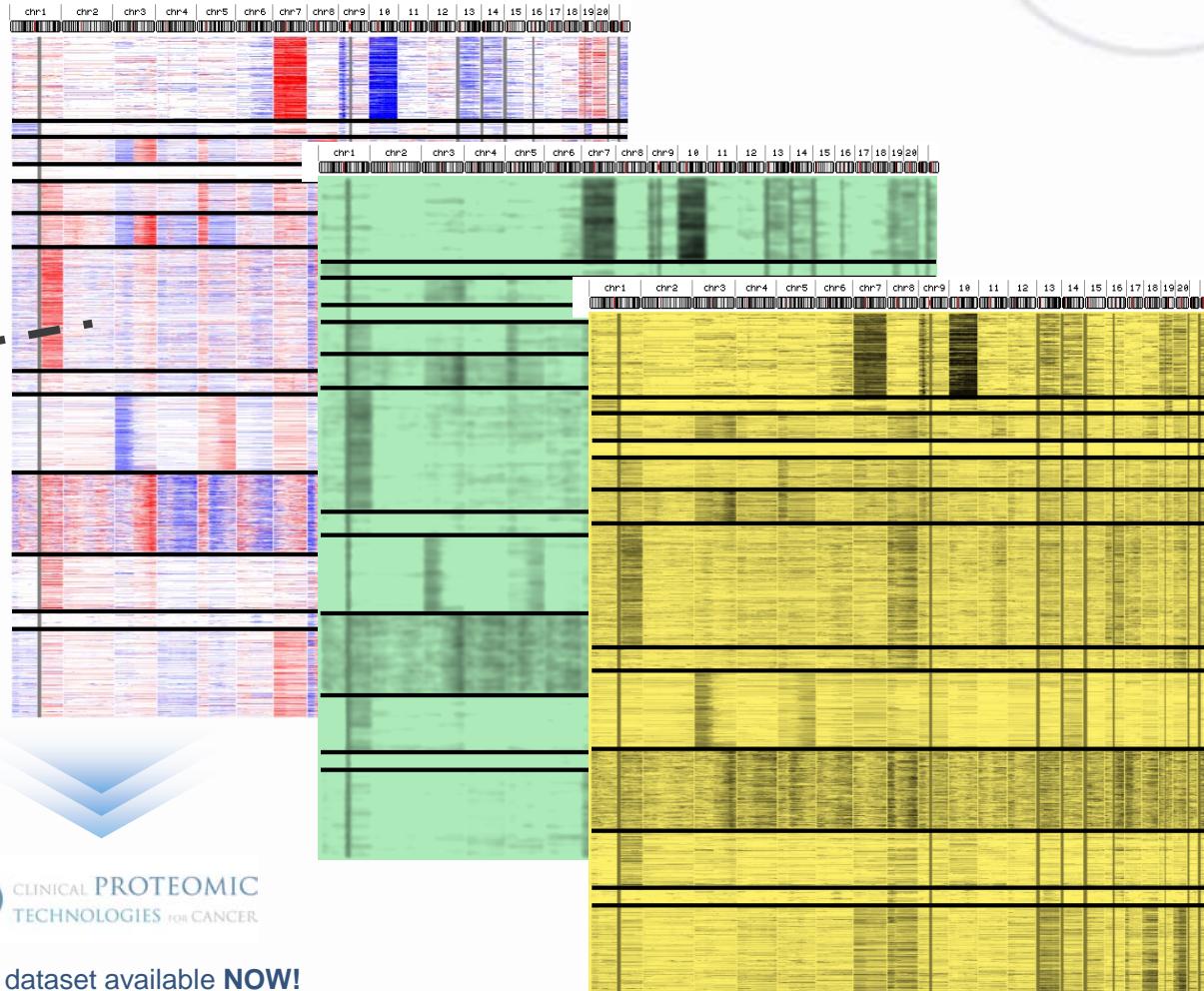
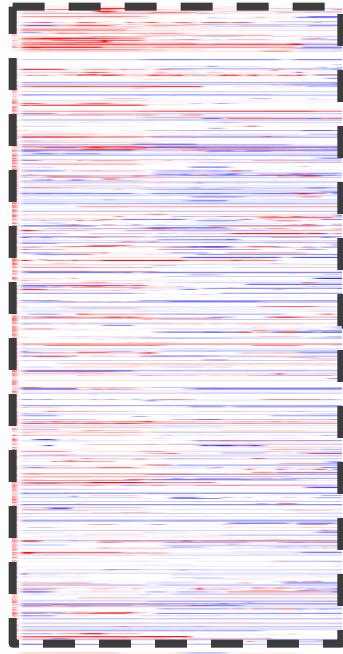


Spring 2013



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:	5979

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

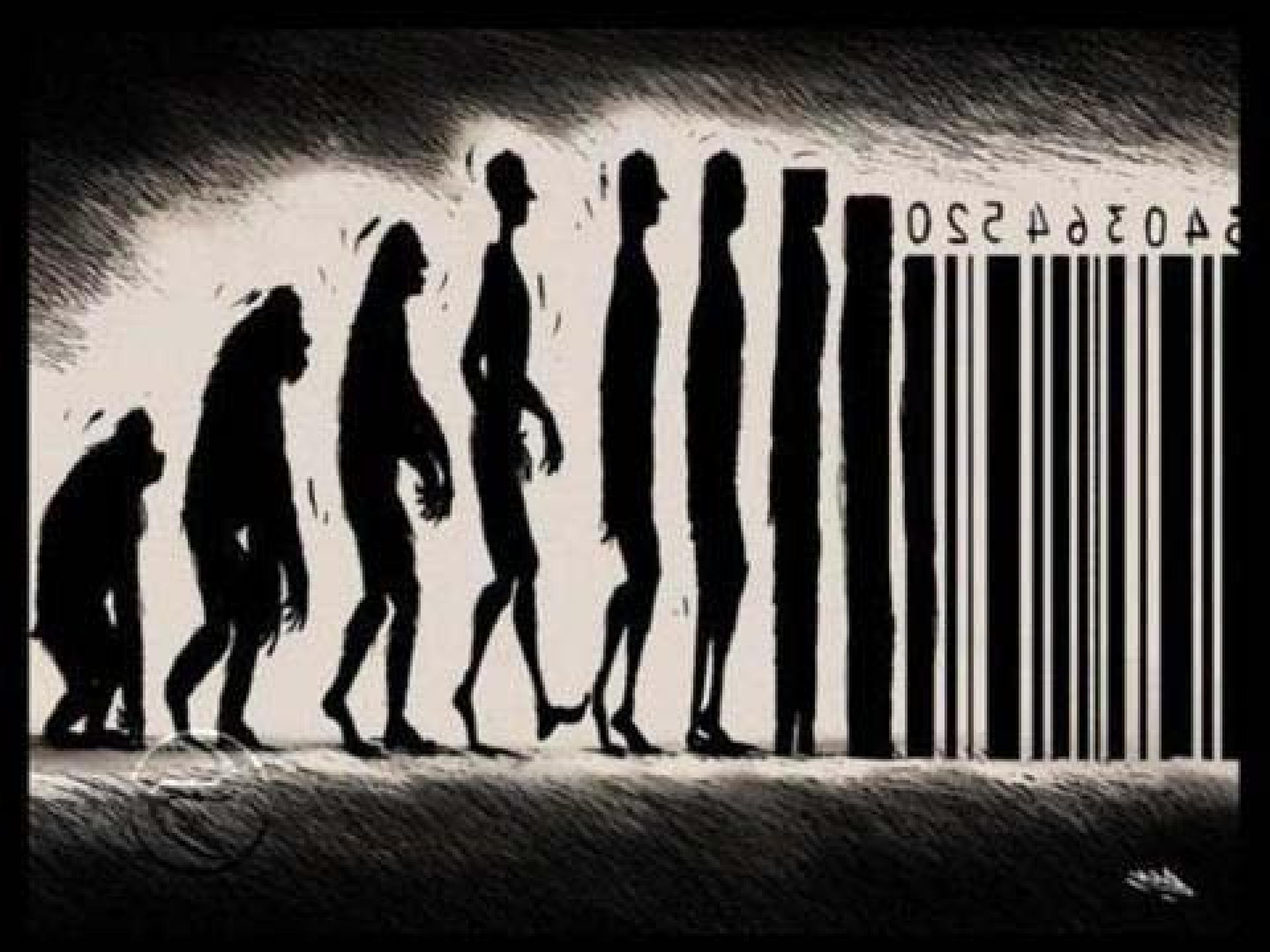


Public dataset available **NOW!**

Time? (Evolution)

Bringing Nanotechnology to Cancer Research & Oncology: ANC Network





4504284250

Extra Motivation to Start Thinking Innovatively...



FORTY YEARS' WAR

Grant System Leads Cancer Researchers to Play It Safe



Bryce Vickmark for The New York Times

Dr. Ewa T. Sicinska turned to a private foundation to finance her research.

By GINA KOLATA

Published: June 27, 2009

Among the recent research grants awarded by the [National Cancer Institute](#) is one for a study asking whether people who are especially

RECOMMEND
[COMMENT](#)

"We have a system that works over all pretty well...we don't fund bad research," said Dr. Raynard S. Kington, "But given that, we also recognize that the system probably provides disincentives to funding really transformative research..."

- ...One major impediment, scientists agree, is the grant system itself. It has become a sort of jobs program, a way to keep research laboratories going year after year with the understanding that the focus will be on **small projects unlikely to take significant steps toward curing cancer...**
- ...In fact, it has **become lore among cancer researchers** that some game-changing discoveries involved projects deemed too **unlikely to succeed** and were therefore denied federal grants, forcing researchers to struggle mightily to continue...
- ...the institute's reviewers choose such projects because, with too little money to finance most proposals, **they are timid about taking chances on ones that might not succeed...**

Bringing In New Perspectives and Teams (2009)



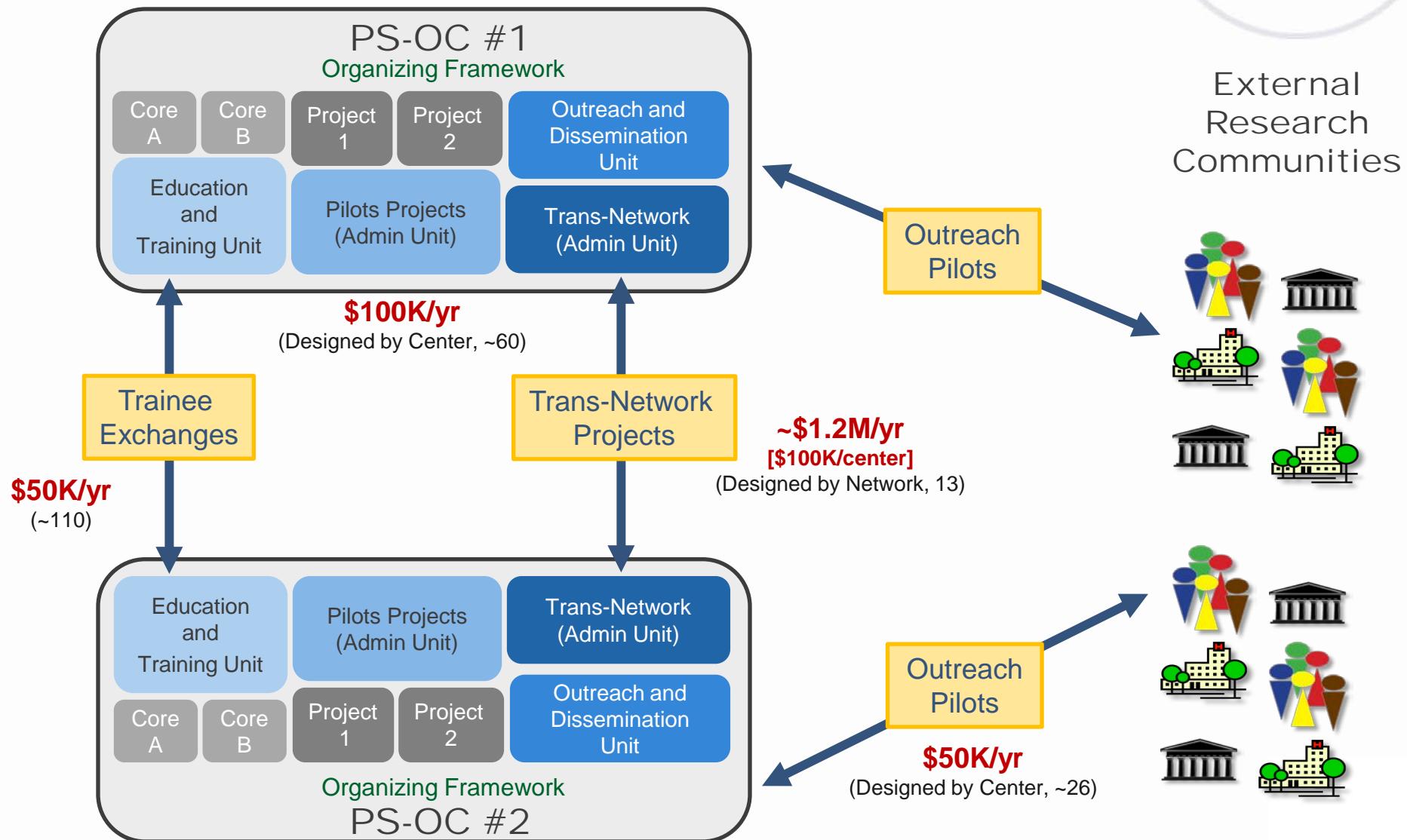
PHYSICAL SCIENCES — in ONCOLOGY

- 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.



New – “Schools of Thought”

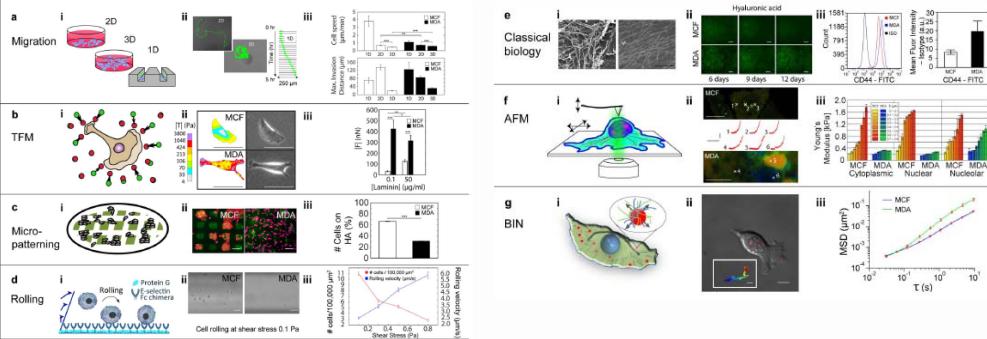
PS-OC Model: PI Driven Interactions Inside/Outside of Network/Center



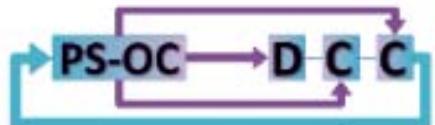
New Collective Insights of Physical Science Parameters: Living Project

A physical sciences network characterization of non-tumorigenic and metastatic cells

The Physical Sciences - Oncology Network*



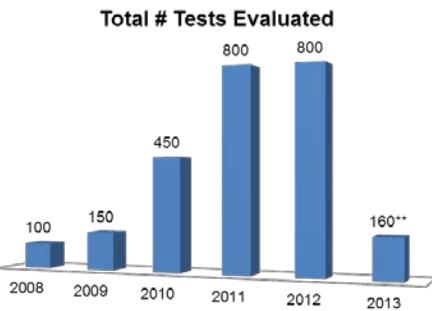
<http://opso.cancer.gov/data/>



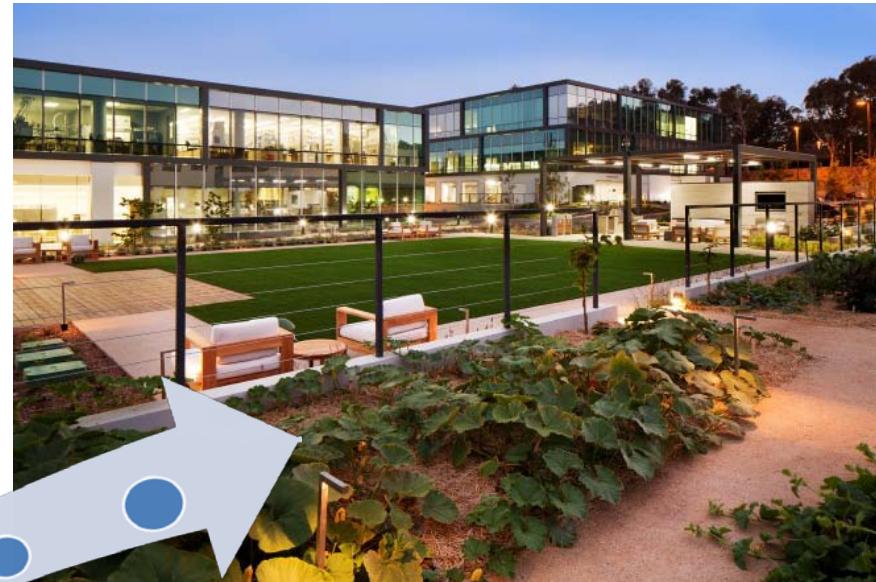
Cells

- First large-scale, comprehensive, biophysical examination of identical cells
 - 17 institutions
 - 20 labs
 - 24 techniques and approaches
- Combined analysis through Data Jamboree
- Continued as a **“living project”** through repository and database
 - Raw data (published/unpublished) for additional analysis
 - Request cells for additional characterization (data upload required post-publication)

PHYSICAL SCIENCES in ONCOLOGY



- Clinical sites: 26
- Global Partners: 4 (UK, NKI, China, Spain)
- Patients enrolled: 2,000
- Patients samples: 5,000
- Observational studies: 19



www.epicsciences.com

Epic Sciences has **40 collaborative projects**

- **10 major Pharma partners** including (Genentech, Pfizer, and Celgene)
- Over ~**2,500 patients** on clinical studies or clinical trials



Then...(2002)



Now...(2012): Moore's Law of Analysts?



200+

~100

Cancer genome characterization centres: Broad Institute/Dana-Farber Cancer Institute Gad Getz¹⁸, Wendy Winkler^{18,22,23}, Roel G. W. Verhaak^{18,22,23}, Michael S.

Comprehensive genomic characterization defines human glioblastoma genes and core pathways

The Cancer Genome Atlas Research Network*

Integrated genomic analyses of ovarian carcinoma

The Cancer Genome Atlas Network*

Comprehensive genomic characterization of squamous cell lung cancers

The Cancer Genome Atlas Network*

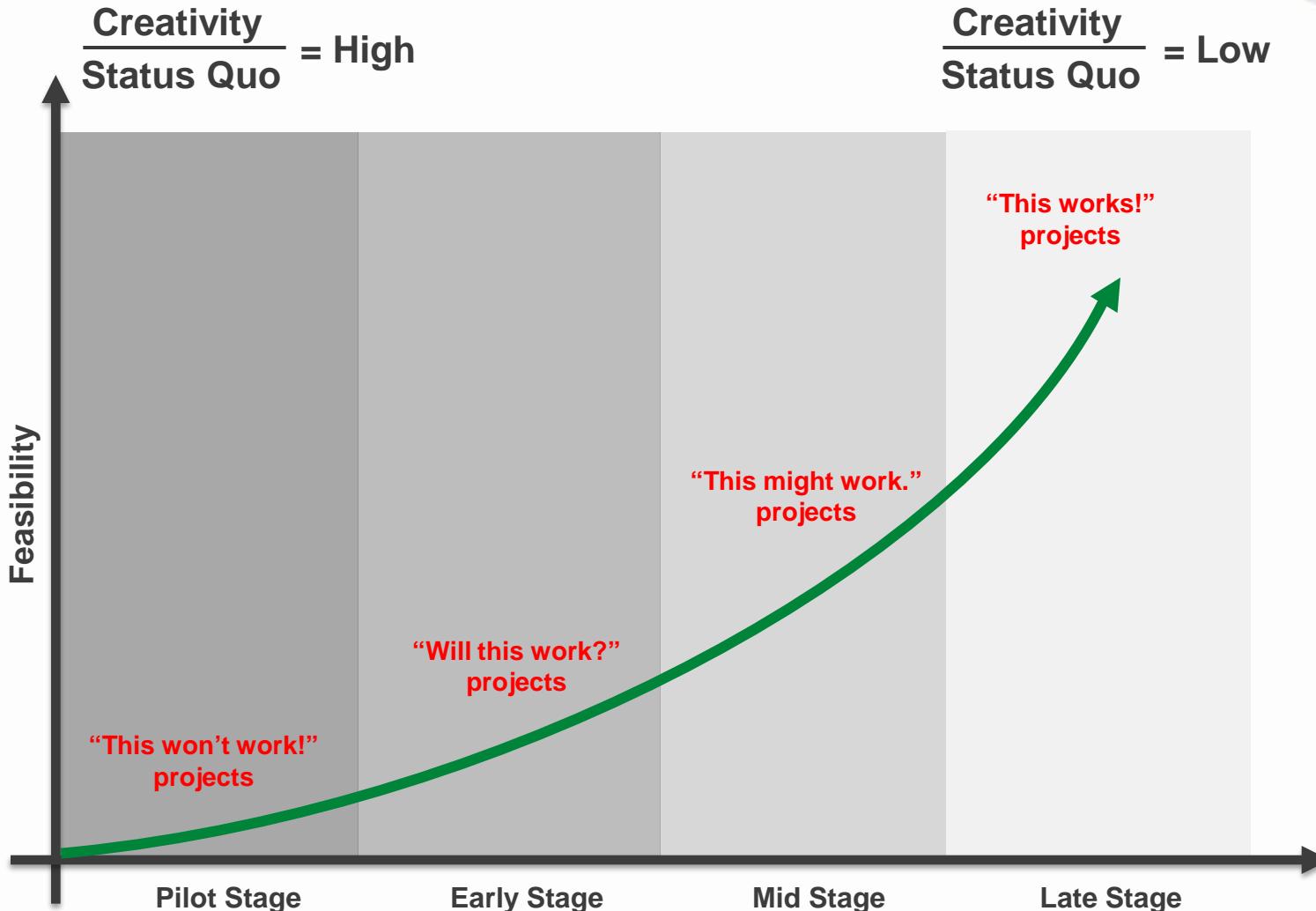
2008

2010

2012

2014

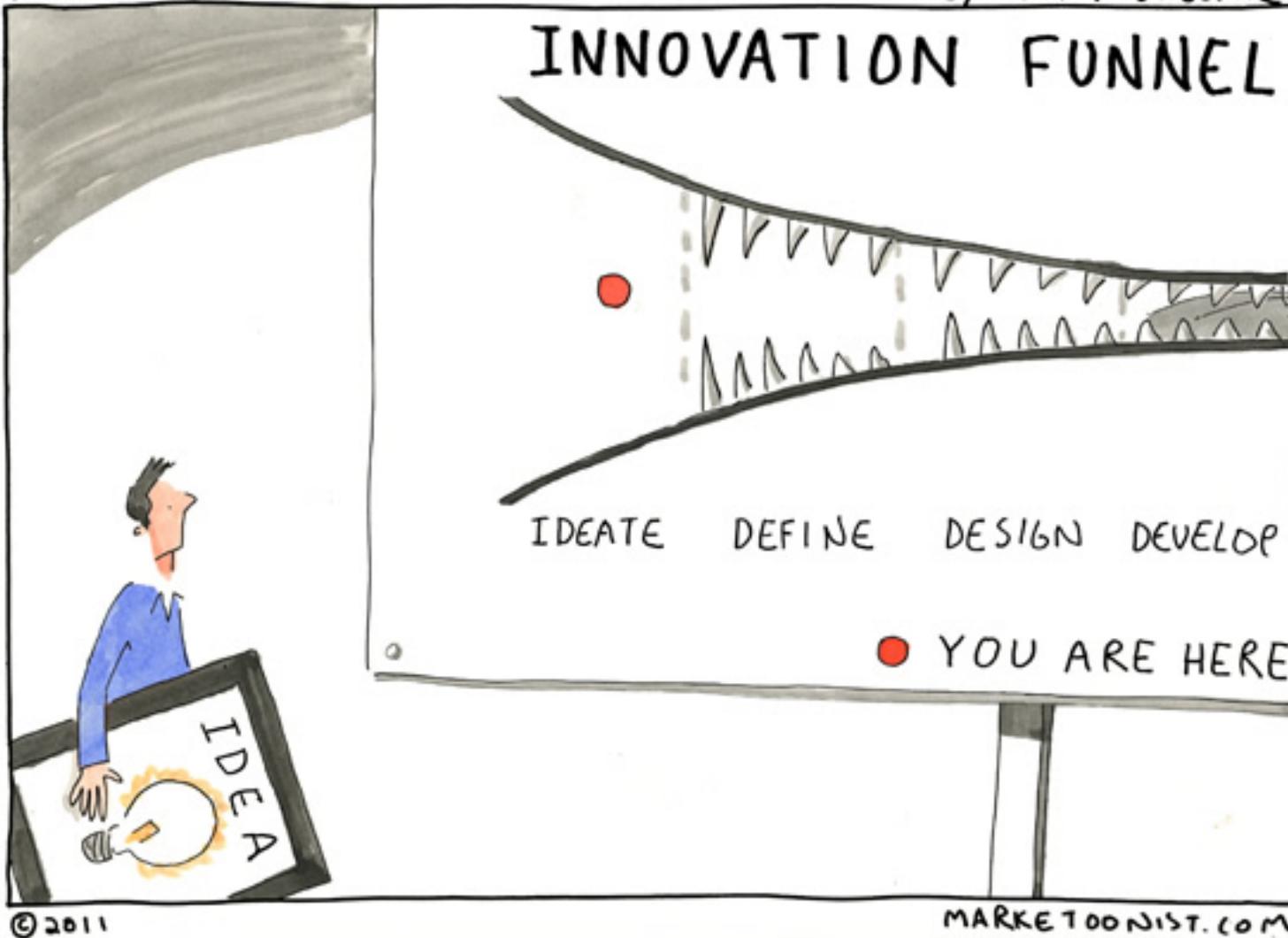
Lessons Learned Thus Far: Creativity vs. Feasibility

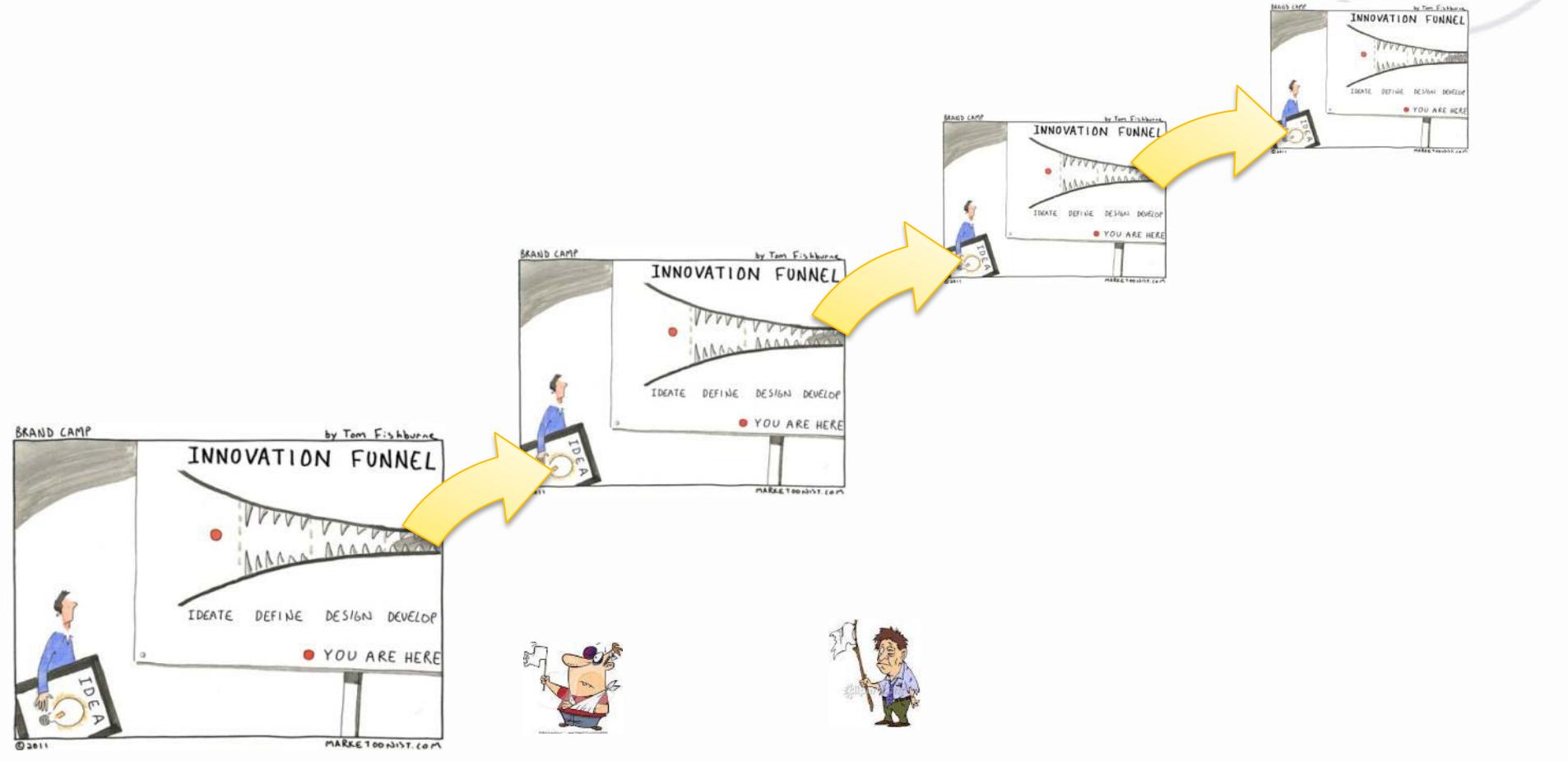


BRAND CAMP

by Tom Fishburne

INNOVATION FUNNEL





Basic

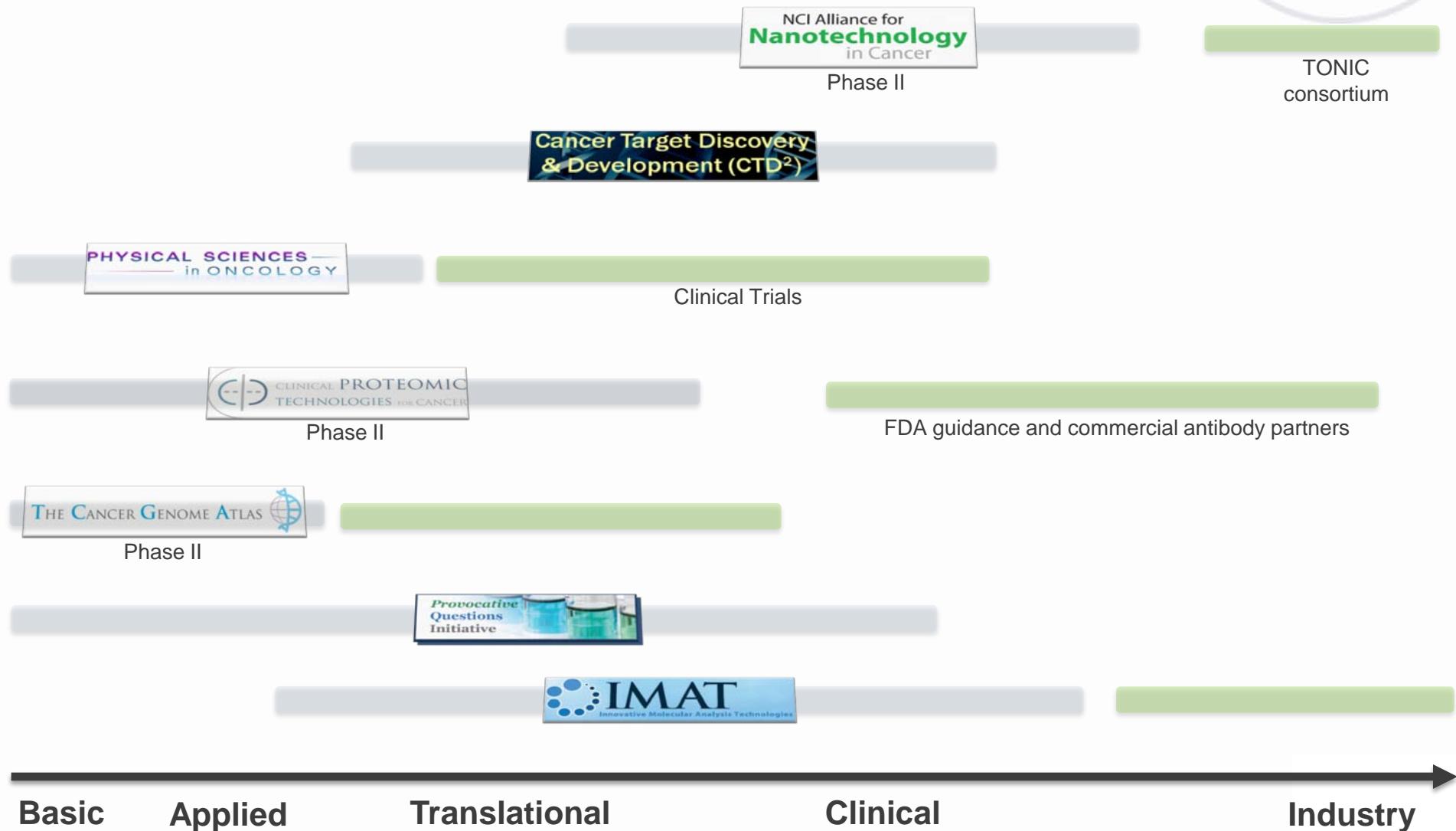
Applied

Translational

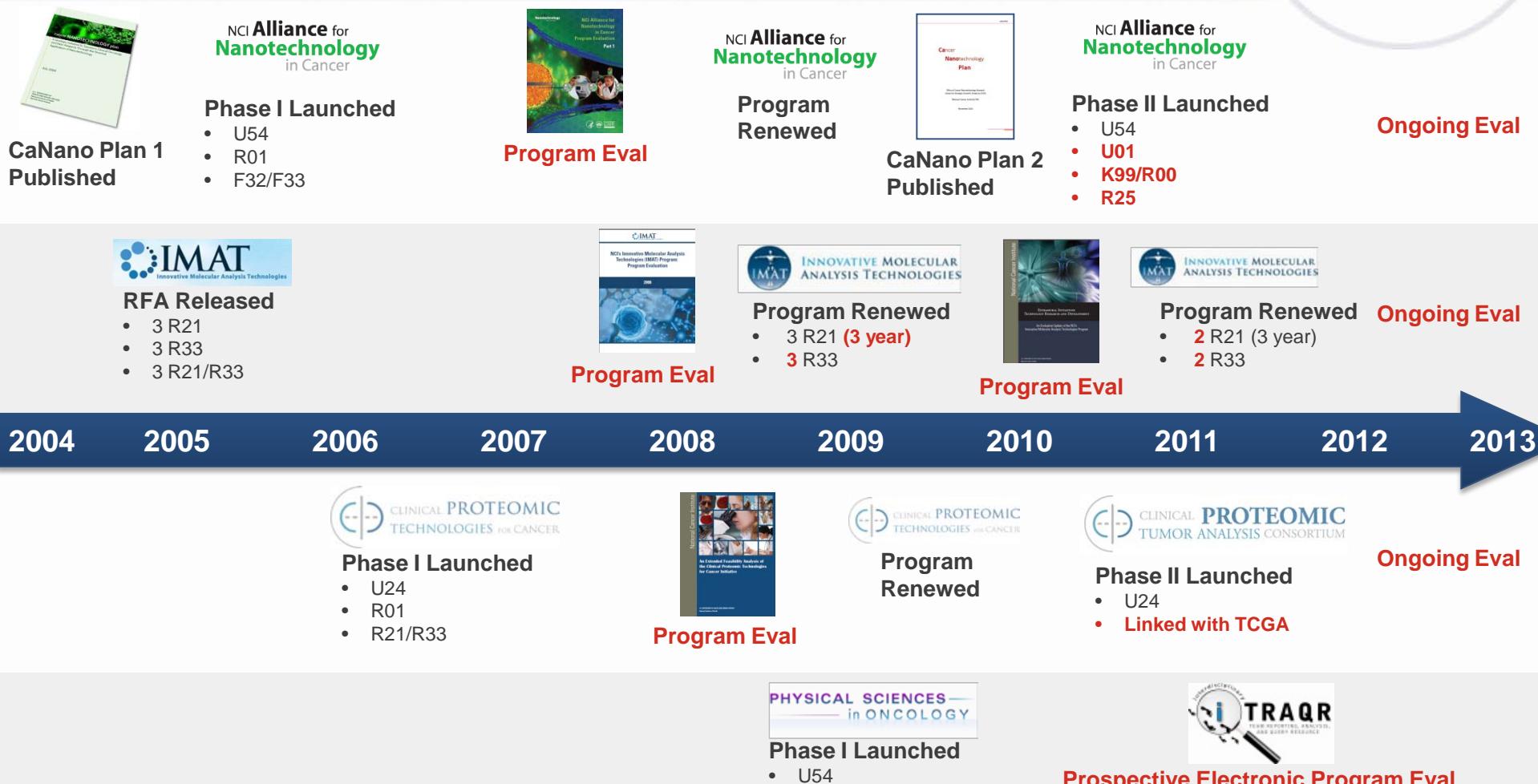
Clinical

Industry

Measuring Innovation & Outcomes: Expectations vs. Realities



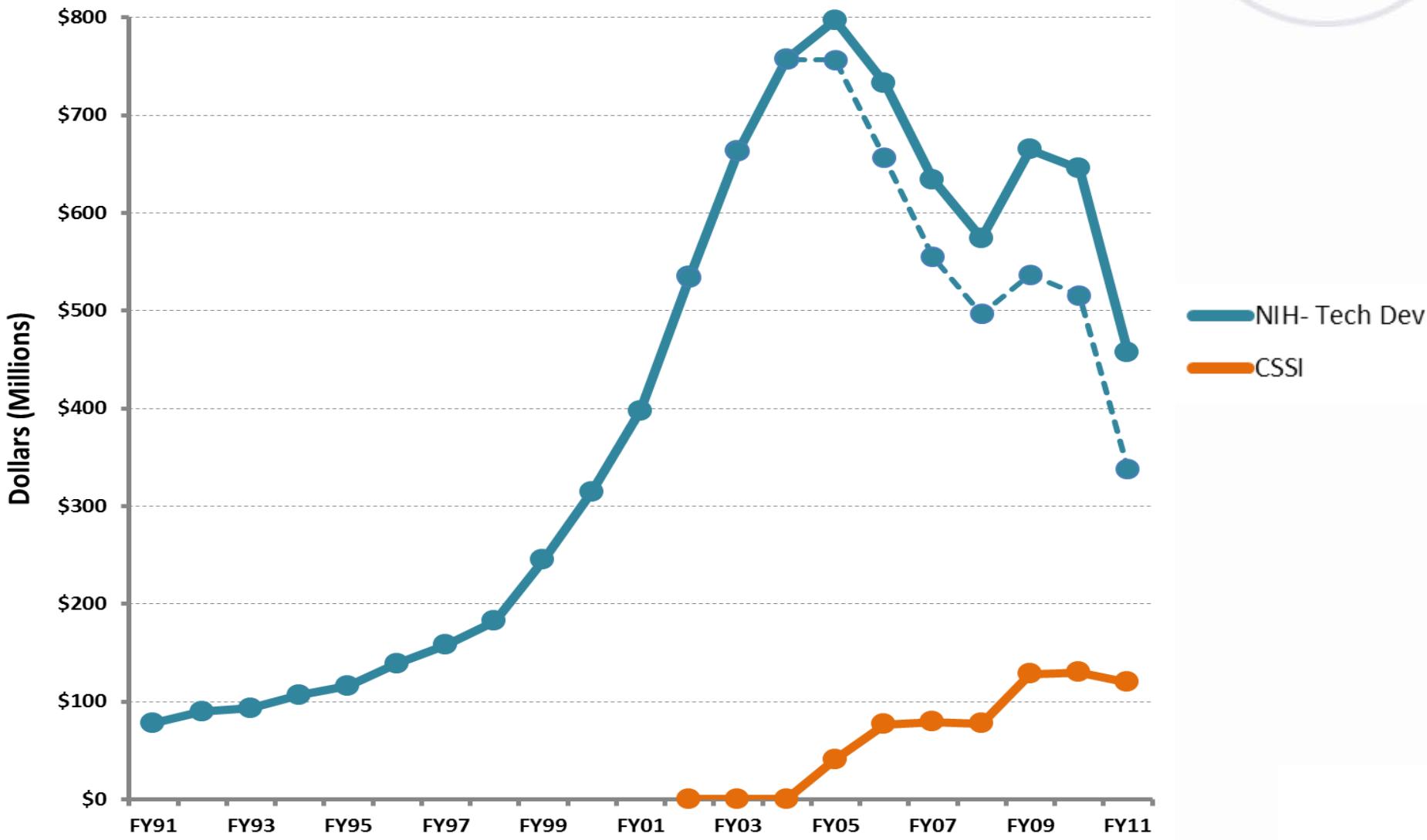
CSSI Programs and Evaluations (2004-2013)



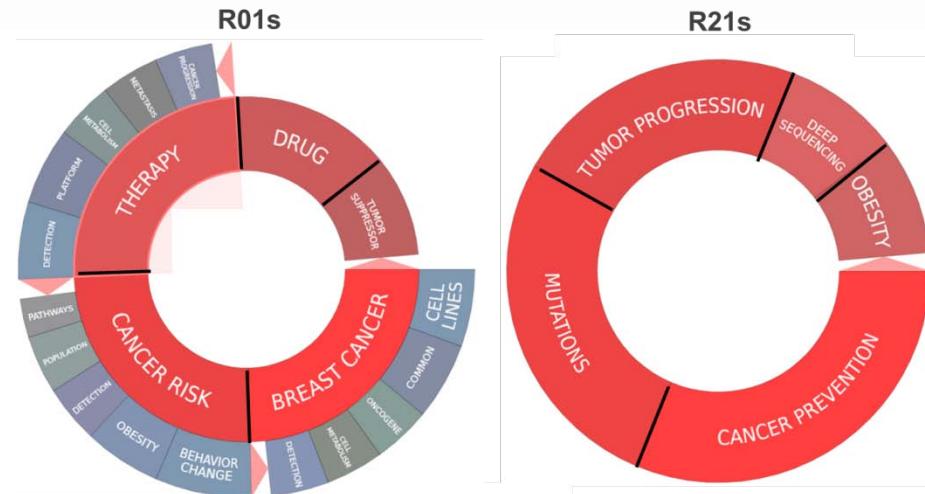
Pre-Review
Applicant Eval



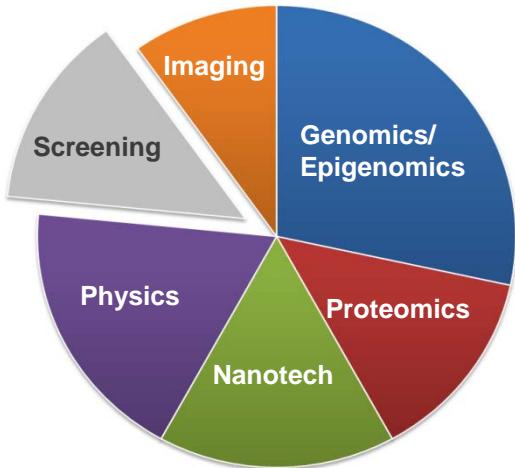
Supporting Innovation: Timing Is Everything



Join the Team! Upcoming Funding Opportunities



Data from projectreporter.nih.gov



Innovative Molecular Analysis Technologies (\$10.5M)



Due Dates 05/20 and 9/20/13

IMAT Program Director
anthony.dickherber@nih.gov



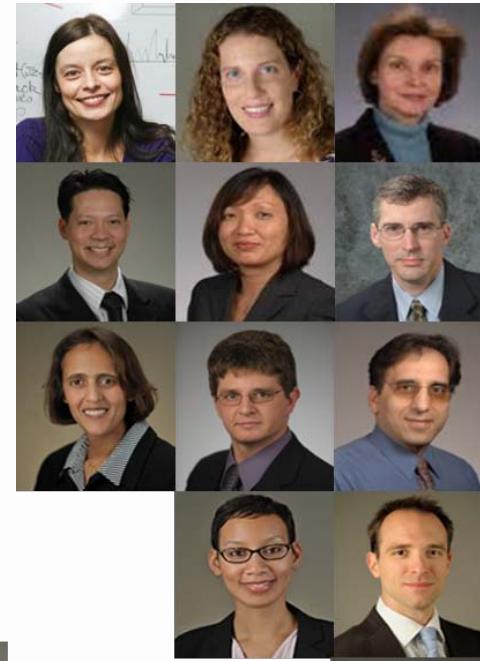
Acknowledgements/Thanks to the “Secret Ingredients”



Clinical Sciences



Life Sciences



Physical Sciences



Learn More About Us...



<http://cssi.cancer.gov>

A screenshot of the CSSI website homepage. The header includes the NCI logo, "National Cancer Institute", and "U.S. National Institutes of Health | www.cancer.gov". The main navigation menu has links for "HOME", "ABOUT CSSI", "CSSI OFFICES", and "CONTACT CSSI". On the left, there is a vertical sidebar with "LEARN MORE" and "A Service of the National Cancer Institute". The main content area features a dark background with a colorful molecular structure graphic. Text on the left reads: "ENABLING PROGRESS IN CANCER RESEARCH THROUGH ADVANCED TECHNOLOGIES, TRANS-DISCIPLINARY PROGRAMS AND RESOURCES". A large, semi-transparent overlay window titled "Timeline:" is centered. It contains a legend for "Offices" (View All, OD CSSI, OIBR, TUGA, OCG, OCCPR, OCNR, OPSO) and a "Zoom Level" selector (1 Year, 3 Years, All Years). Below these are two timelines: a horizontal one at the bottom and a circular one in the center. The circular timeline shows various colored circles representing different offices, each containing a small icon related to cancer research.

Jerry S.H. Lee, PhD
jerry.lee@nih.gov

Questions?