



CENTER for
STRATEGIC
SCIENTIFIC INITIATIVES

NATIONAL CANCER INSTITUTE

Advancing Innovation and Convergence In Cancer Research

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

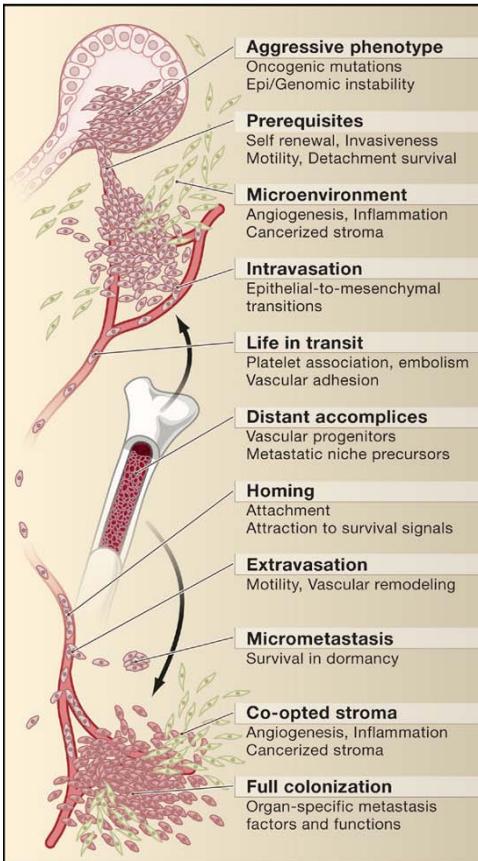
April 25, 2013

INTERNATIONAL CONFERENCE
INNOVATION
IMPERATIVE
SLOVAKIA'S FUTURE

Sponsored by:



What is It? Tumor, Cancer, and Metastasis



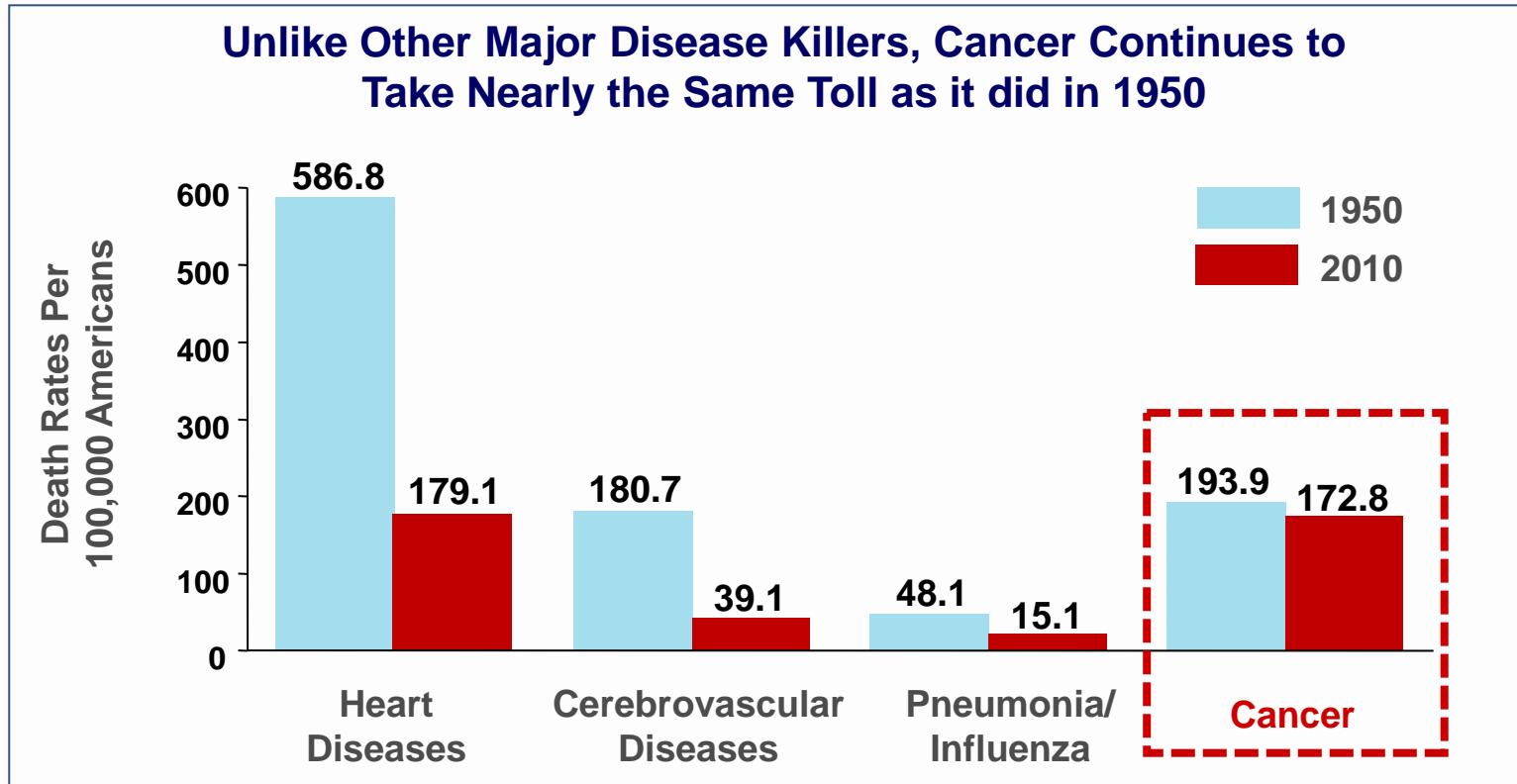
| Organ Site | All Stages | Localized | Regional | Distant |
|-------------------|------------|-----------|----------|---------|
| Prostate | 99 | 100 | 100 | 28 |
| Breast | 89 | 98 | 84 | 24 |
| Ovary | 44 | 92 | 72 | 27 |
| Uterine Cervix | 68 | 91 | 57 | 16 |
| Melanoma | 91 | 98 | 62 | 15 |
| Urinary Bladder | 78 | 70 | 33 | 6 |
| Kidney | 71 | 91 | 64 | 12 |
| Colon and rectum | 64 | 90 | 70 | 12 |
| Esophagus | 17 | 38 | 20 | 3 |
| Lung and bronchus | 16 | 52 | 25 | 4 |
| Liver | 15 | 28 | 10 | 3 |
| Pancreas | 6 | 23 | 9 | 2 |

“...>90% of deaths is caused by disseminated disease or metastasis...

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

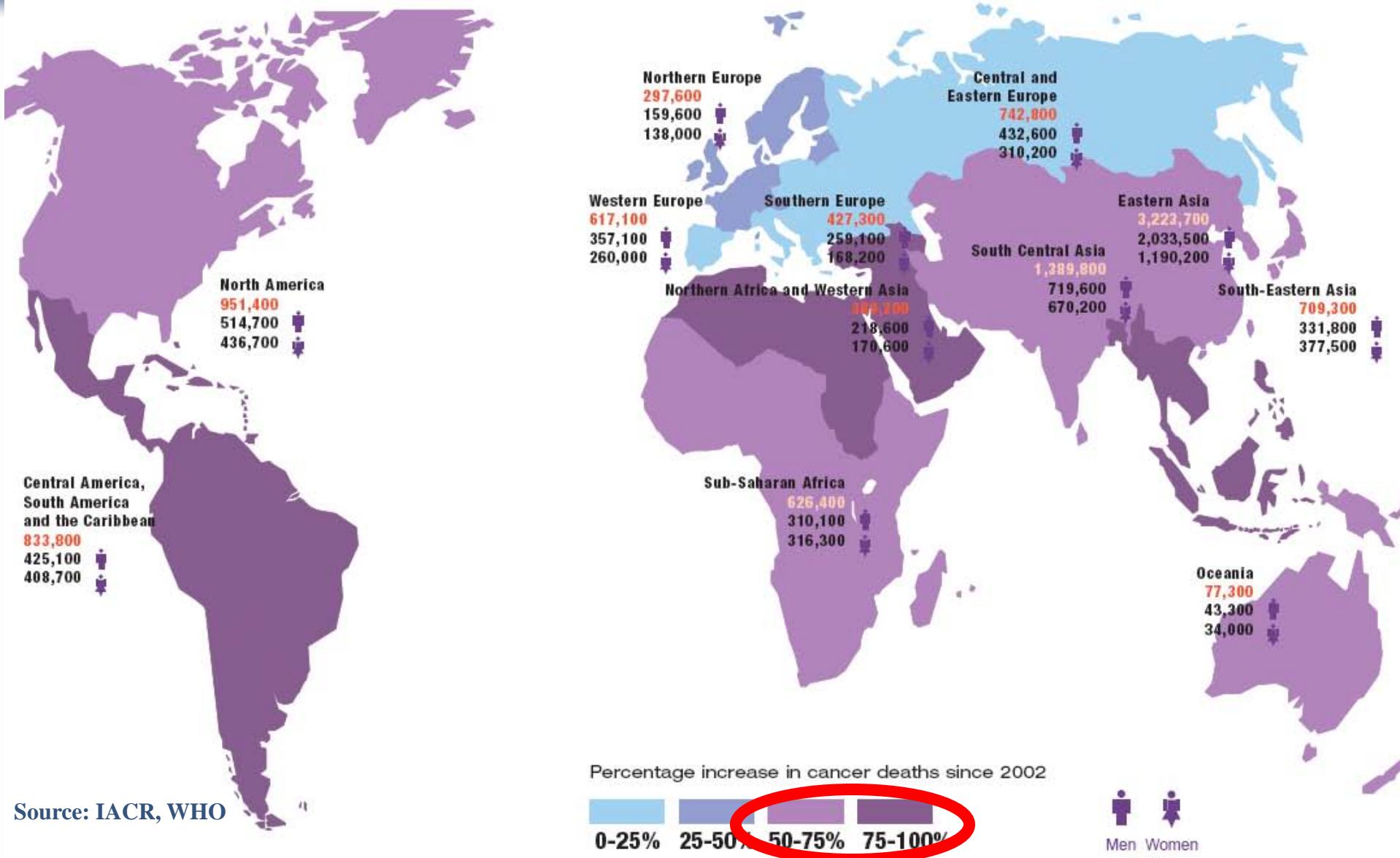


- **567,628** Americans died of cancer in 2009 (**580,350** projected for 2013)
- **1,660,290** Americans will be newly diagnosed with cancer in 2013 (projected)
- **\$124.6 billion** in 2010 for cancer healthcare costs

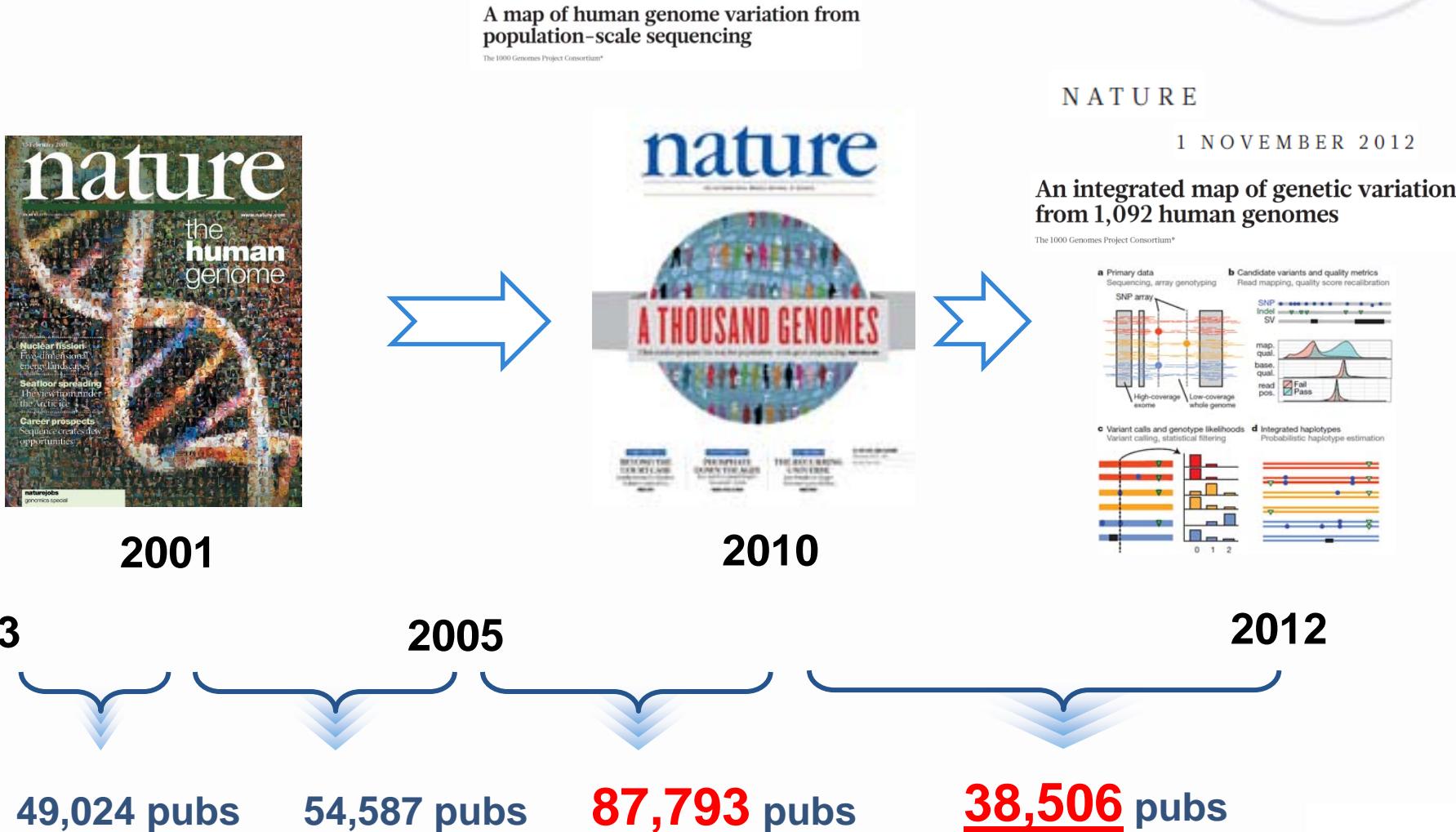


Source for 2013 projected deaths and diagnoses: Siegel et. al, Cancer Statistics, 2013
Source for 2010 age-adjusted death rate: National Center for Health Statistics, NCHS Public-use file for 2010 deaths.

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

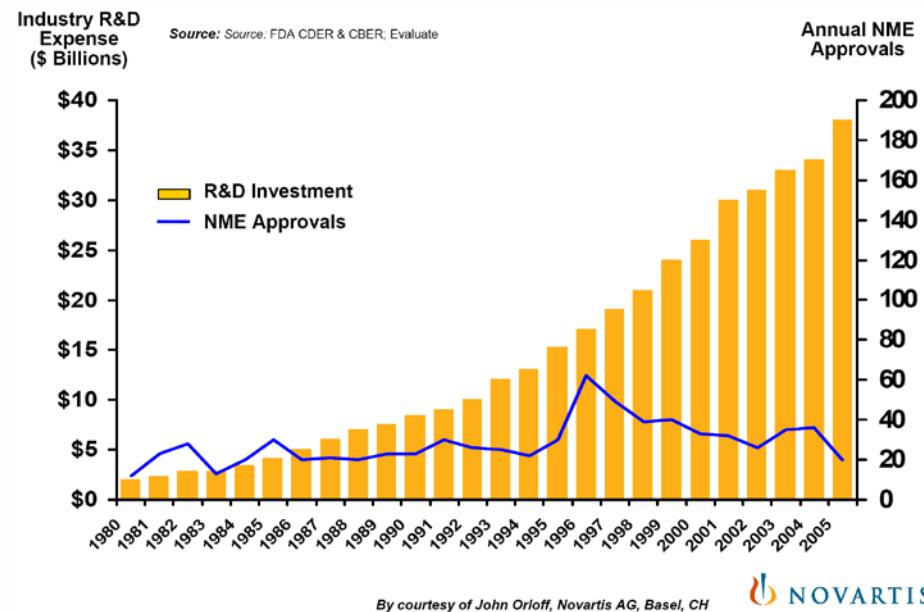


Unprecedented Amount of Scientific Knowledge: Omics(ssss)

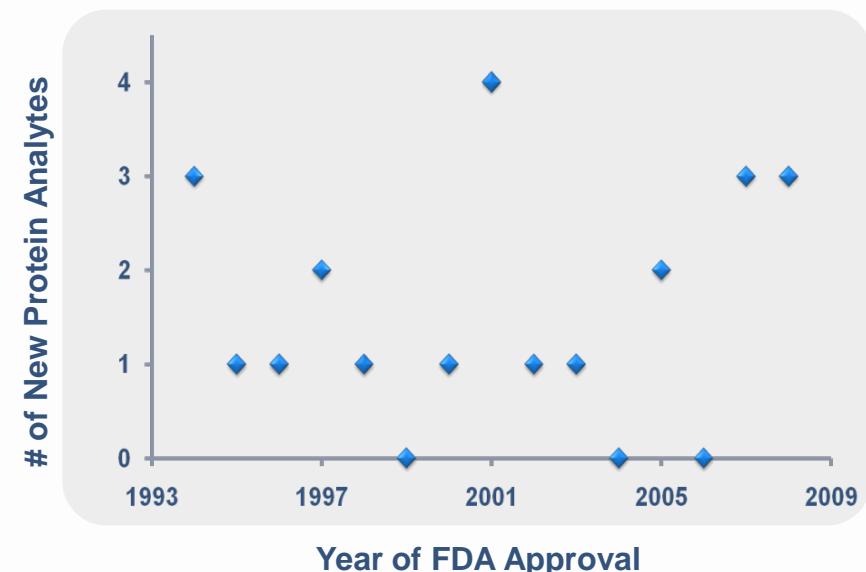


Is More Knowledge Yielding More Solutions for Patients?

Drug Discovery and Development



Diagnostic Biomarkers



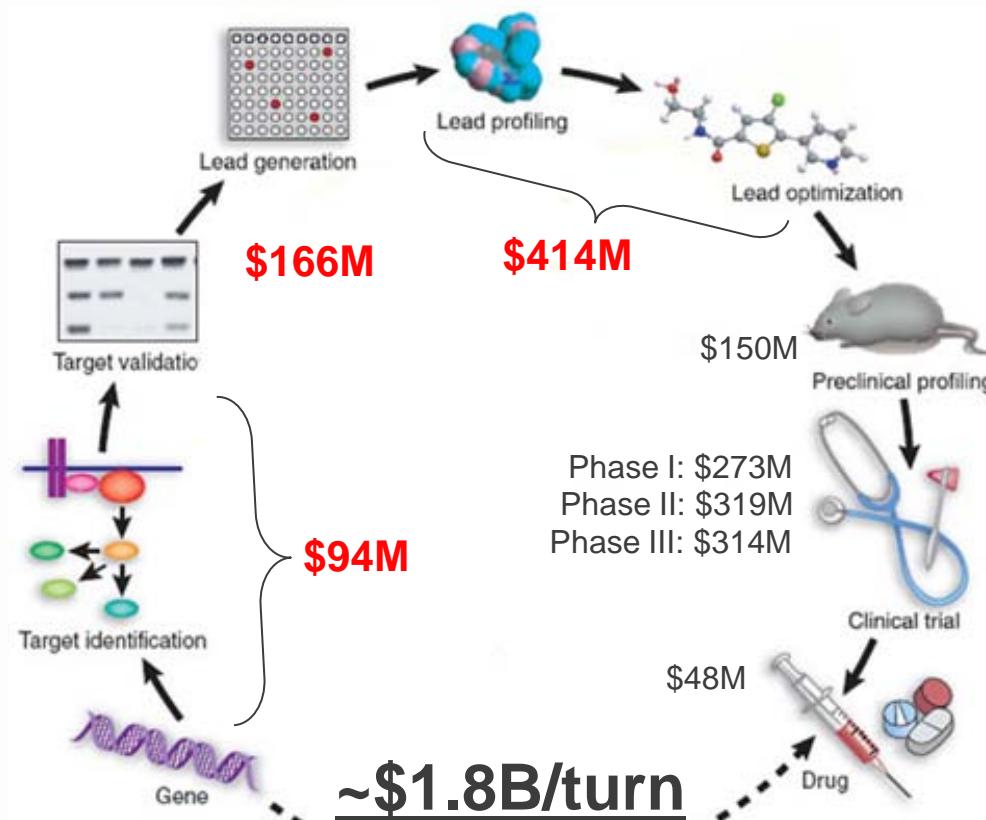
- 10 – 15 years at ~ \$1.8 billion*
- 2007: 19 NMEs [lowest since 1983]
- 2008: 21 NMEs [29% new-in-class]
- 2009: 24 NMEs [17% new-in-class]

- 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?

*Paul et. al, *Nature Rev. Drug Discovery*, March 2010; †Leigh Anderson, *Clin Chem*, 2010

Translation Pace: How To Break Out of Current Paradigm?



Turning the Crank...

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 diagnostics

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



NHGRI



NIA



NIDA



NIH Campus – Bethesda, Maryland



NINDS



NIDCD



NIMH



NEI



NIAAA



CIT



FIC



CSR



NIBIB



NIGMS



NICHD



CC



NINR



NLM



NIDDK



NIAMS



NCCAM



NIAID



NCI



NHLBI



NCATS

NIH Budget ~ \$30.8 Billion (FY12)

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

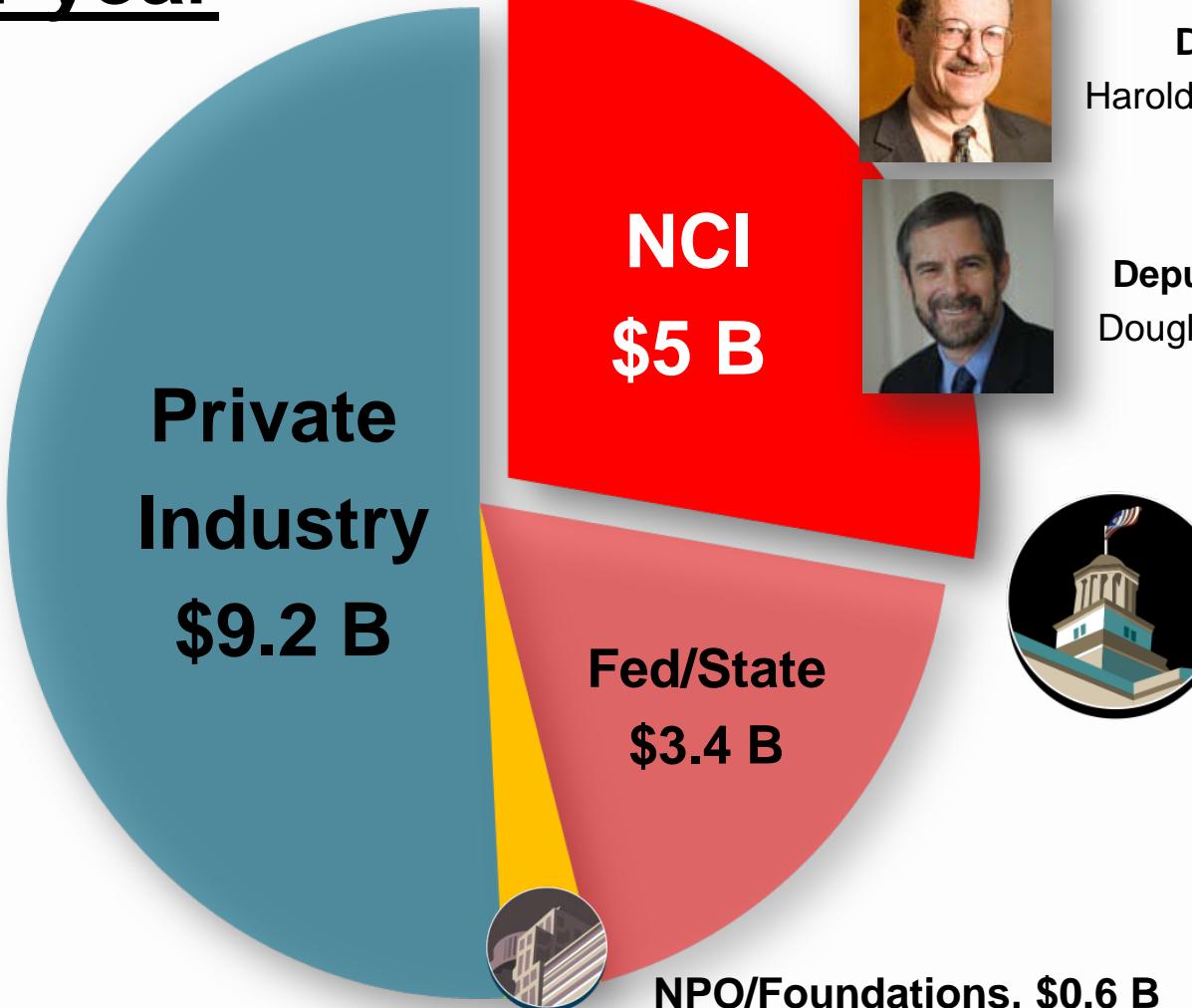
NCI Budget ~ \$ 5.07 Billion (FY12)

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

National Cancer Program: Stakeholders



~\$18 B per year



Director
Harold Varmus, MD



Deputy Director
Douglas Lowy, MD



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

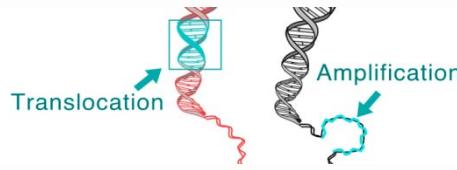


2010

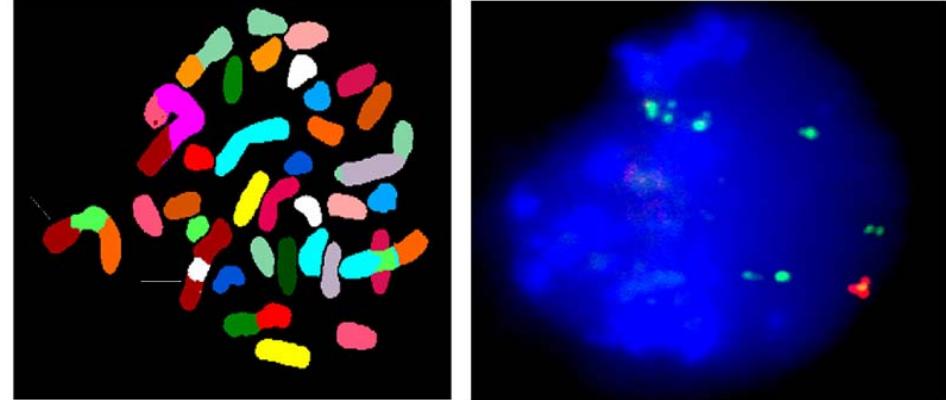
First Step(back)- Cancer Genomics: Taking a Page from Engineers

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 |

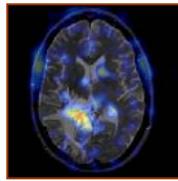
Steam table (Reference)

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

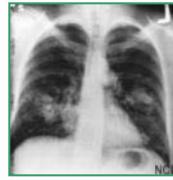


Three Cancers- Pilot

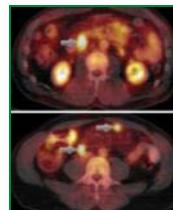
glioblastoma multiforme
(brain)



squamous carcinoma
(lung)

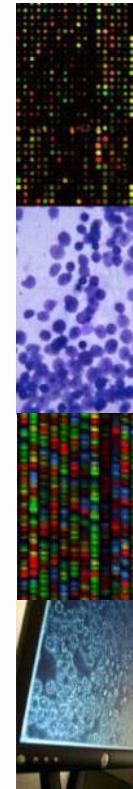


serous
cystadenocarcinoma
(ovarian)



Multiple data types

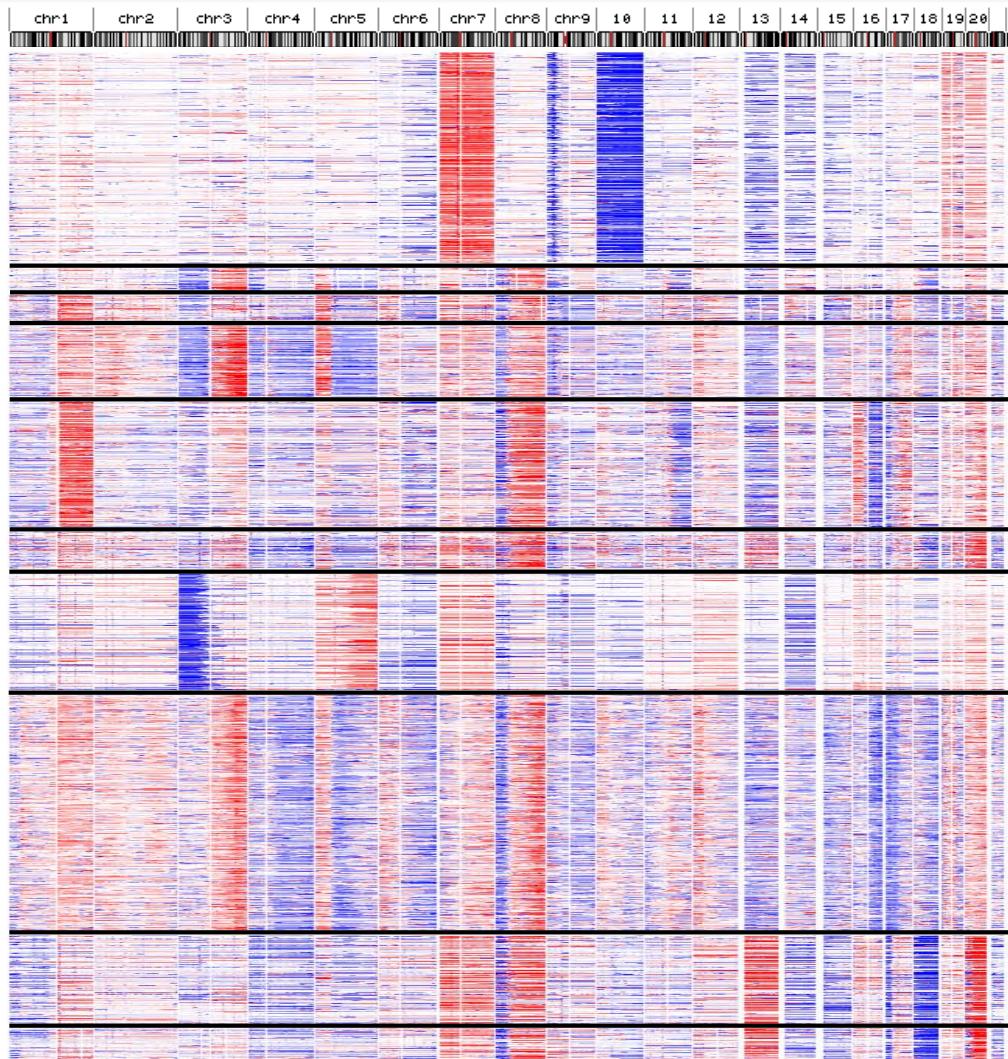
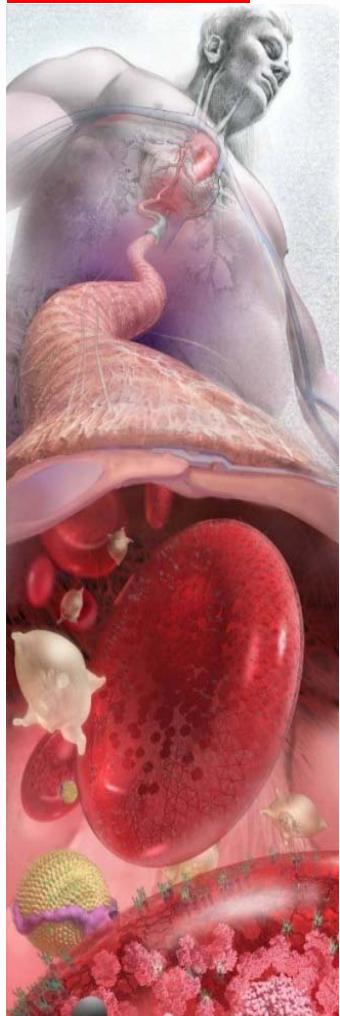
- Clinical diagnosis
- Treatment history
- Histologic diagnosis
- Pathologic status
- Tissue anatomic site
- Surgical history
- Gene expression
- Chromosomal copy number
- Loss of heterozygosity
- Methylation patterns
- miRNA expression
- DNA sequence



Genomic “Steam Table”



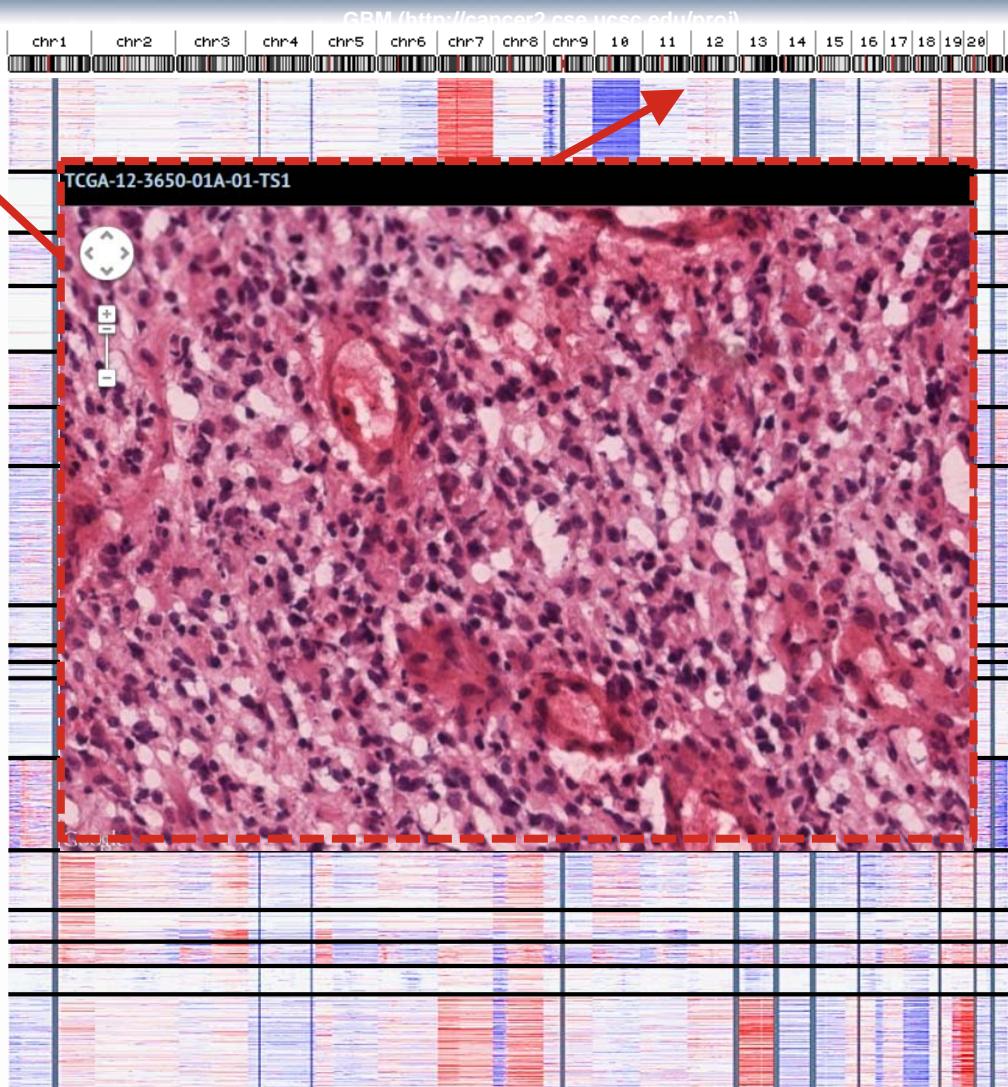
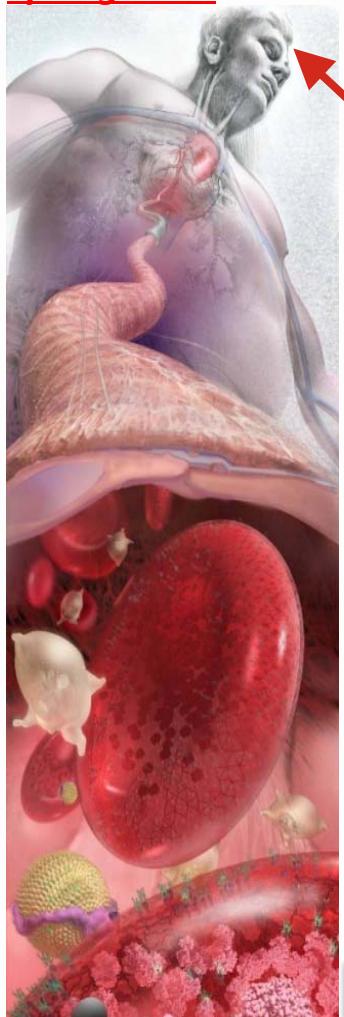
Summer 2011



| | |
|--------------------|-------------|
| 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: | 74 |
| Total: | 2053 |

Genomic “Steam Table”

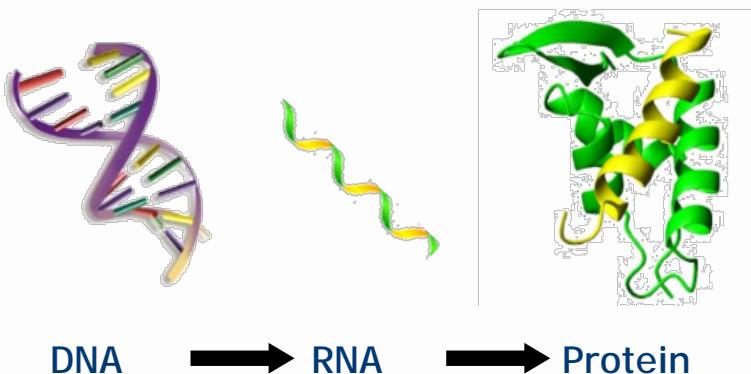
Spring 2013



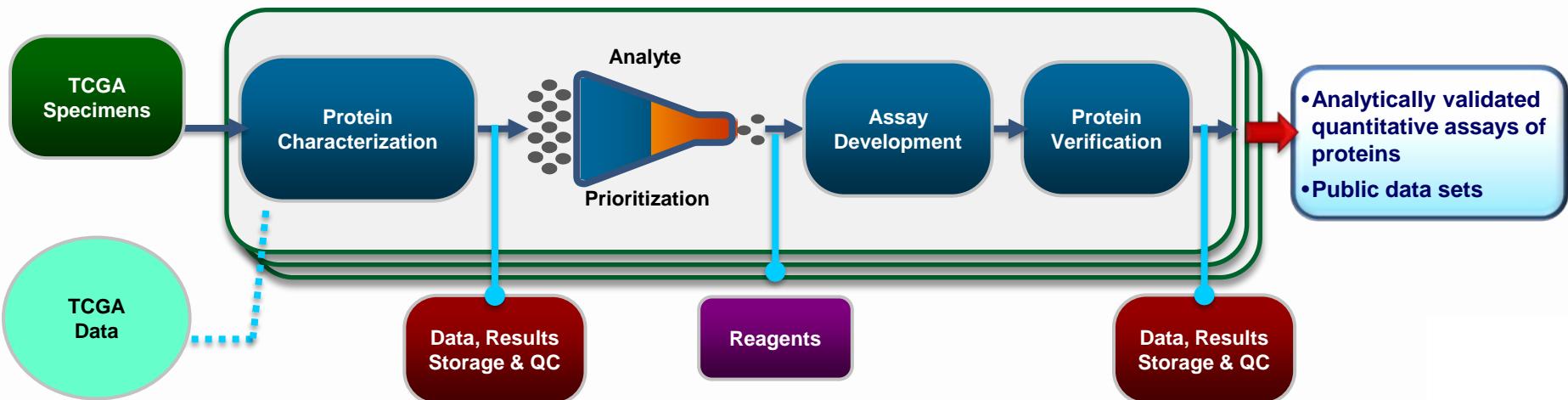
| | |
|---------------------------|-------------|
| Glioblastoma: | 563 |
| Brain lower grade glioma: | 180 |
| Head & neck: | 306 |
| Thyroid carc: | 401 |
| Lung adeno: | 356 |
| Lung squamous: | 343 |
| Breast carc: | 866 |
| Stomach adeno: | 237 |
| Liver hep. carc: | 97 |
| Kidney pap. cell carc: | 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: | 575 |
| Total: | 5979 |

What about Biomarkers? Clinical Proteomics Tumor Analysis Program

Phase II Launched Sept 2011

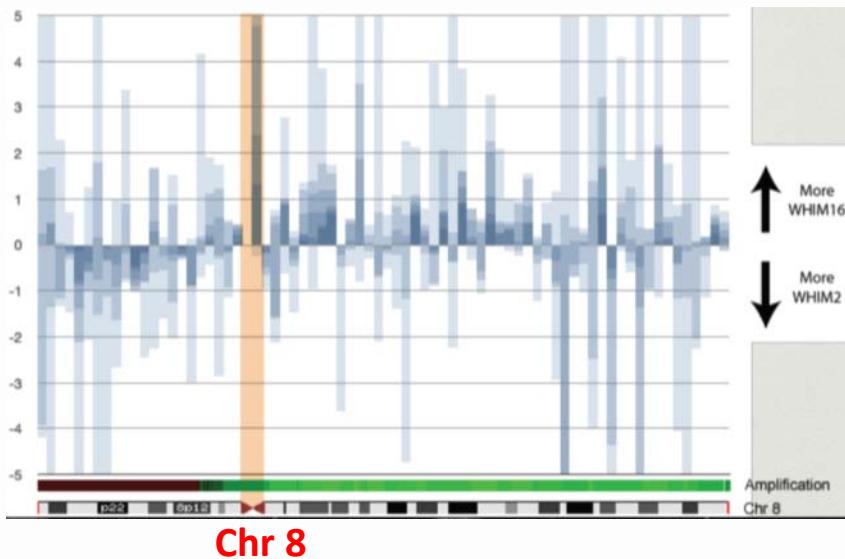


- Analyze matched TCGA samples using two approaches
 - Targeting genome to proteome
 - Mapping proteome to genome
- Develop **validated and quantitative** assays and reagents
 - Lessons from Phase I (mock 510K submission)
 - Antibody Characterization Lab
- Distribute raw and analyzed data via public data portal



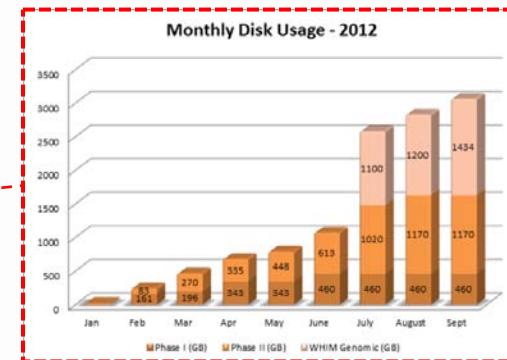
CPTAC Phase II: Highlights, Progress to Date, and Data Release

Status Update: Fall 2012

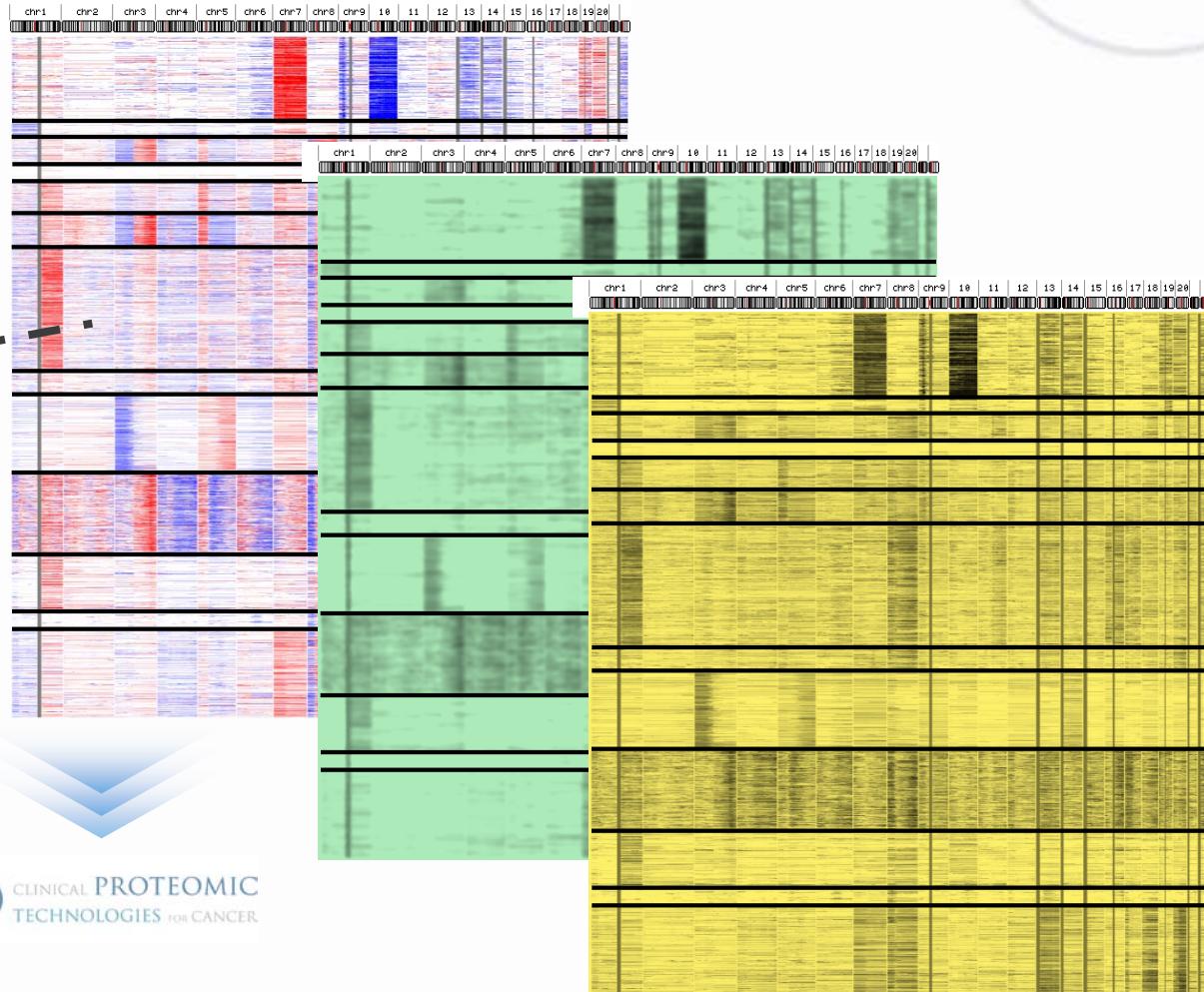
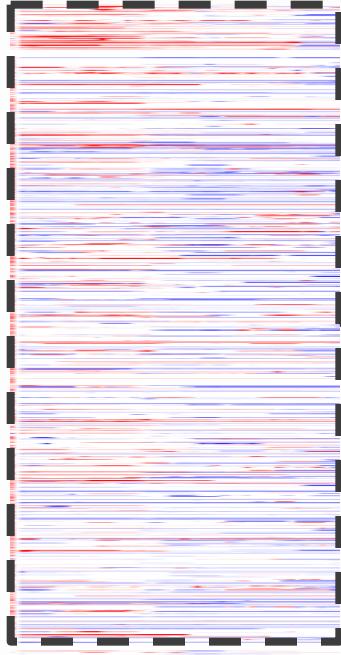


- Due diligence studies near completion
 - Cross network experiments show comparable lab-to-lab measurements
- Orthogonal proteomic platforms and analysis (proteome → genome vs. genome → proteome) reveal additional unexpected complexities
- Verifying new insights will require additional sample sets and development of novel analysis algorithms and techniques
- Public data portal access OPEN!
(Phase I: 351 GB, Phase II: 616 GB)

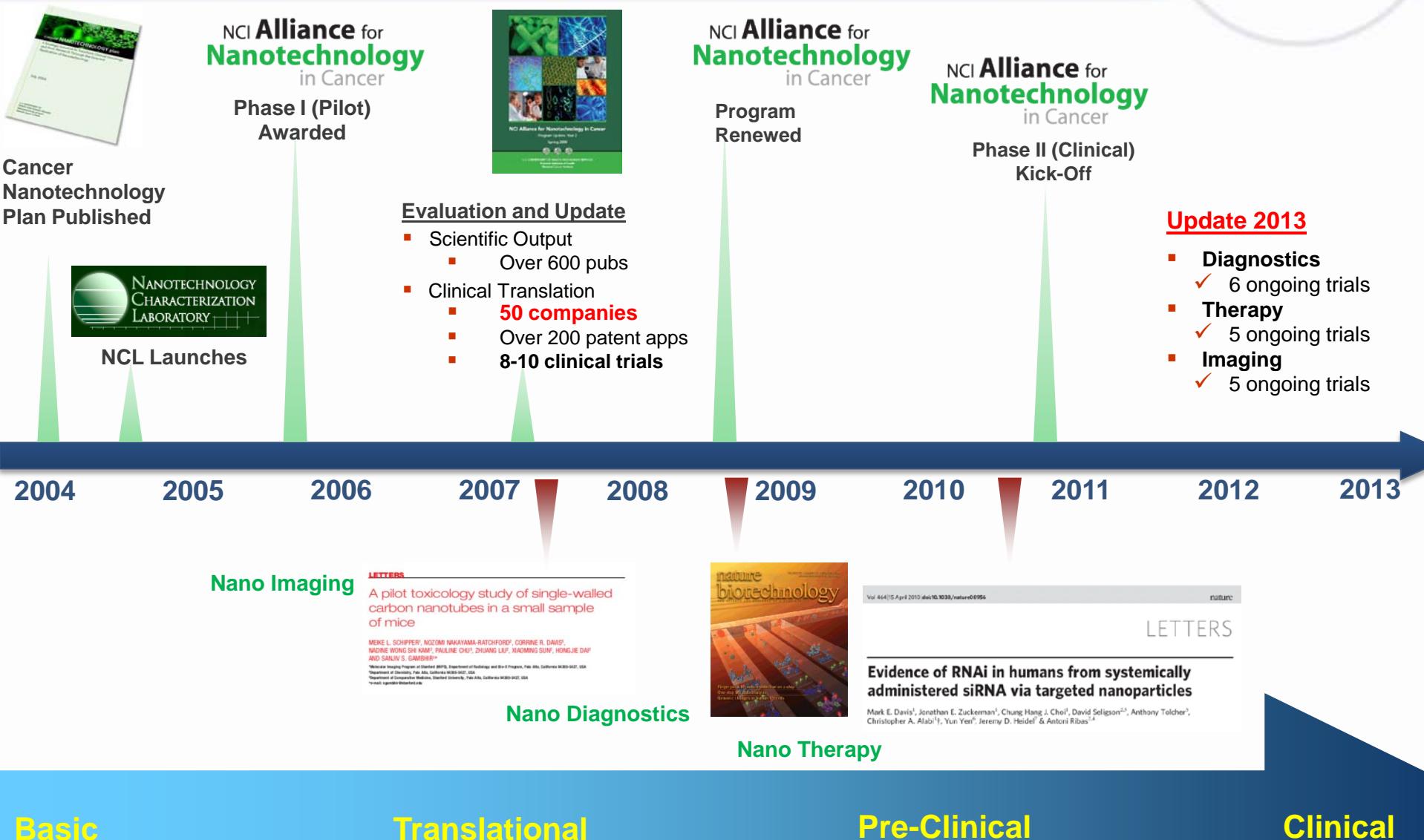
The CPTAC Data Portal interface features a navigation bar with links to Contact Us, Launch Analytics Portal, Home, and Stay Up to Date Updates. The main area displays the 'CPTAC DATA PORTAL Open Access to Proteomic Data' section, which includes a map of Proteome Characterization Centers and Partners, a flowchart of data processing steps, and a 'CPTAC Phase I Data Download >>' button. A sidebar provides information about the CPTAC Phase I Data and its coordination with TCGA.



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



Bringing Nanotechnology to Cancer Research & Oncology: ANC Network



Bringing In New Perspectives and Teams (2009)



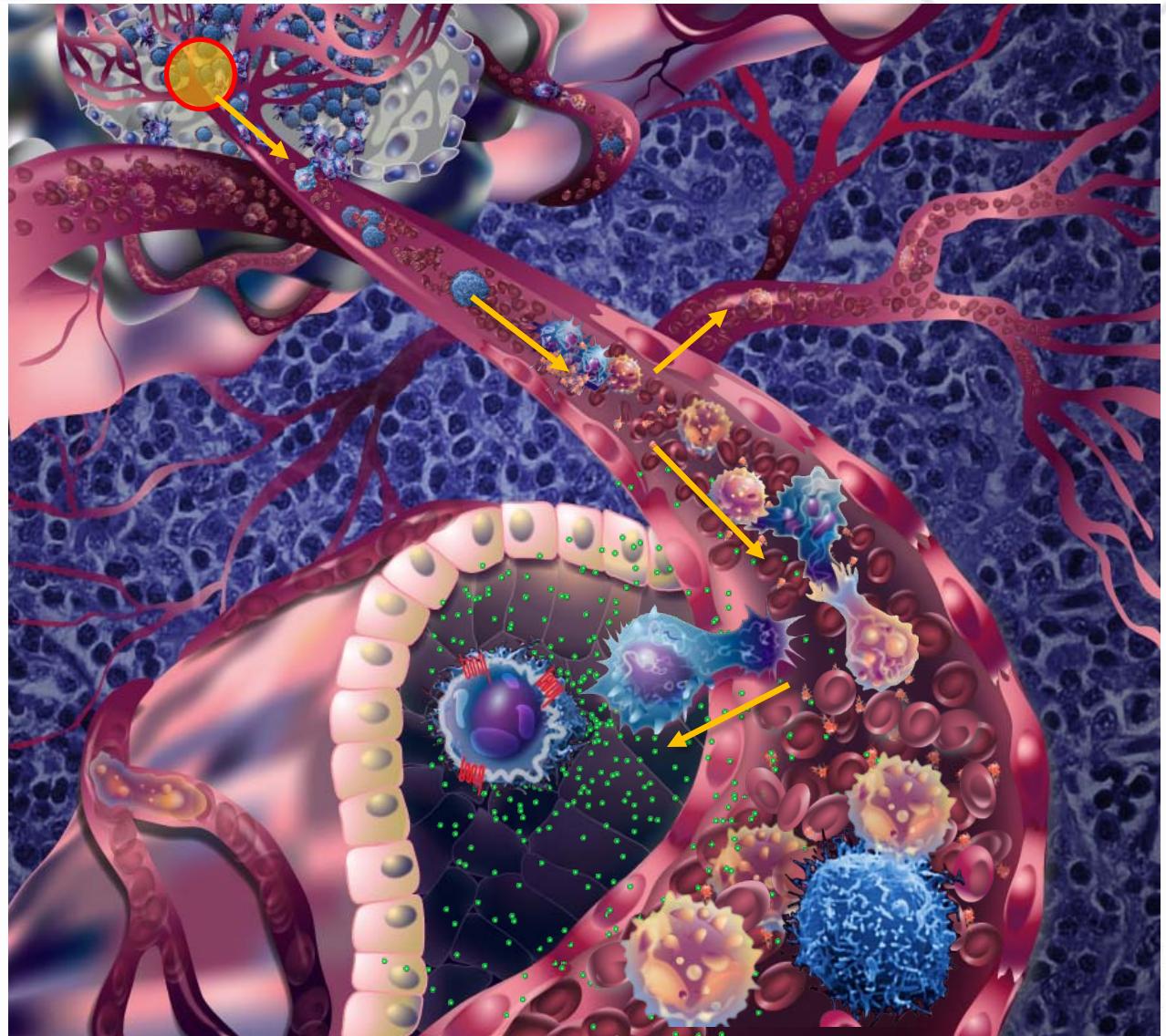
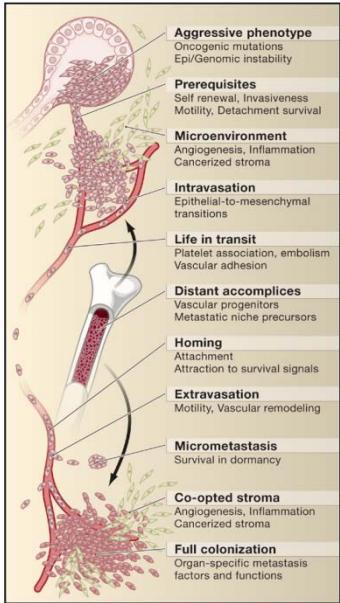
PHYSICAL SCIENCES — in ONCOLOGY

- 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”

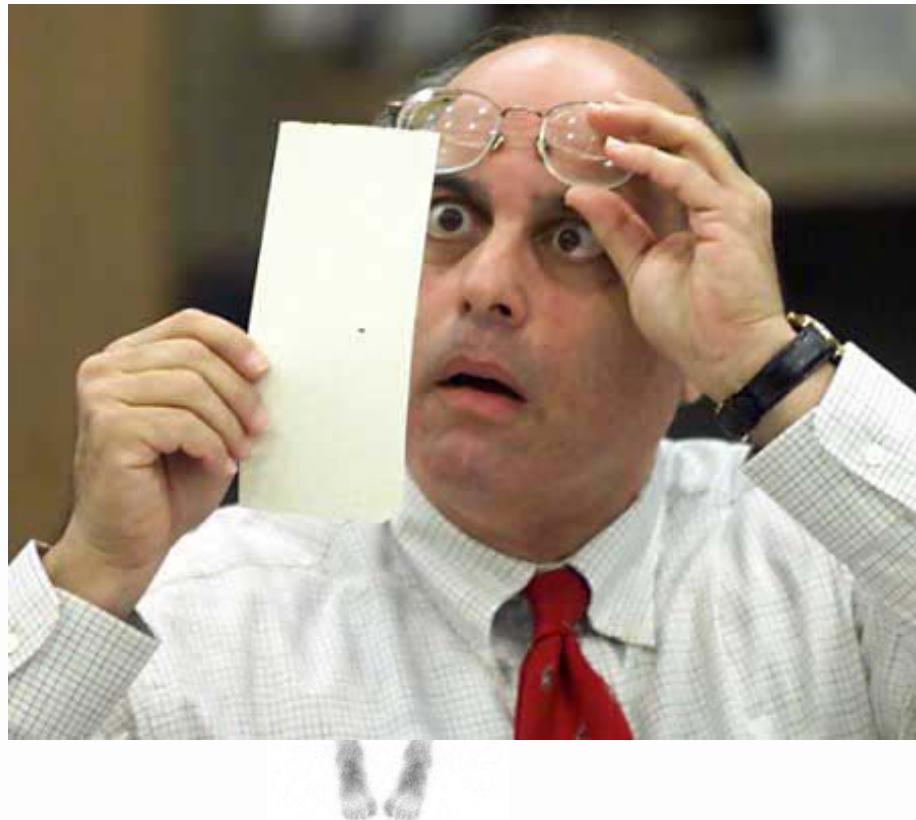
Physical Science Perspective: Space and Time Are Critical



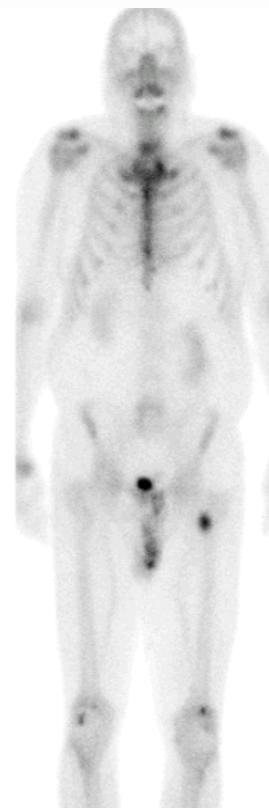
Metastasis known
to be an inefficient
process (0.01%)

From the Clinician's Perspective, Metastasis is More of a Binary Event ...

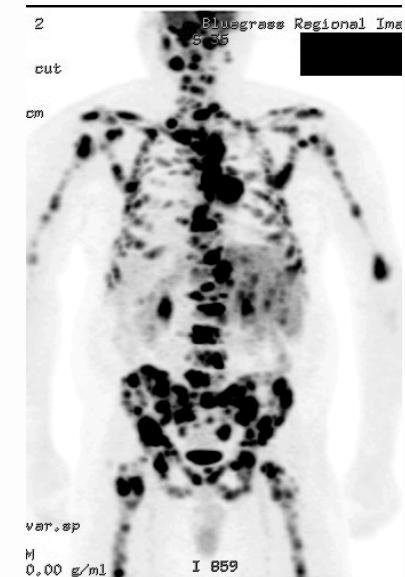
M0



M1



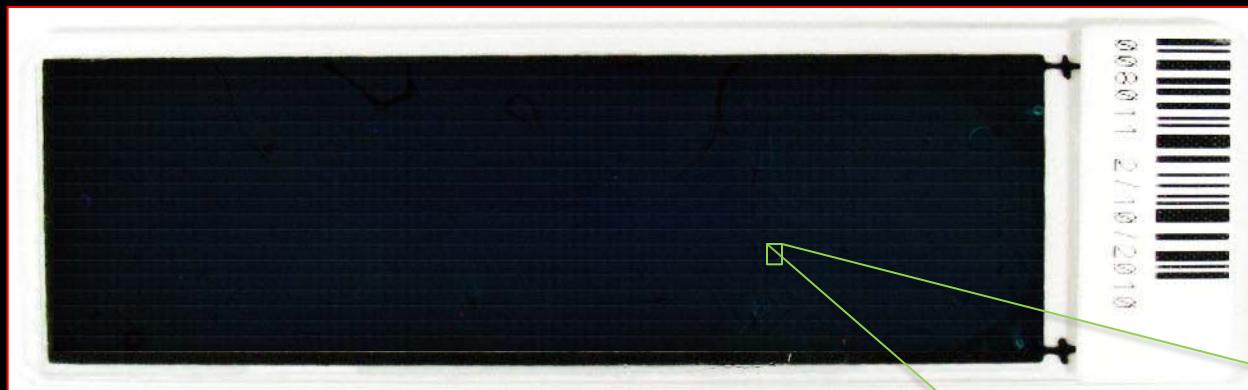
M1



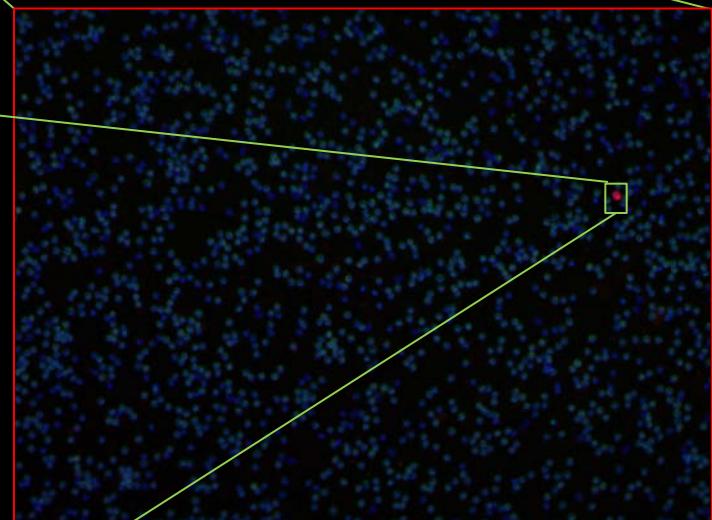
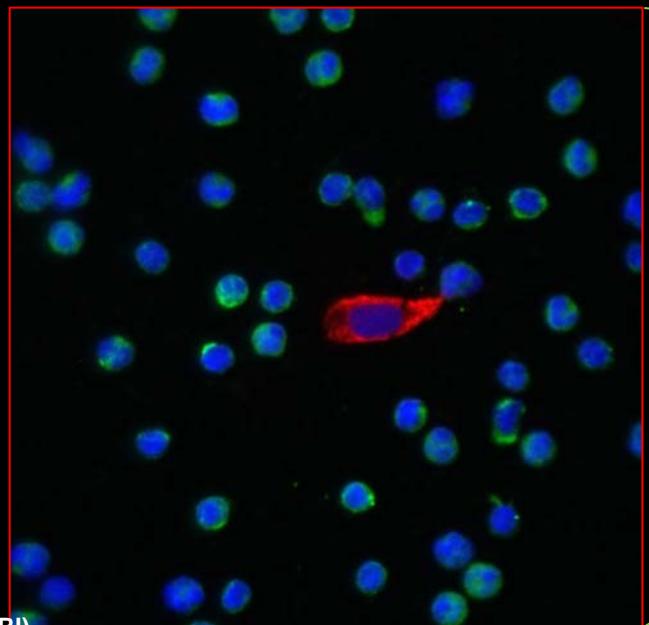
Distant metastasis (M)§

| | |
|----|-----------------------|
| M0 | No distant metastasis |
| M1 | Distant metastasis |

Finding Rare Events: Circulating Tumor Cells from Blood on Glass Slides



~3 Million Cells
9216 images/slides
25GB/slide
4 slides/test
200 TB of data/year



Scripps PSOC Clinical Studies

LUNG:

- **PSOC0043** (UCSD, Billings)
- **PSOC0044** (Scripps Clinic, UCSD, Billings)
- **PSOC0046** (UCSD)
- **PSOC0047** (NKI, UCSD, Billings)
- **PSOC0048** (NKI, Amsterdam)
- **PSOC0049** (Stanford, USC)
- **PSOC0064** (UCSD)
- **PSOC0065** (UCSD)

LIVER:

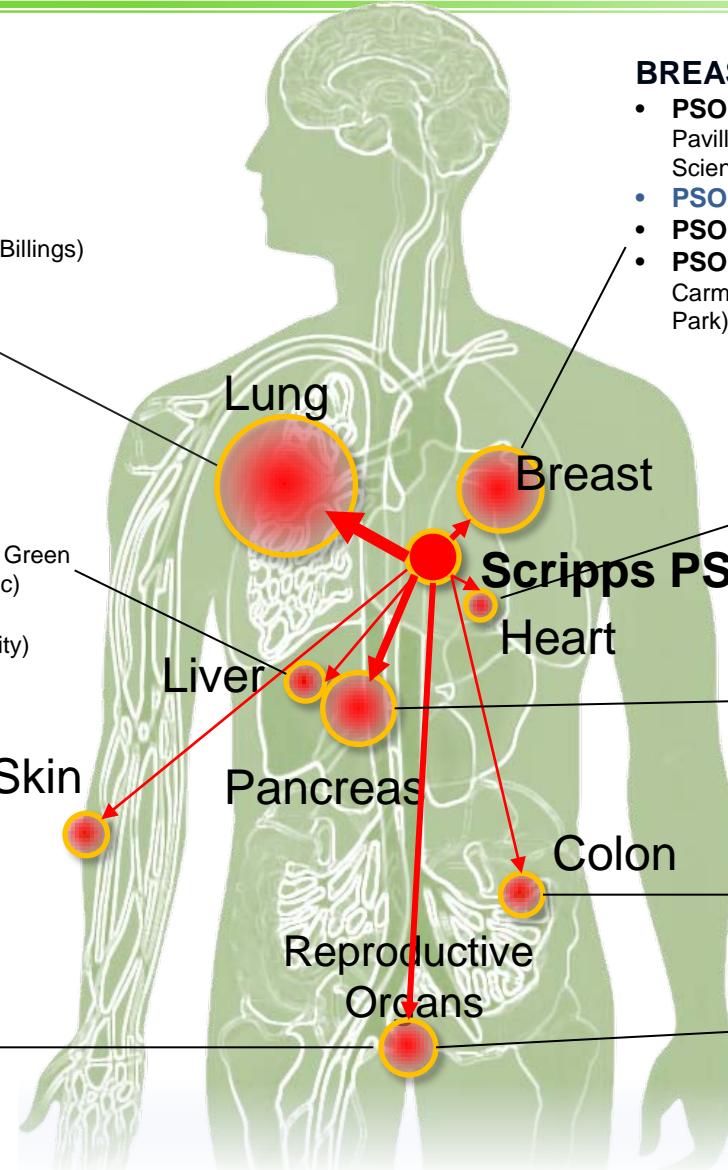
- **PSOC0050** (Scripps Green Hospital, Scripps Clinic)
- **PSOC0055** (UCSF, Northwestern University)

SKIN:

- **PSOC0056** (Pacific Oncology and Hematology)
- **PSOC0061** (Nevada Cancer Center)

PROSTATE:

- **PSOC0045** (Scripps Clinic: Anderson Outpatient Pavilion, Carmel Valley, Rancho Bernardo, Torrey Pines Science Park)
- **PSOC0051** (USC)
- **PSOC0058** (USC)
- **PSOC0060** (Scripps Health)
- **PSOC0063** (NorthShore)



BREAST:

- **PSOC0045** (Scripps Clinic: Anderson Outpatient Pavilion, Carmel Valley, Rancho Bernardo, Torrey Pines Science Park)
- **PSOC0053** (Duke University)
- **PSOC0060** (Scripps Health)
- **PSOC0062** (Scripps Clinic: Anderson Outpatient Pavilion, Carmel Valley, Rancho Bernardo, Torrey Pines Science Park)

HEART:

- **PSOC0057** (Scripps Health)

PANCREAS:

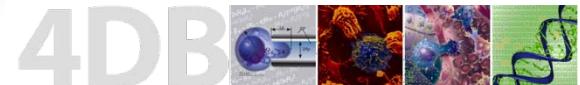
- **PSOC0045** (Scripps Clinic: Anderson Outpatient Pavilion, Carmel Valley, Rancho Bernardo, Torrey Pines Science Park)
- **PSOC0054** (UCSF)
- **PSOC0059** (Scripps Green Hospital)
- **PSOC0060** (Scripps Health)

COLON:

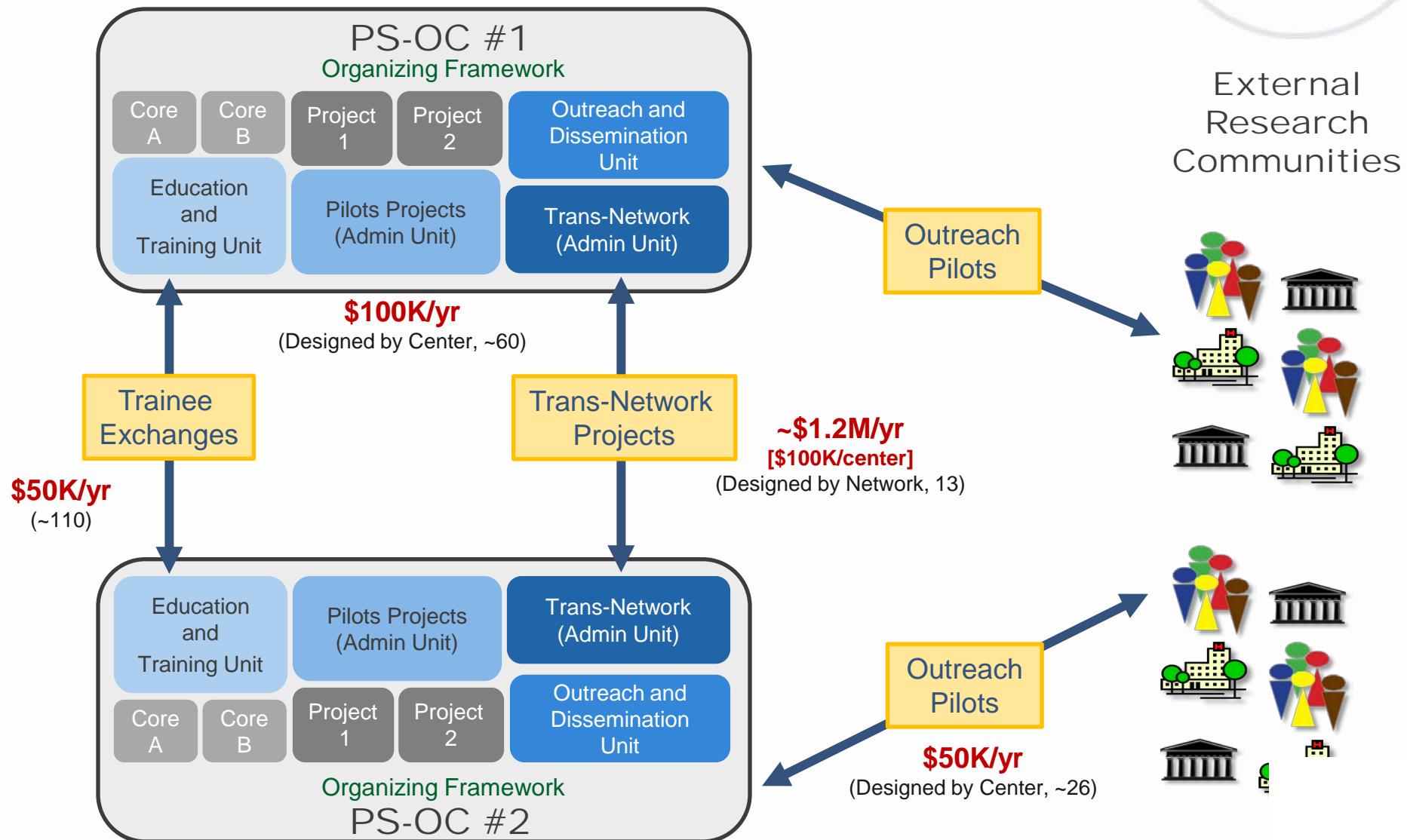
- **PSOC0066** (Scripps Clinic)

OVARIAN:

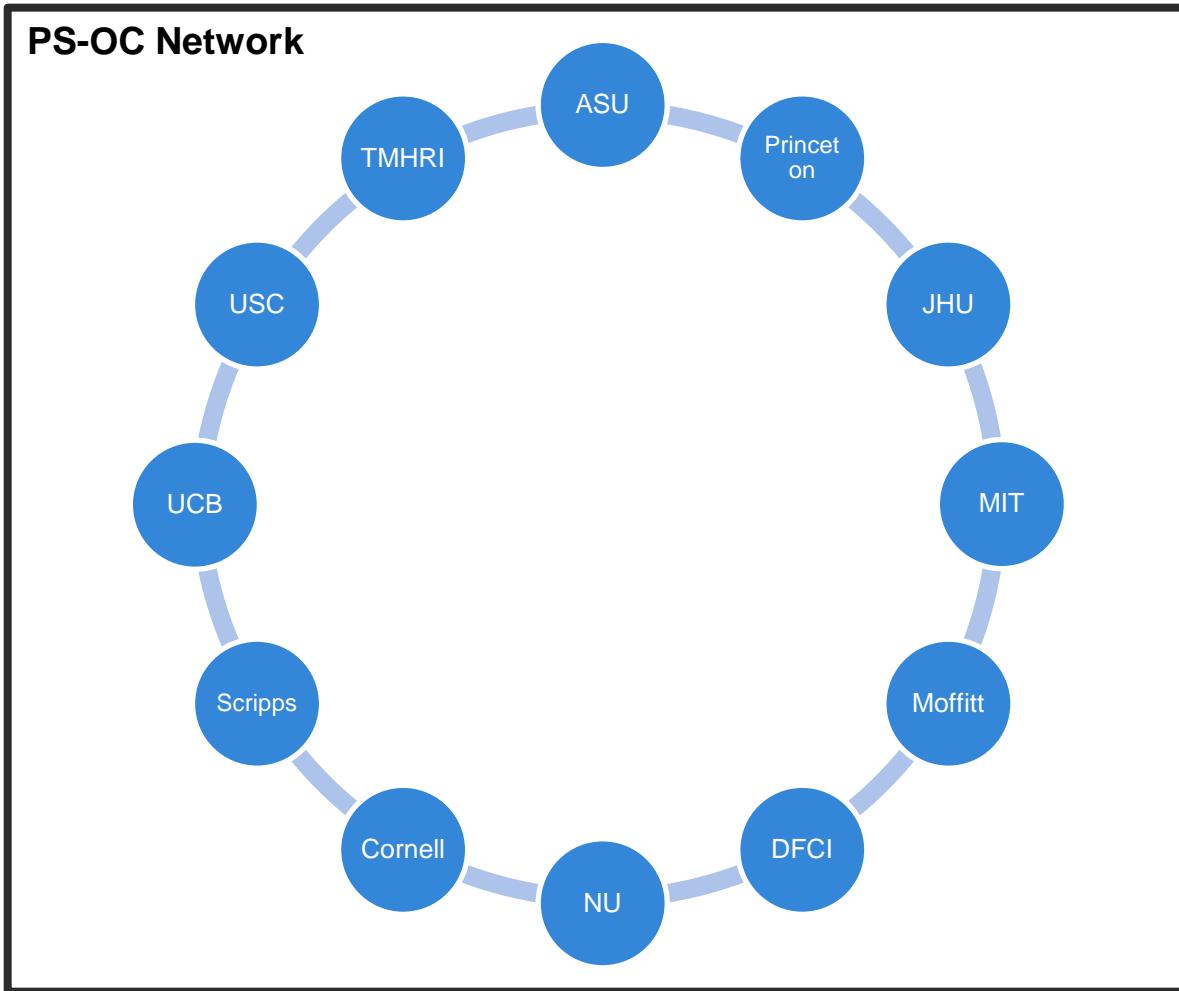
- **PSOC0052** (Scripps Memorial Hospital, South Coast Gynecologic Oncology)

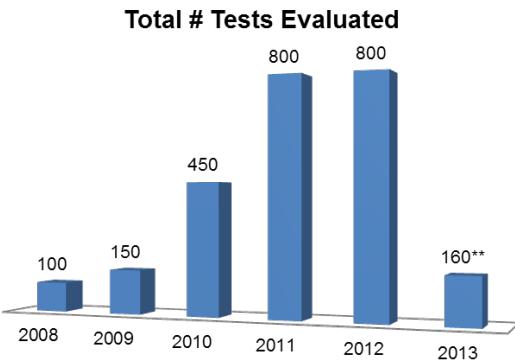


PS-OC Model: PI Driven Interactions Inside/Outside of Network/Center



Transition and Spread of Future “Physical Science-Oncologists”





- Global clinical sites: 26
- Patients enrolled: 2,000
- Patients samples: 5,000
- Observational studies: 19



we find it, we fight it!

The Kuhn Lab at Scripps Research • <http://kuhn.scripps.edu>



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



A Member of the Roche Group

Then...(2002)



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



200+

~100

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

Lawrence¹⁸, Michael O'Kelly¹⁹, J. Robinson²⁰, Gabriele Alexie¹⁸, Ramen Beroukhim²⁰, Scott Carter²¹, Derek Chang²², Jon Gould²³, Supriya Gupta¹⁹, José Kom²⁴, Craig Merrell²², Jill Mesirov²⁵, Stéphane Monj²⁶, Huy Nguyen²⁶, Melissa Parkin²⁷, Michael Reich²⁸, Nicolas Strancky²⁹, Barbara A. Well^{22,23}, Levi Garraway^{22,23}, Todd Golub^{23,28}, Matthew Meyerson^{22,23}, **Harvard Medical School/Dana-Farber Cancer Institute** Lydia Chin^{23,24}, Alexei Protopopov²⁴, Jianhua Zhang¹, Liana Perna², Sandy Aronson¹, Narayanan Sathiamoorthy²⁶, Georgia Ren¹, Jun Yao²⁴, W. Ruprecht Wiedenmeyer¹, Hyunsoo Kim²⁴, Sek Won Kang²⁴, Daniel Kornblith²⁴, Isaac S. Kohl²⁴, Daniel G. Meltzer²⁴, Daniel P. Poff²⁴, Jennifer R. Pomeroy²⁴, John Hwang¹, University of Southern California Stephen W. Lane²⁴, Leslie Cole²⁴, George H. Gershenson²⁴, David J. Wiesenerger¹, Fei Fan¹, David Van Den Berg¹, Leander Van Neste¹, Jon M. Yiz¹⁸, Korrel E. Schanbel¹, Stephen B. Baylin¹, **HudsonAlpha Institute** University Design M. Absher¹⁶, Jun Zhu¹⁶, Audrey Southwest¹, Brannon Sharp¹, Amita Agarwalla¹⁶, Tisha Chung¹⁷, Gavin Shero¹⁷, James D. Brooks¹⁸, Richard M. Myers¹⁹, **Lawrence Berkeley National Laboratory** Paul T. Spellman²⁰, Elizabeth Purdon²⁰, Lakshmi R. Jakkula²⁰, Anna V. Lupu²³, Henry Man²³, Shannon Doerton²³, Yoon Gi Choi²³, Ju Han²³, Amitra Ray²³, Victoria Wang²³, Steven Durnak²³, Mark Robinson²³, Nicholas J. Wang²³, Karen Wanzen²³, Vivian Peng²³, Eric Van Name²³, Gerald F. Vorster²³, John Ngal²³, John G. Corboy²³, Barbara Parvin²³, Heidi S. Feier²³, Terence P. Speed²³, Joe W. Gray²³, **Memorial Sloan-Kettering Cancer Center** Cammenga Brennan²⁴, Nicholas D. Socci²⁴, Adam Olshan²⁴, Barry S. Taylor²⁴, Alexandru Schulz²⁴, Ethan Cerami²⁴, Reva Yesayan Antipin²⁴, Alexey Stekulav²⁴, Alex Benjamin Gross²⁴, Ethan Cerami²⁴, Wei Qin Gao²⁴, Li-Xuan Qin²⁴, Venkataraman E. Seshan²⁴, Liliana Villanueva²⁴, Magali Cavatorta²⁴, Laetitia Borsig²⁴, Agnes Vilchez²⁴, William Gerald²⁴, Chris Sander²⁴, Marc Ladanyi²⁴, **University of North Carolina**, Chapel Hill Charles M. Perou²⁴, David Nell Hayes²⁴, Michael D. Tepko²⁴, Katherine A. Hoadley²⁴, Yuan Qiu²⁴, Zhenyu Li²⁴, Yan

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 Network²

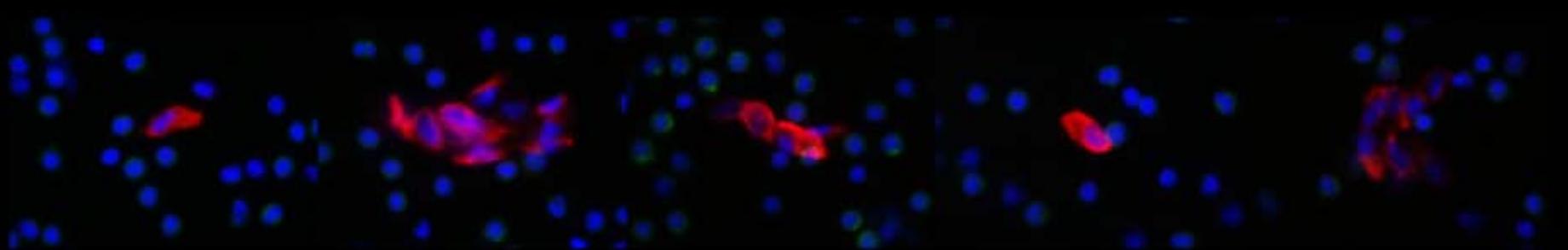
2008

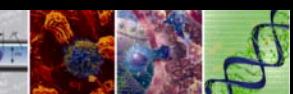
2010

2012

2014

Identify CTC Candidates by Orthogonal Analytics

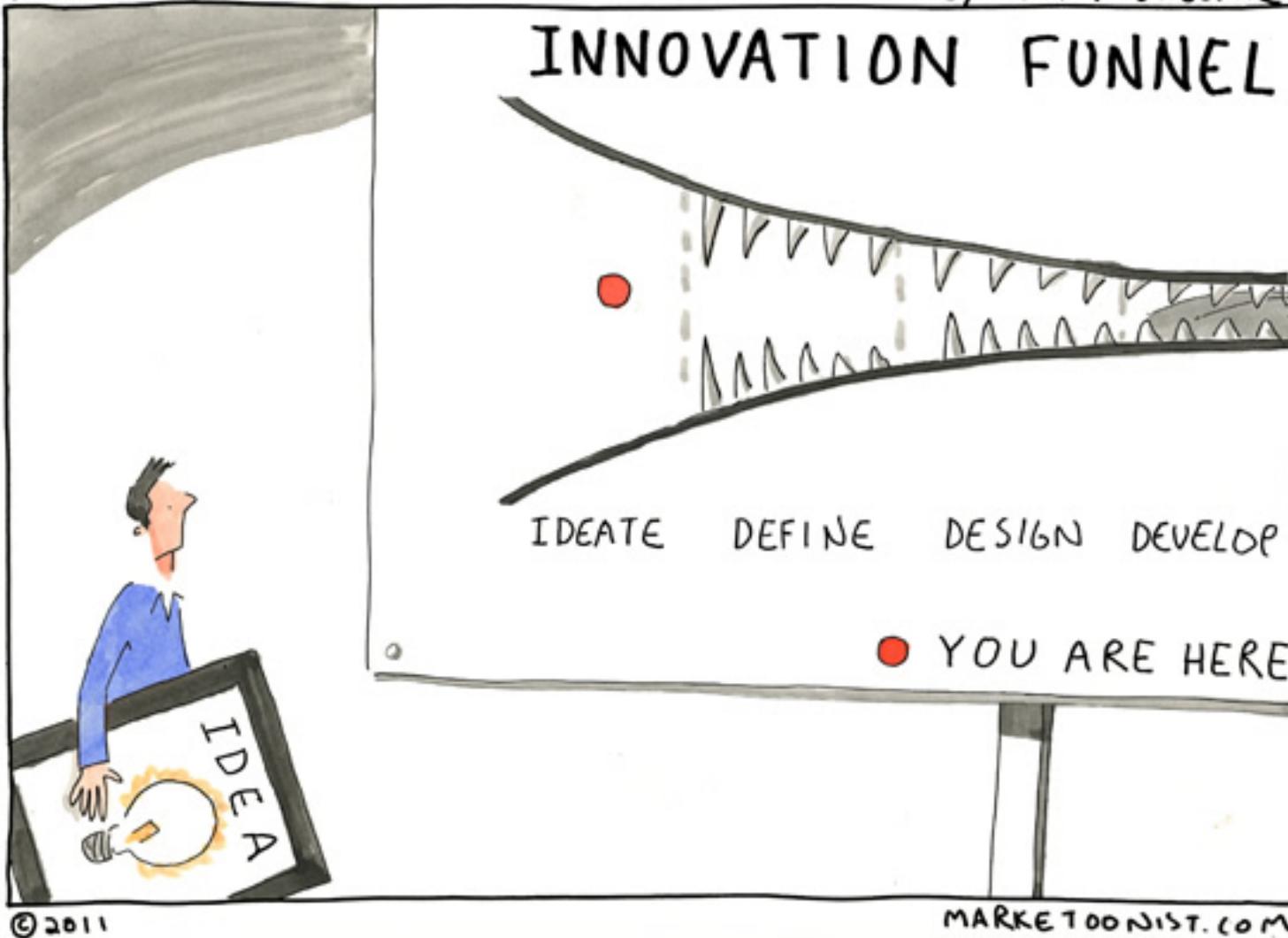


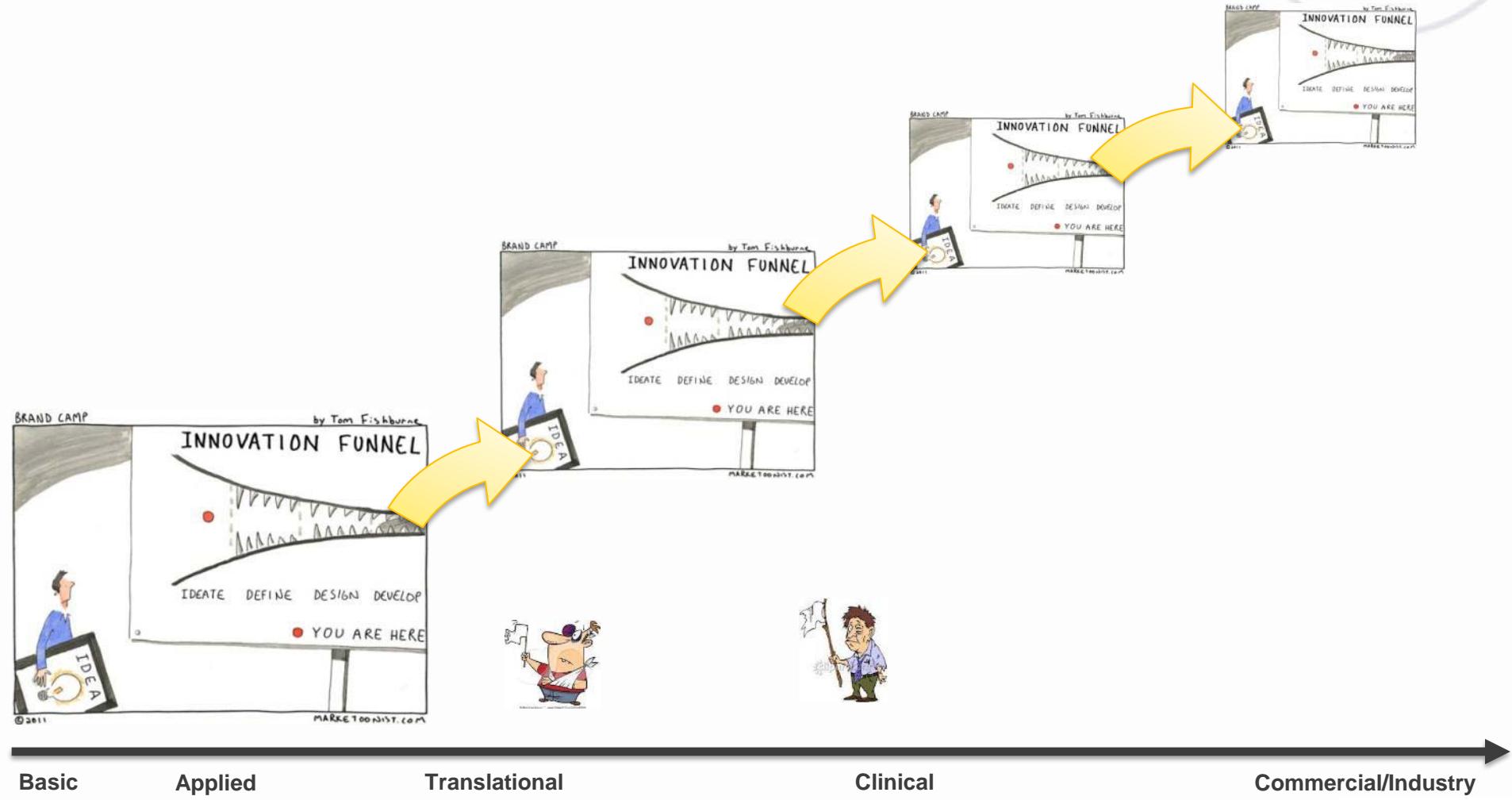
4DB 

BRAND CAMP

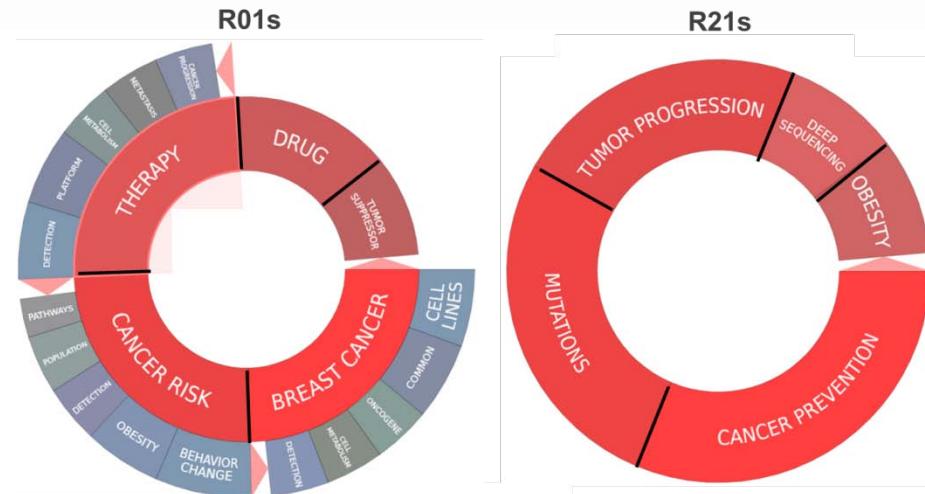
by Tom Fishburne

INNOVATION FUNNEL

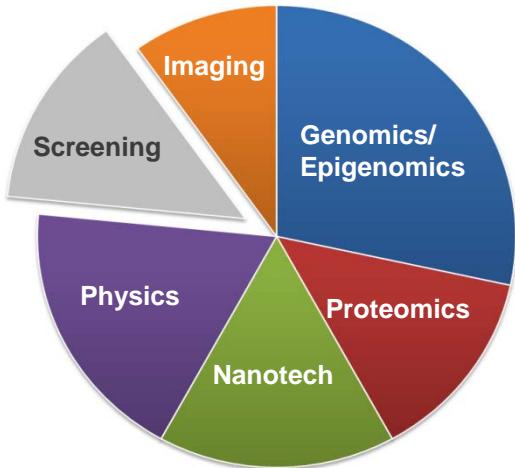




Join the Team! Upcoming Funding Opportunities



Data from projectreporter.nih.gov



98 active projects at the end of 2011

Provocative Questions (\$30M)



Due Date 06/20/13

PQ Program Director
emily.greenspan@nih.gov

Innovative Molecular Analysis Technologies (\$10.5M)



Due Dates 05/20 and 9/20/13

IMAT Program Director
anthony.dickherber@nih.gov



NCI CSSI: Major Programs and Public Resources



Office of the Director



Director
Douglas R. Lowy, MD



Deputy Director
Jerry S.H. Lee, PhD

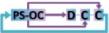


Provocative Questions Initiative

Office of Physical Sciences-Oncology (OPS-O)



Director
Larry A. Nagahara, PhD



Office of Cancer Nanotechnology Research (OCNR)



Director
Piotr Grodzinski, PhD



Office of Cancer Clinical Proteomics Research (OCCPR)



Director
Henry Rodriguez, PhD, MBA



Learn More About Us...



<http://cssi.cancer.gov>



The screenshot shows the homepage of the Center for Strategic Scientific Initiatives (CSSI). At the top, there is a red header bar with the National Cancer Institute logo and the text "National Cancer Institute" and "U.S. National Institutes of Health | www.cancer.gov". Below the header, the CSSI logo is displayed, followed by a navigation menu with links to "HOME", "ABOUT CSSI", "CSSI OFFICES", and "CONTACT CSSI". The main content area features a dark background with a colorful molecular structure graphic on the right. On the left, the text "ENABLING PROGRESS IN CANCER RESEARCH THROUGH ADVANCED TECHNOLOGIES, TRANS-DISCIPLINARY PROGRAMS AND RESOURCES" is displayed, along with a "LEARN MORE" button. At the bottom, there are links to "NCI Home", "CSSI Home", "Contact Us", "Policies", and "Access". A "A Service of the National Cancer Institute" note is also present, along with the NCI and USA logos. A large, semi-transparent overlay window titled "Timeline:" is overlaid on the page. This window contains a circular timeline visualization where each circle represents an event or office. The interface includes dropdown menus for selecting offices ("View All", "OD CSSI", "OIBR", "TOGA", "OCG", "OCCPR", "OCNR", "OIPSO") and zoom levels ("1 Year", "3 Years", "All Years"). A horizontal timeline at the bottom shows the years from 2000 to 2012.

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