
# Advancing Innovation and Convergence In Cancer Research

**Jerry S.H. Lee, Ph.D.**

**Health Sciences Director**

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

Georgia Tech Parker H. Petit Institute for Bioengineering & Bioscience

**Petit Institute Seminar**

**March 20, 2014**

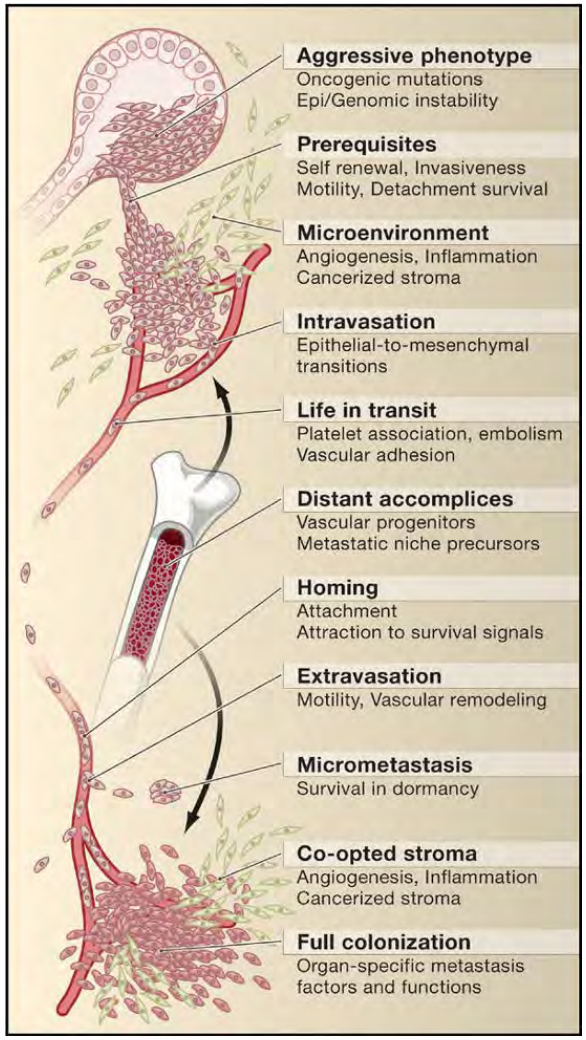
CLINICAL PROTEOMIC TUMOR ANALYSIS CONSORTIUM

NCI Alliance for Nanotechnology in Cancer

IMAT INNOVATIVE MOLECULAR ANALYSIS TECHNOLOGIES

Provocative Questions Initiative

# What is It?
# Tumor, Cancer, and Metastasis



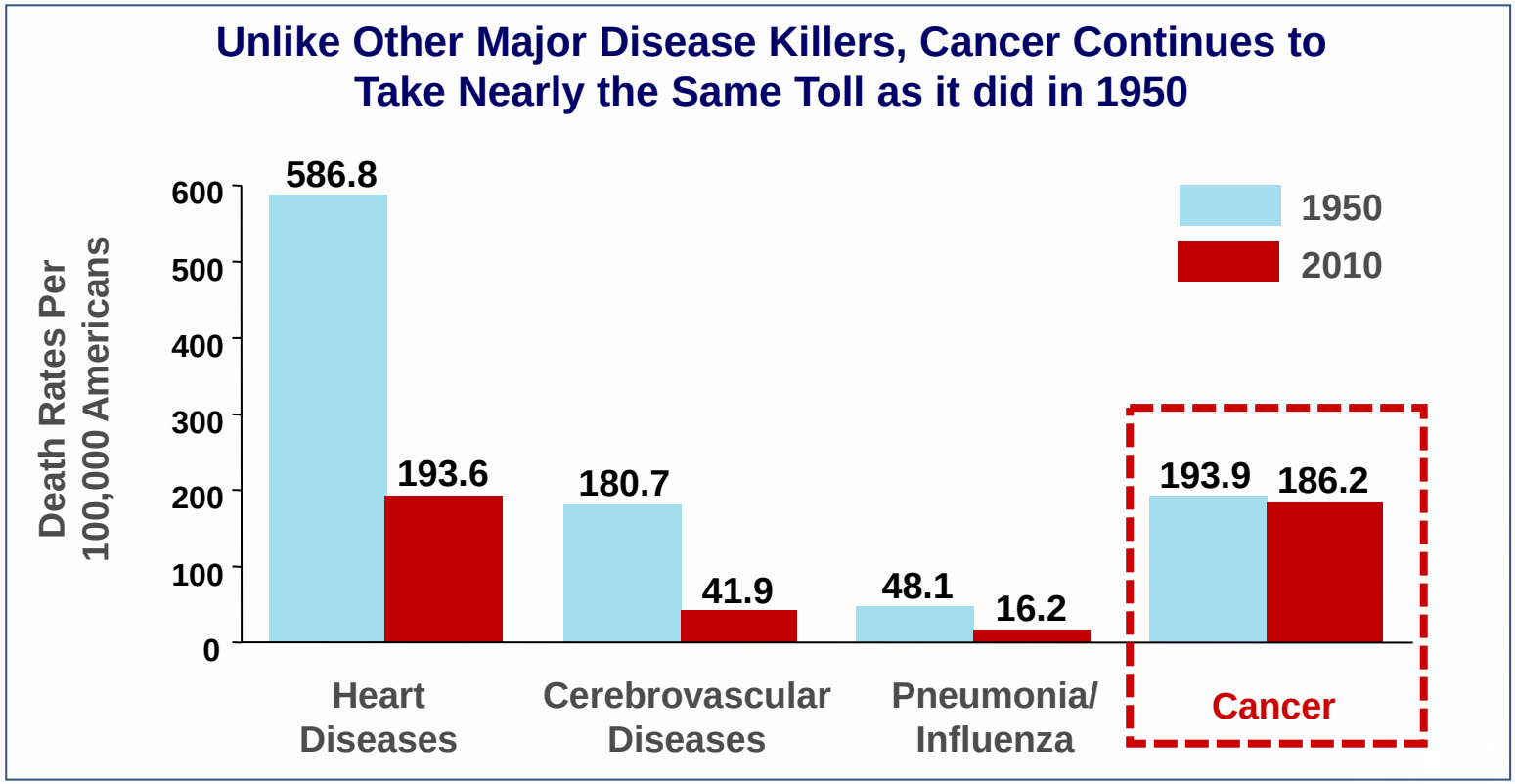

| Organ Site | All Stages | Localized | Regional | Distant |
|---|---|---|---|---|
| Prostate | 99 | **100** | 100 | **28** |
| Breast | 89 | **99** | 84 | **24** |
| Ovary | 44 | **92** | 72 | **27** |
| Uterine Cervix | 68 | **91** | 57 | **16** |
| Melanoma | 91 | **98** | 62 | **16** |
| Urinary Bladder | 78 | **70** | 33 | **5** |
| Kidney | 72 | **92** | 64 | **12** |
| Colon and rectum | 65 | **90** | 70 | **13** |
| Esophagus | 17 | **39** | 21 | **4** |
| Lung and bronchus | 17 | **54** | 26 | **4** |
| Liver | 16 | **29** | 10 | **3** |
| Pancreas | 6 | **24** | 9 | **2** |

***"…>90% of deaths is caused by disseminated disease or metastasis…***

Gupta et. al., *Cell,* 2006 and Siegel et. al. *CA Cancer J Clin*, Feb 2014

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

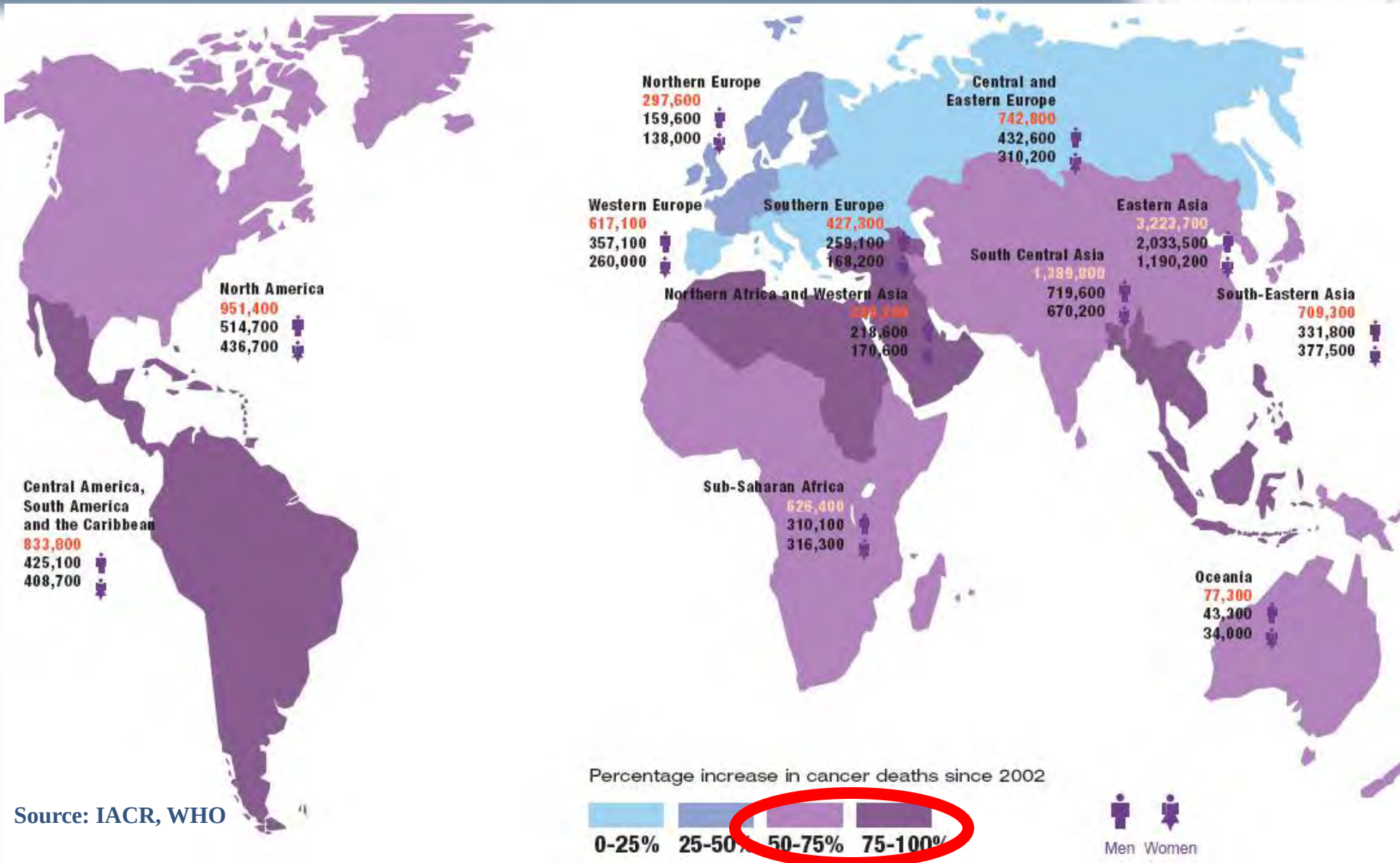
- **574,743** Americans died of cancer in 2010 (**585,720** projected for 2013)
- **1,665,540** Americans will be newly diagnosed with cancer in 2014 (projected)
- **$216.6 billion** in 2009 for cancer healthcare costs (**$86.6 billion** for direct medical)




Source for 2014 projected deaths and diagnoses: Siegel et. al, Cancer Statistics, 2014
Source for 2010 age-adjusted death rate: National Center for Health Statistics, National Vital Statistics Report, Dec 2013

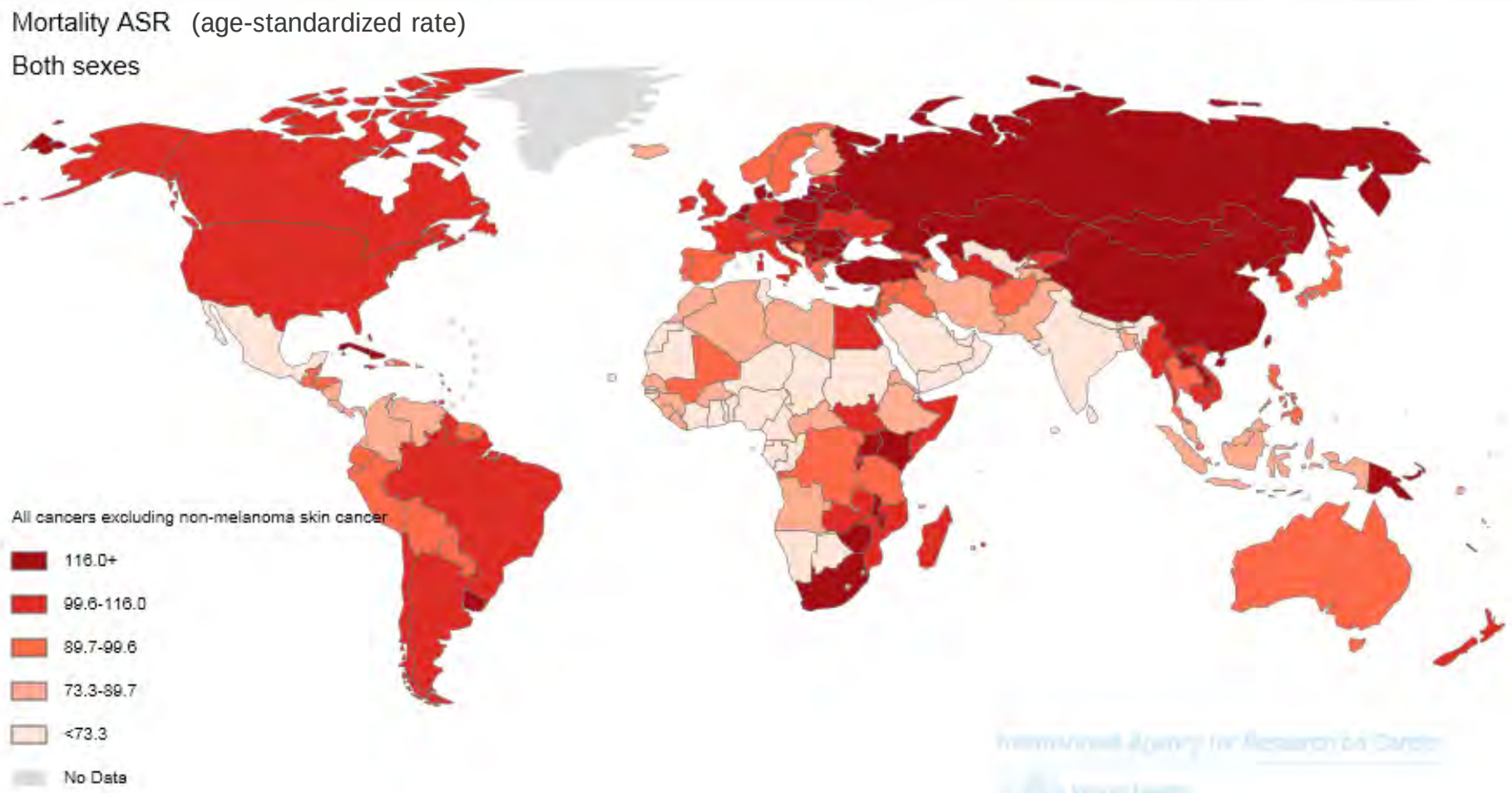
# Global Burden: By 2020, Cancer Incidence 16 M/yr (Mortality 10 M/yr)






Source: IACR, WHO

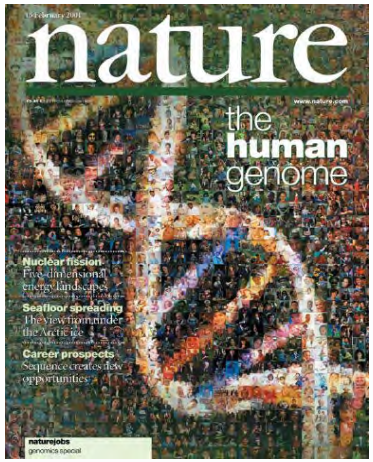
# GLOBOCAN 2012: In 2012, Cancer Incidence 14.1 M (Mortality 8.2 M)




Source: GLOBOCAN 2012 (IARC)

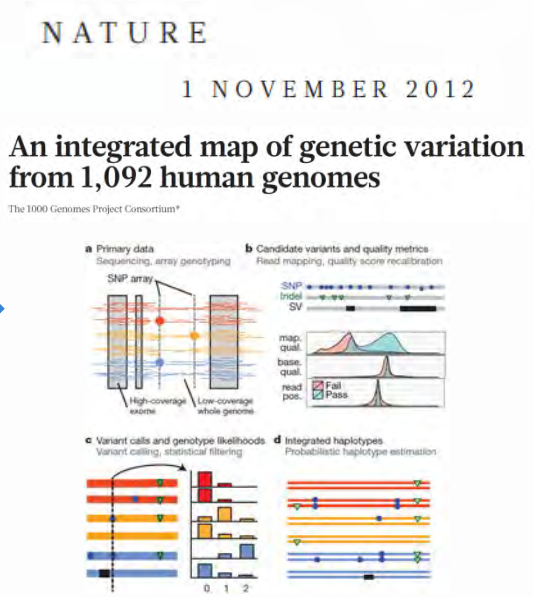
# Unprecedented Amount of Scientific Knowledge: Omics(ssss)

CENTER for STRATEGIC SCIENTIFIC INITIATIVES




2001


2010




2012

1923 — 2005 — 2012

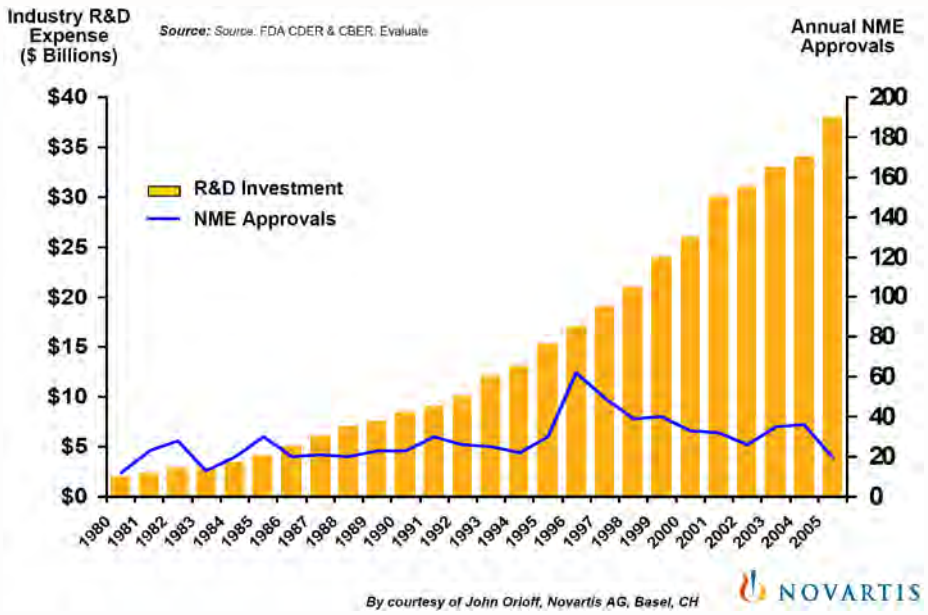
49,024 pubs | 54,587 pubs | **87,793** pubs | **38,506** pubs

ISI search for genomics, proteomics, transcriptomics, metabolomics, phenomics, interactomics, glycomics

# Is More Knowledge Yielding More Solutions for Patients?

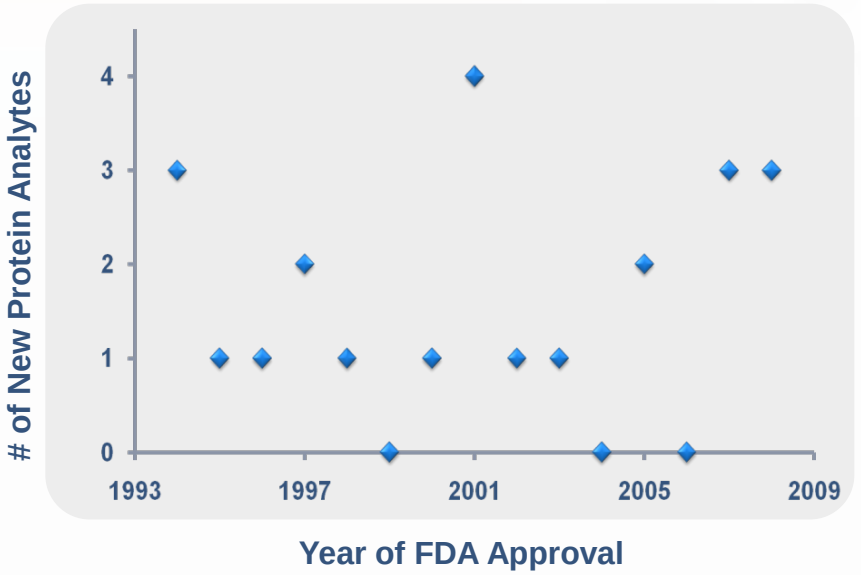
CENTER for STRATEGIC SCIENTIFIC INITIATIVES

## Drug Discovery and Development




- 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]

## Diagnostic Biomarkers

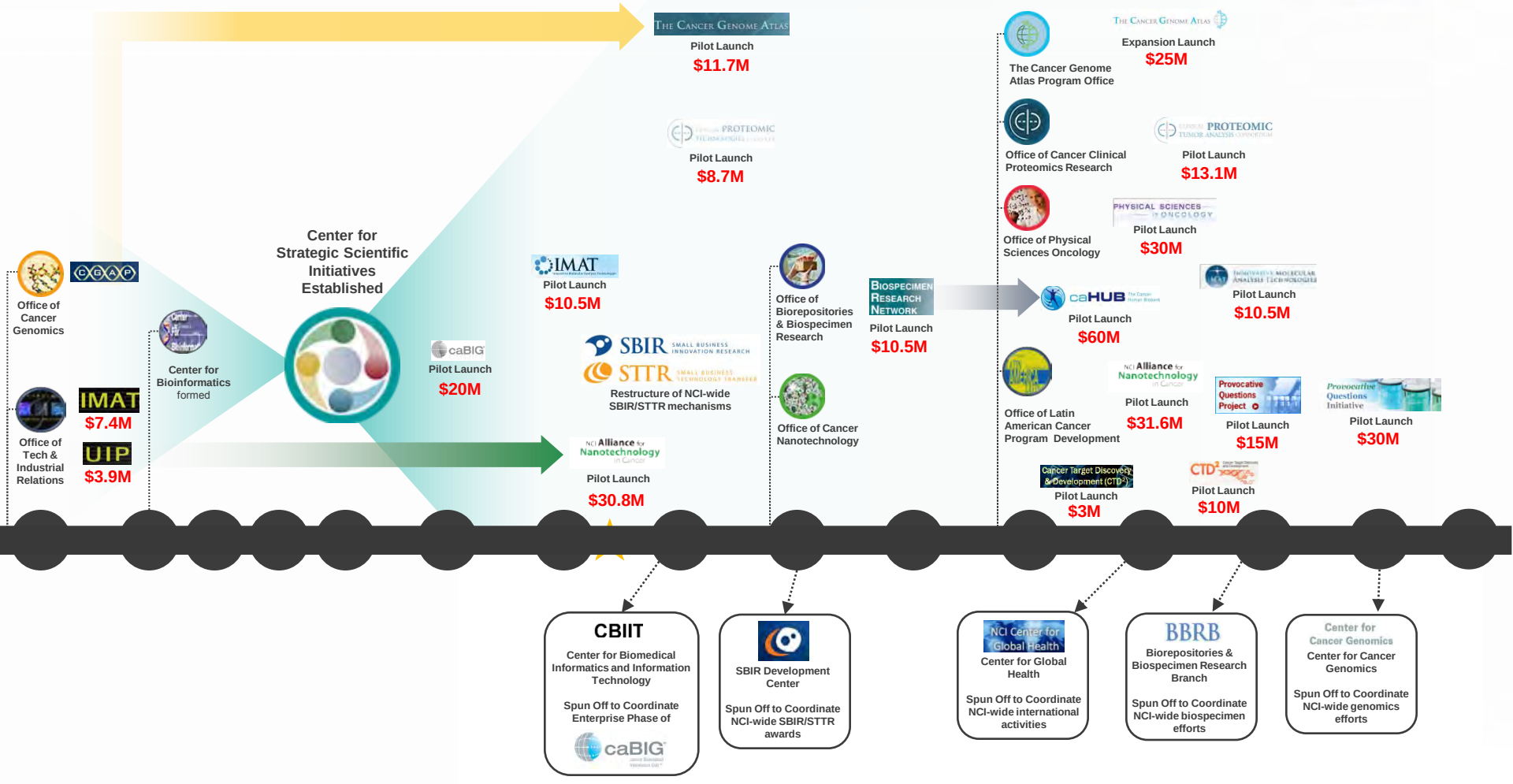



- Averaging 1.5 FDA approvals per year†
- 1000's of samples
- Balancing complexity of biology against heterogeneity of patients

***Maybe…but can it be more efficient?***

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

# NCI Center for Strategic Scientific Initiatives (FY99 – FY13)




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

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


NHGRI NIA NIDA NINDS NIDCD NIMH

NEI NIAAA CIT NINR NLM NIDDK

FIC CSR NIBIB NIMHD NIDCR NIEHS

NIGMS NICHD CC

NIAMS NCCAM NIAID NCI NHLBI NCATS

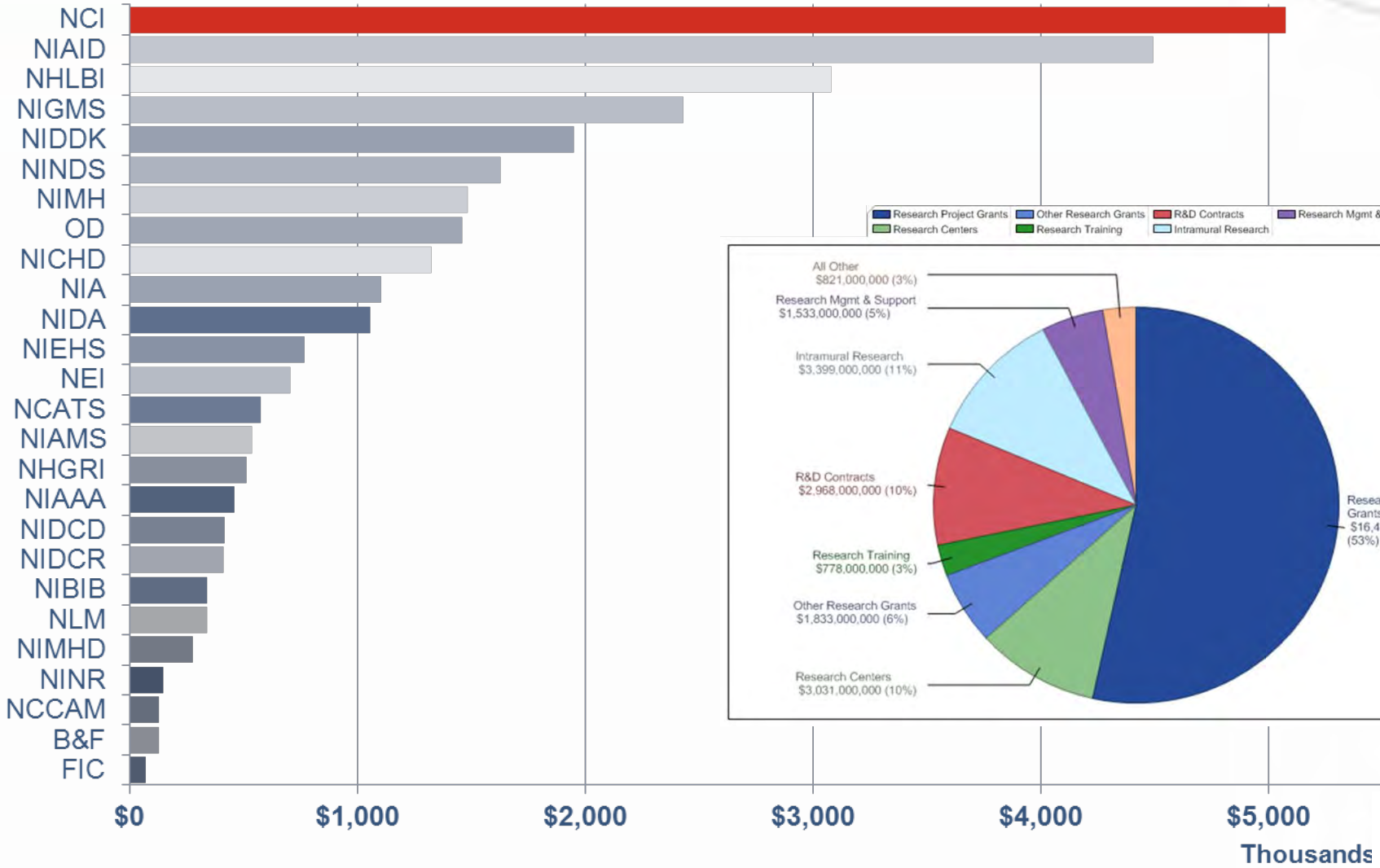
***NIH Budget ~ $30.8 Billion (FY12)***

- ***~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 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: Types of Funding Announcements (FOAs)

Center for Strategic Scientific Initiatives

http://grants.nih.gov/grants/planning_application.htm


**~575 in FY12**

## Parent Announcements

- Non-specific, **investigator-initiated "unsolicited" research**
- May submit **any topic** within the breadth of the NIH mission.
- **No money set-aside**
- Competition tied mainly to an **IC's overall payline**

**~53% NIH-wide**
**~47% NCI-only**

## IC-Specific Program Announcements (PA)

- Often broadly defined or a **reminder of a scientific need**
- Investigator-initiated **"unsolicited" research**
- **No money set asides (unless PAS)**
- Competition tied mainly to the **IC's overall payline**
- **High-priority** applications may be **funded beyond the payline**

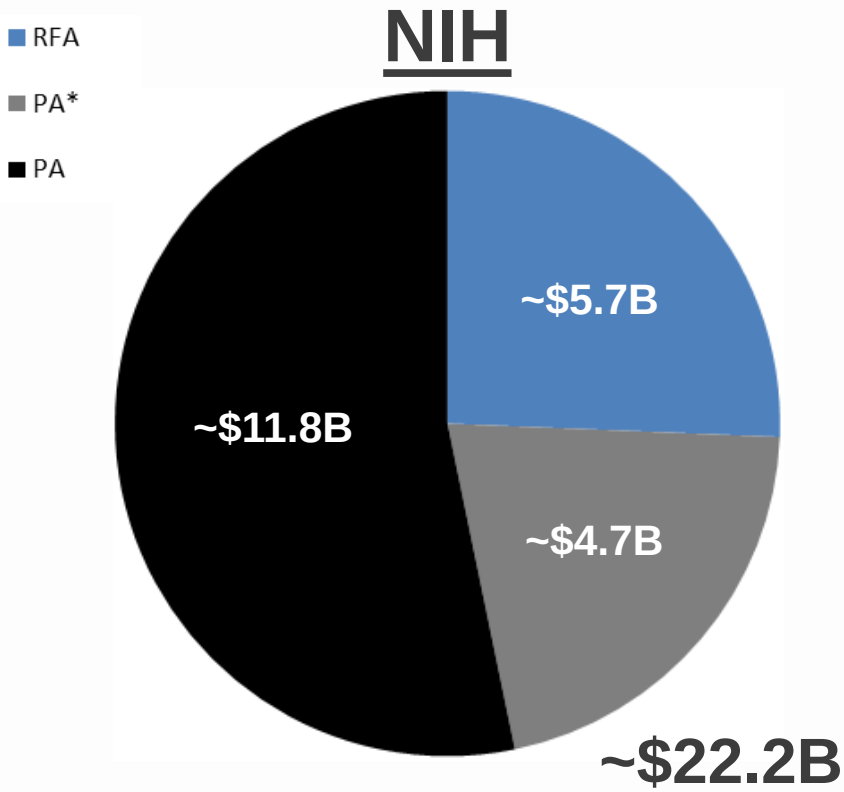
**~21% NIH-wide**
**~34% NCI-only**

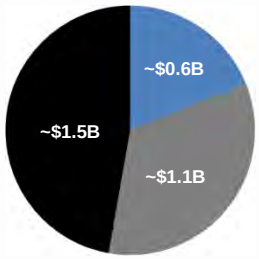
## Requests for Applications (RFA)

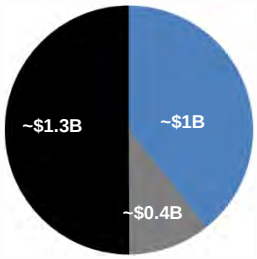
- **NIH-Requested Research**; Well-defined scientific area
- **Specifies funds** and targets **number of awards**
- Competition depends on **number of applicants** and **dollars set aside**

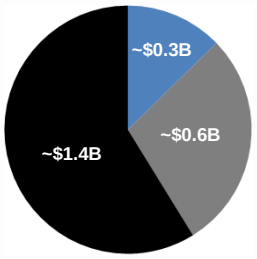
**~26% NIH-wide**
**~19% NCI-only**

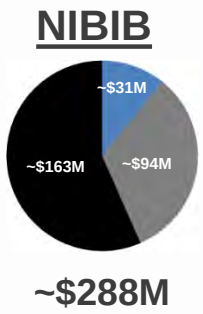
# NIH Research Portfolio Online Reporting Tools (RePORT)

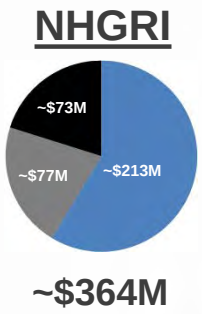



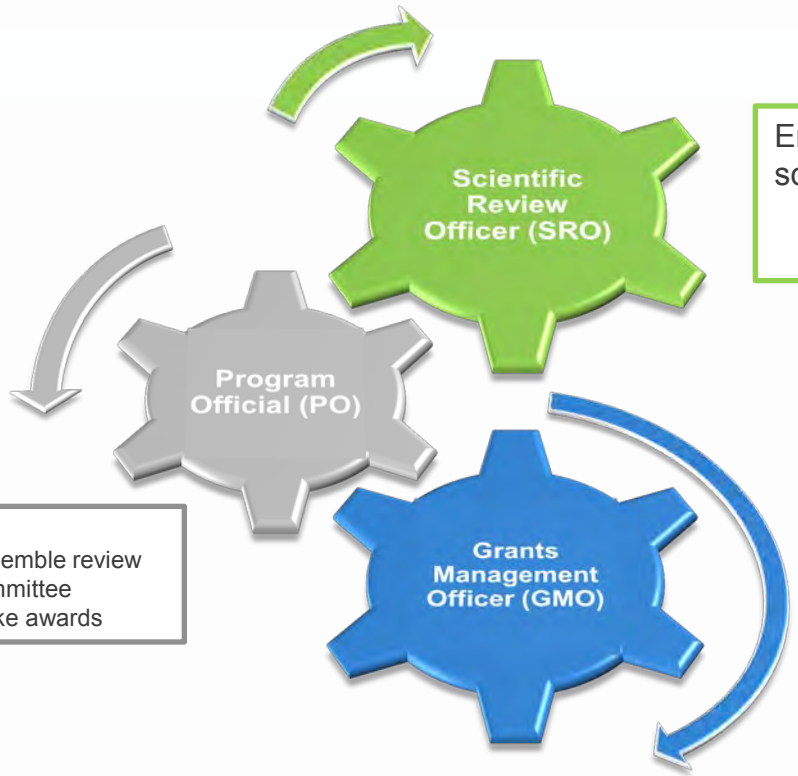




FY12 grants data from http://projectreporter.nih.gov

# The NIH Extramural Team: Checks & Balances




Ensure **fair** and **unbiased** evaluation of the scientific and technical merit of proposed research

- Manages study sections
- Prepares/issues summary statements

**Does not**

- Assemble review committee
- Make awards

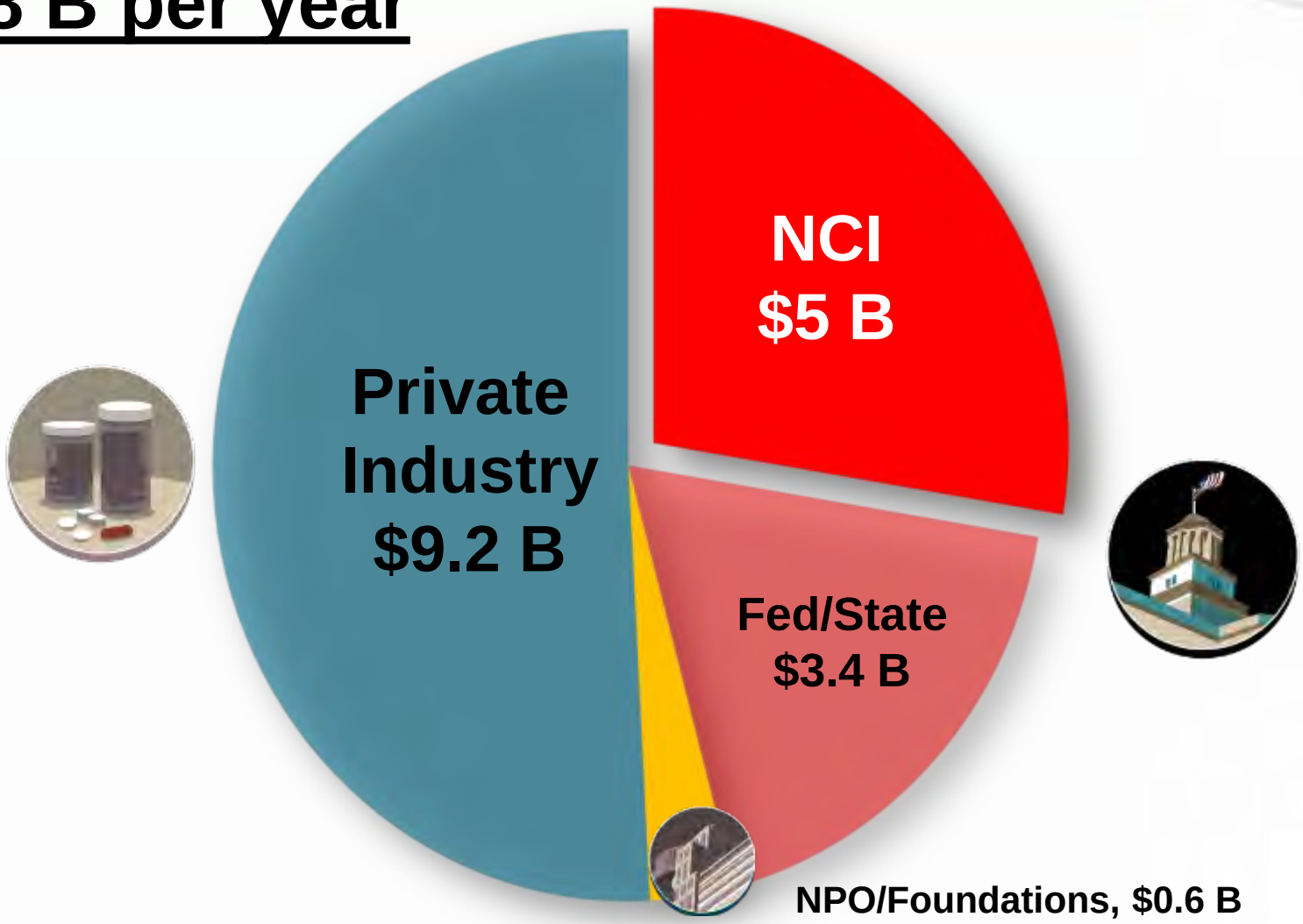
Ensure all required business management actions are performed by the grantee and federal government

- Participates in budget negotiations
- Prepares/issues **Notice of Awards (NoA)**

# National Cancer Program: Stakeholders



## ~$18 B per year




NCAB Working Group Report, 2010

# 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's Federally Funded Research and Development Center (FFRDC)

Center for Strategic Scientific Initiatives

operated by
Leidos Biomedical Research, Inc.
**Frederick National Laboratory** for Cancer Research

**Established in 1972** as one of the nation's **39** FFRDC's and the **only one devoted exclusively to biomedical research and development**

## Facts

As one of Frederick County's major employers, the contractor Leidos Biomedical Research Inc. employs approximately 1,800 employees.

### Economic Impact

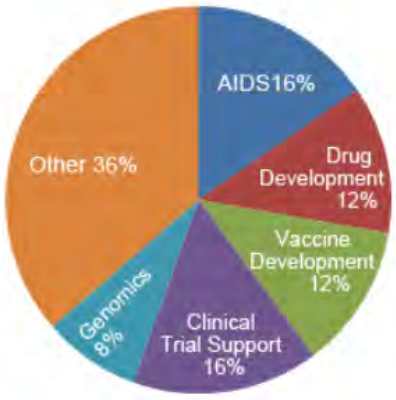
In addition to payroll, Leidos Biomedical Research contributes:

- Dollars spent via Leidos Biomedical Research (formerly SAIC-Frederick) purchase orders, Contract Year 2011
  - Frederick County...$16,820,351
  - Maryland.....$183,086,783
- Dollars spent via Leidos Biomedical Research (formerly SAIC-Frederick) purchase orders, 9/26/08–8/10/11
  - Frederick County...$35,695,585
  - Maryland.....$286,944,880

### Physical

- 68 acres deeded to the Department of Health and Human Services (HHS)
- 991,217 net square feet
- 1,654,035 gross square feet
- 113 buildings on site

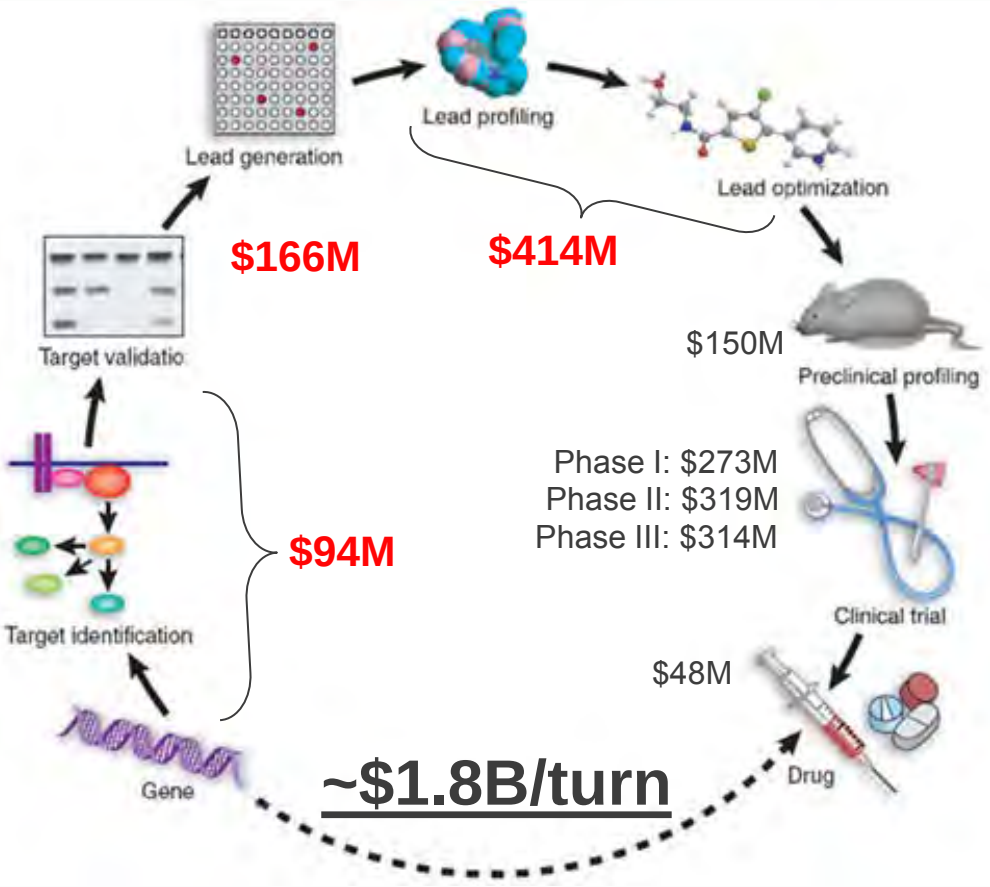
### Frederick National Lab Distribution of Effort




**NCI Funding in FY12 $238,204**

http://frederick.cancer.gov/About/Facts.aspx

# 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**

Paul et. al, *Nature Rev. Drug Discovery*, March 2010

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

**Director**
Douglas Lowy, MD

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

**~$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**…"

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**

# 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** **Industry**

# CSSI Programs (FY99-FY14): Diverse Mechanisms

Center for Strategic Scientific Initiatives

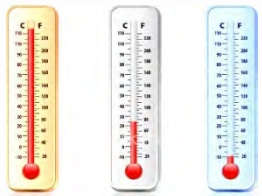
| Program | Grants | | Cooperative Agreements | Contracts | FFRDC | | Interagency Collaborations (Co-funds/joint programs) |
|---|---|---|---|---|---|---|---|
| | Research | Training | | | Resource | R&D Subs | |
| Unconventional Innovations Program | | | | ✓ | | | |
| Innovative Molecular Analysis Technologies | ✓ | ✓ | | | | | |
| 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 | ✓ | | | | | | |

# Center Framework: "What is Water?"- Measurements → Insights

Color (clear, yellow, brown)
Taste (none, metallic, awful)

Phase (liquid, gas, solid)
Phase change (boil, melt, freeze)

***Qualitative Descriptions***

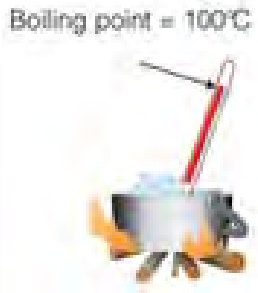


***Measurements Taken***

| Pressure (kg/cm²) | Temp (°C) | Saturated steam: Vapour enthalpy (kcal/kg) | Saturated steam: Specific volume (m³/kg) | Saturated steam: Density (kg/m³) | Superheated steam: Specific volume (m³/kg) at 250°C | Superheated steam: Specific volume (m³/kg) at 300°C |
|---|---|---|---|---|---|---|
| 1 | 99,1 | 638,8 | 1,725 | 0,580 | 2,454 | 2,691 |
| 2 | 119,6 | 646,2 | 0,902 | 1,109 | 1,223 | 1,342 |
| 3 | 132,9 | 650,6 | 0,617 | 1,621 | 0,812 | 0,893 |
| 4 | 142,9 | 653,7 | 0,471 | 2,123 | 0,607 | 0,668 |
| 5 | 151,1 | 656,0 | 0,382 | 2,618 | 0,484 | 0,533 |
| 6 | 158,1 | 657,0 | 0,321 | 3,115 | 0,402 | 0,443 |
| 7 | 164,2 | 659,5 | 0,278 | 3,597 | 0,343 | 0,379 |
| 8 | 169,6 | 660,8 | 0,245 | 4,082 | 0,299 | 0,331 |
| 9 | 174,5 | 661,9 | 0,219 | 4,566 | 0,265 | 0,293 |
| 10 | 179,1 | 662,9 | 0,198 | 5,051 | 0,238 | 0,263 |
| 12 | 187,1 | 664,5 | 0,166 | 6,024 | 0,196 | 0,218 |
| 14 | 194,1 | 665,7 | 0,143 | 6,993 | 0,167 | 0,186 |
| 16 | 200,4 | 666,7 | 0,126 | 7,937 | 0,145 | 0,162 |
| 18 | 206,1 | 667,4 | 0,112 | 8,929 | 0,128 | 0,143 |
| 20 | 211,4 | 668,0 | 0,101 | 9,901 | 0,114 | 0,128 |
| 22 | 216,2 | 668,4 | 0,092 | 10,870 | 0,103 | 0,116 |
| 24 | 220,7 | 668,7 | 0,085 | 11,765 | 0,093 | 0,106 |
| 26 | 225,0 | 669,0 | 0,078 | 12,821 | 0,085 | 0,097 |
| 28 | 229,0 | 669,1 | 0,073 | 13,699 | 0,078 | 0,089 |
| 30 | 232,7 | 669,2 | 0,068 | 14,706 | 0,072 | 0,083 |

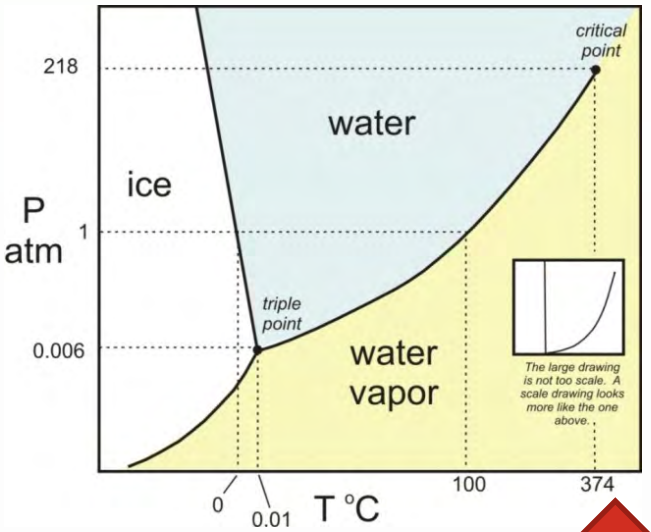
***LOTS of Quantitative "Data"***

***But also LOTS of disagreements…***

# Standards and Sharing of Data → New Insights and Understanding

- Define *samples & protocols*
- ***Share collected data***




**New Understanding**

- **Phase boundaries**
  - V/L equilibrium
- **Triple Point**

**(Phase Diagram)**




**New Parameter**

**"Pressure"**

| Saturated steam | | | | | Superheated steam | |
|---|---|---|---|---|---|---|
| Pressure (kg/cm²) | Temp (°C) | Vapour enthalpy (kcal/kg) | Specific volume (m³/kg) | Density (kg/m³) | Specific volume (m³/kg) at 250°C | at 300°C |
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| 10 | 179,1 | 662,9 | 0,198 | 5,051 | 0,238 | 0,263 |
| 12 | 187,1 | 664,5 | 0,166 | 6,024 | 0,196 | 0,218 |
| 14 | 194,1 | 665,7 | 0,143 | 6,993 | 0,167 | 0,186 |
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| 26 | 225,0 | 669,0 | 0,078 | 12,821 | 0,085 | 0,097 |
| 28 | 229,0 | 669,1 | 0,073 | 13,699 | 0,078 | 0,089 |
| 30 | 232,7 | 669,2 | 0,068 | 14,706 | 0,072 | 0,083 |

**LOTS of Quantitative and Reproducible Data**

**(Steam Table)**

# 2003 Launch of the Technology Dashboard of CSSI: IMAT

Center for Strategic Scientific Initiatives

INNOVATIVE MOLECULAR ANALYSIS TECHNOLOGIES

*To support the **development**, **maturation**, and dissemination of **innovative and/or potentially transformative** next-generation technologies*

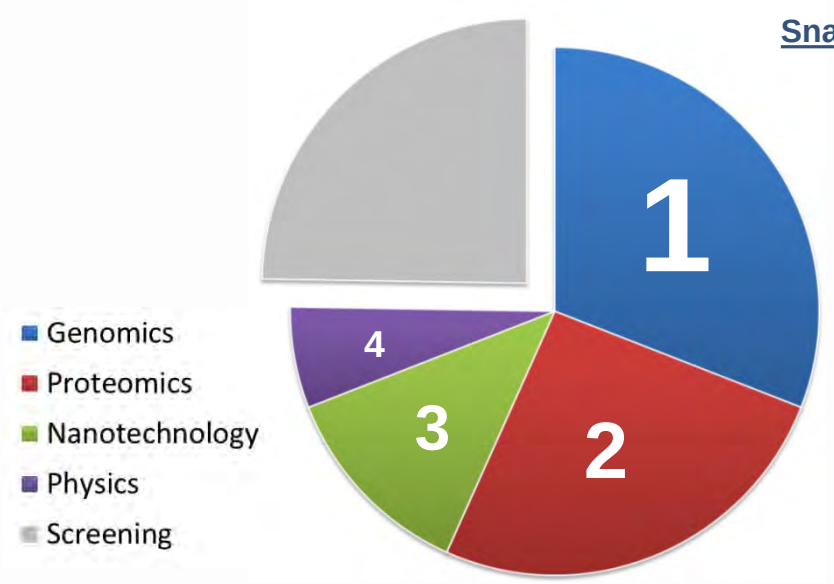
## Innovative Technologies for Molecular Analysis of Cancer

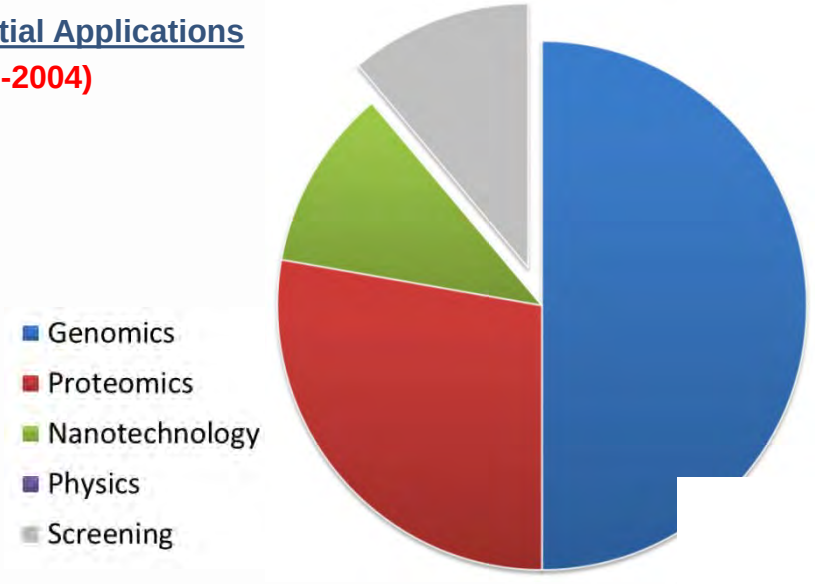
- Proof-of-concept technologies/projects encouraged
- Milestone and technology development driven (no biology)

## Application of Emerging Technologies for Cancer Research

- Validation and dissemination of platforms
- Demonstration of impact on basic and clinical research

**Snapshot of Initial Applications**
**(2003-2004)**



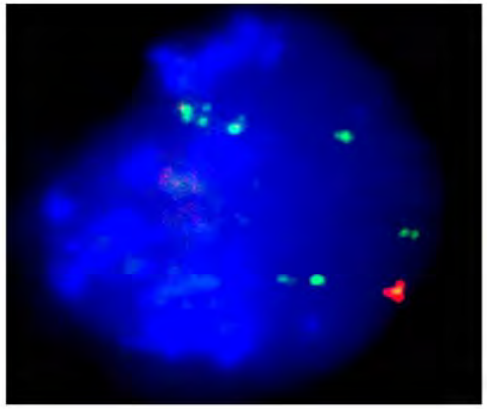



# First Step(back)- Cancer Genomics: Taking a Page from Engineers

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

## Disease of Genomic Alterations

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



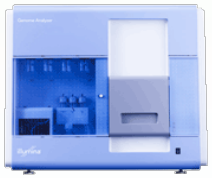

- **Systematic identification of all genomic changes**
- **Repeat (a lot) for individual cancer**
- **Repeat for many cancers**
- **Make it publically available**

| | Saturated steam | | | Superheated steam | | |
|---|---|---|---|---|---|---|
| Pressure (kg/cm²) | Temp (°C) | Vapour enthalpy (kcal/kg) | Specific volume (m³/kg) | Density (kg/m³) | Specific volume (m³/kg) at 250°C | Specific volume (m³/kg) at 300°C |
| 1 | 99,1 | 638,8 | 1,725 | 0,580 | 2,454 | 2,691 |
| 2 | 119,6 | 646,2 | 0,902 | 1,109 | 1,223 | 1,342 |
| 3 | 132,9 | 650,6 | 0,617 | 1,621 | 0,812 | 0,893 |
| 4 | 142,9 | 653,7 | 0,471 | 2,123 | 0,607 | 0,668 |
| 5 | 151,1 | 656,0 | 0,382 | 2,618 | 0,484 | 0,533 |
| 6 | 158,1 | 657,0 | 0,321 | 3,115 | 0,402 | 0,443 |
| 7 | 164,2 | 659,5 | 0,278 | 3,597 | 0,343 | 0,379 |
| 8 | 169,6 | 660,8 | 0,245 | 4,082 | 0,299 | 0,331 |
| 9 | 174,5 | 661,9 | 0,219 | 4,566 | 0,265 | 0,293 |
| 10 | 179,1 | 662,9 | 0,198 | 5,051 | 0,238 | 0,263 |
| 12 | 187,1 | 664,5 | 0,166 | 6,024 | 0,196 | 0,218 |
| 14 | 194,1 | 665,7 | 0,143 | 6,993 | 0,167 | 0,186 |
| 16 | 200,4 | 666,7 | 0,126 | 7,937 | 0,145 | 0,162 |
| 18 | 206,1 | 667,4 | 0,112 | 8,929 | 0,128 | 0,143 |
| 20 | 211,4 | 668,0 | 0,101 | 9,901 | 0,114 | 0,128 |
| 22 | 216,2 | 668,4 | 0,092 | 10,870 | 0,103 | 0,116 |
| 24 | 220,7 | 668,7 | 0,085 | 11,765 | 0,093 | 0,106 |
| 26 | 225,0 | 669,0 | 0,078 | 12,821 | 0,085 | 0,097 |
| 28 | 229,0 | 669,1 | 0,073 | 13,699 | 0,078 | 0,089 |
| 30 | 232,7 | 669,2 | 0,068 | 14,706 | 0,072 | 0,083 |

**Steam table (Reference)**

# Many “Thermometers”: Heterogeneity of Platforms

454



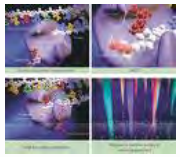
Illumina

SOLiD

Complete Genomics

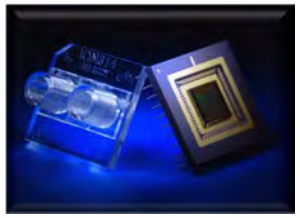
Complete Genomics

Helicos

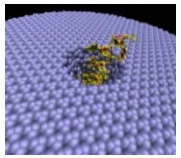


Visigen

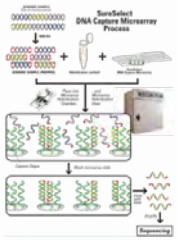
PacBio



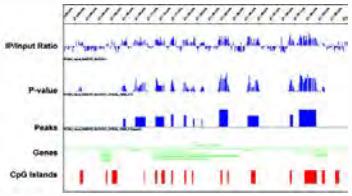
Ion-Torrent



Oxford Molecular



Agilent



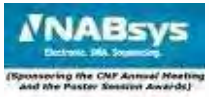
Nimblegen

LaserGen, Inc.

LaserGen

ZSGenetics

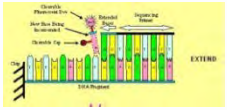
NABsys




Raindance

febit

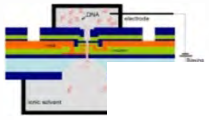
Febit



Intelligent Biosystems

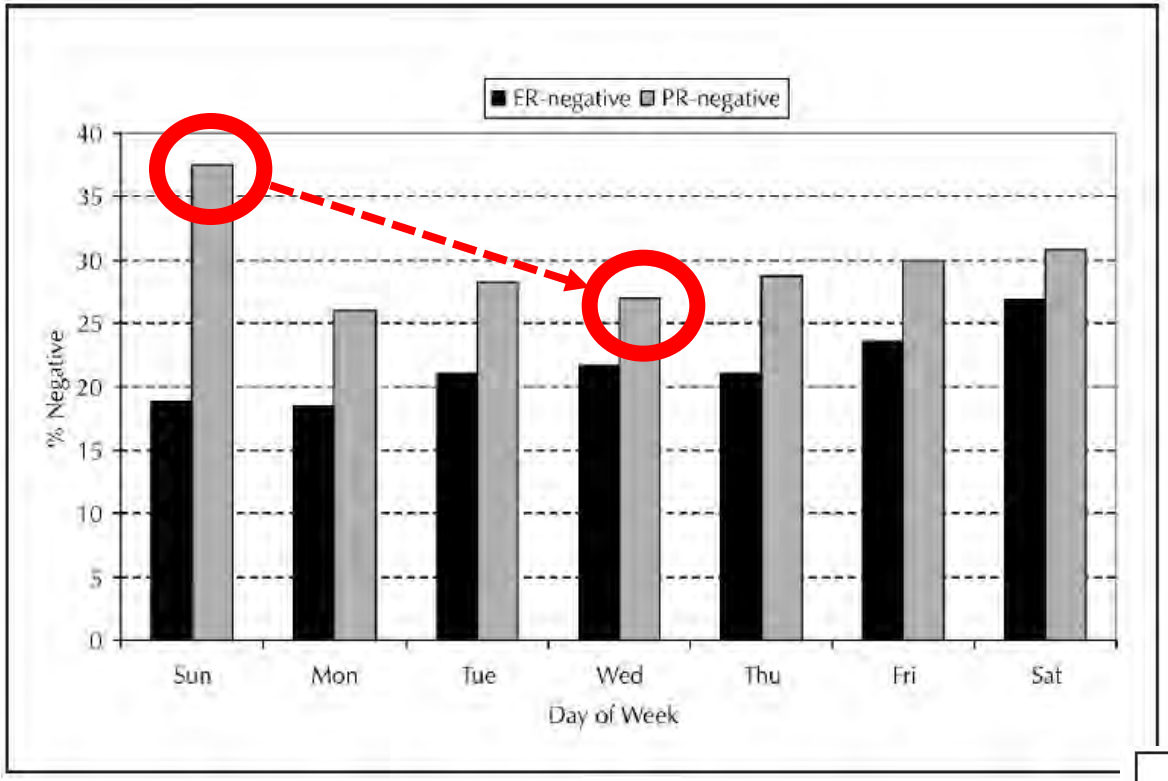
Halycon

IBM



# Getting "Water" Right: Samples AND Handling Matter!

CENTER for STRATEGIC SCIENTIFIC INITIATIVES




caHUB The Cancer Human Biobank

*"Garbage In…Garbage Out"*

"…We found that specimens **obtained late in the week** (prolonged specimen handling) are **more likely to be ER/PR negative** than specimens **obtained on other weekdays** (regular specimen handling)…"

Nkoy et. al., Arch Pathol Lab Med, April 2010

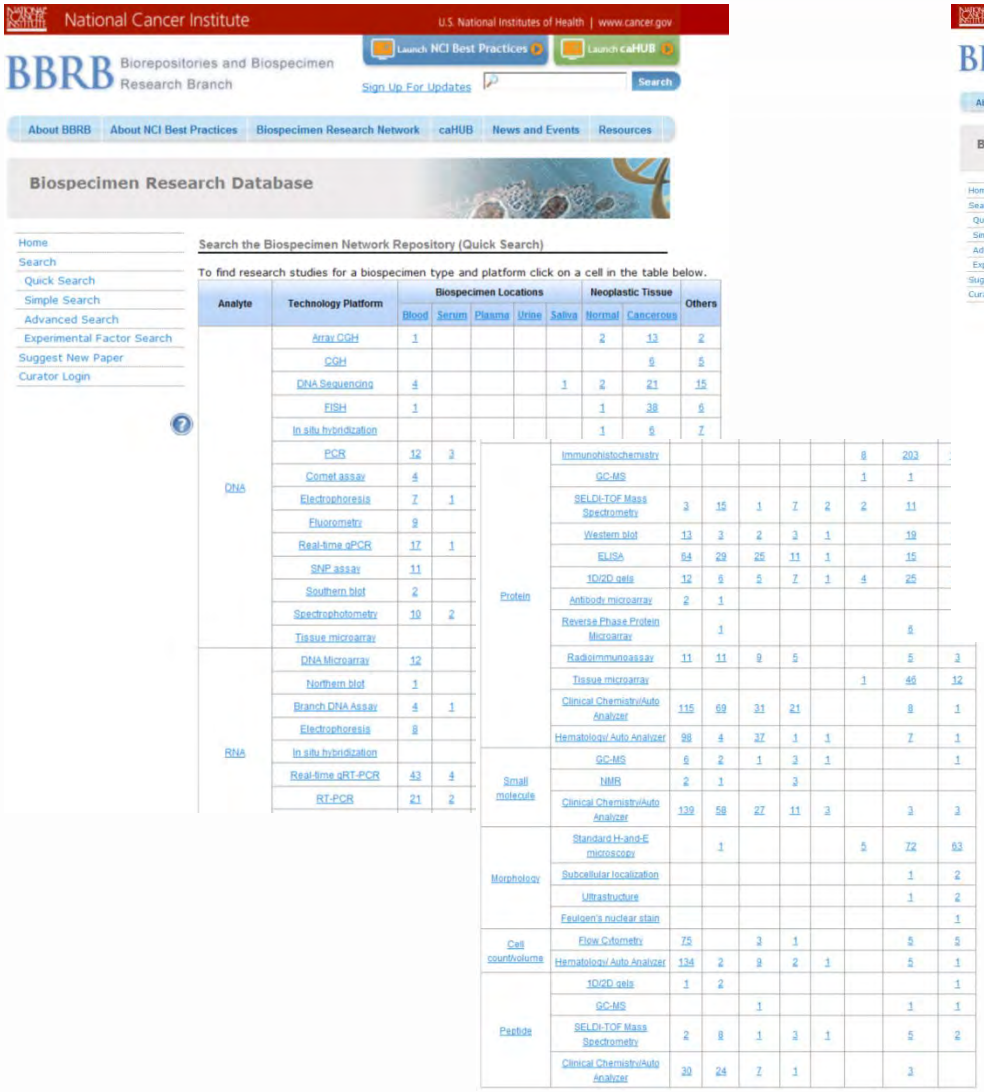
**Table 1. Frequency of Specimen Removal by Day of the Week**

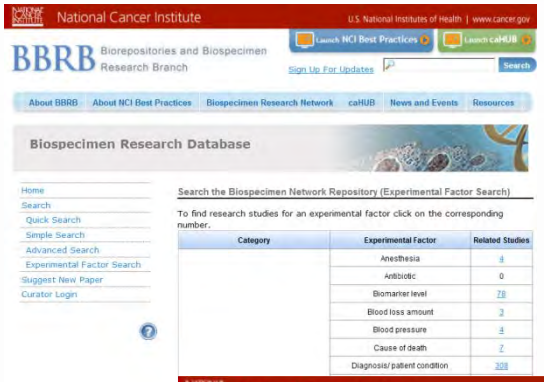
| Day | Cases | ER-Negative | PR-Negative |
|---|---|---|---|
| Sunday | 16 | 3 | 6 |
| Monday | 1252 | 230 | 325 |
| Tuesday | 1176 | 248 | 332 |
| Wednesday | 784 | 170 | 212 |
| Thursday | 904 | 191 | 259 |
| Friday | 919 | 216 | 276 |
| Saturday | 26 | 7 | 8 |
| **System** | **5077** | **1065** | **1418** |

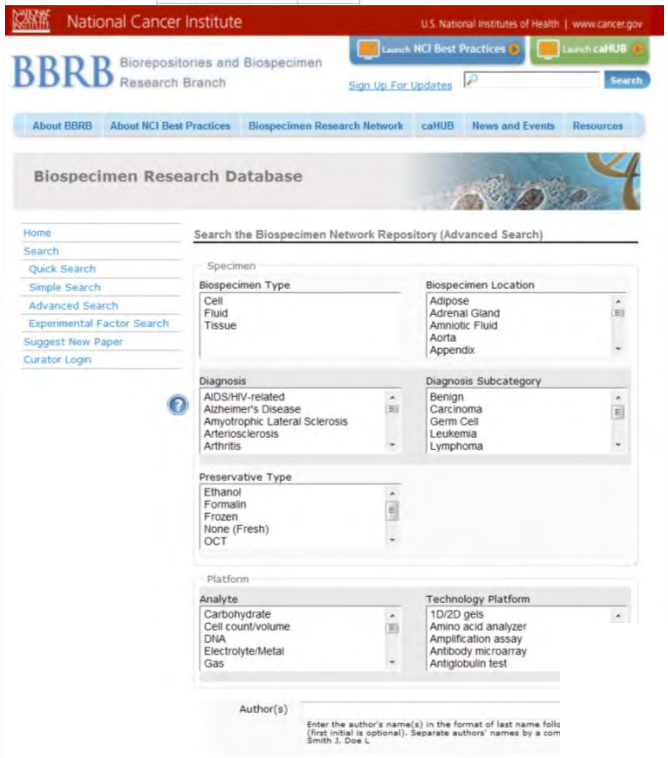
Abbreviations: ER, estrogen receptor; PR, progesterone receptor.

# Biospecimen Research Database (http://brd.nci.nih.gov)

CENTER for STRATEGIC SCIENTIFIC INITIATIVES



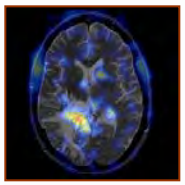
# TCGA: Connecting Multiple Standardized Sources, Experiments, and Data Types

Center for Strategic Scientific Initiatives

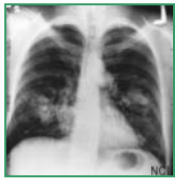
The Cancer Genome Atlas

**Three Cancers- Pilot**

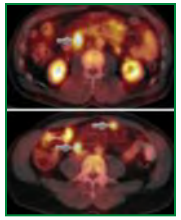
**glioblastoma multiforme (brain)**



**squamous carcinoma (lung)**



**serous cystadenocarcinoma (ovarian)**



**Biospecimen Core Resource with more than 13 Tissue Source Sites**

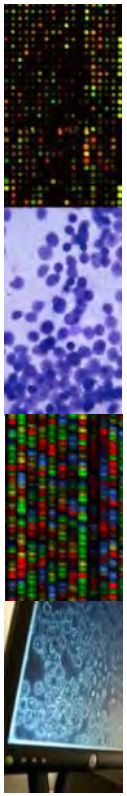
**7 Cancer Genomic Characterization Centers**

**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



# 1st Reference Released in 2008: Subsequent Use by Community

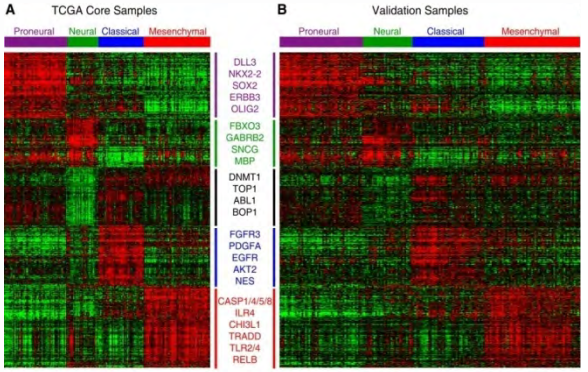
CENTER for STRATEGIC SCIENTIFIC INITIATIVES

## Mid- 2008

- Reference cancer genome for GBM
- Single author paper (TCGA Network)
  - 300+ authors
- Unanticipated Scientific Discoveries
  - Hypothesis on a possible resistance mechanism to temozolomide (TMZ)

**Comprehensive genomic characterization defines human glioblastoma genes and core pathways**

The Cancer Genome Atlas Research Network*

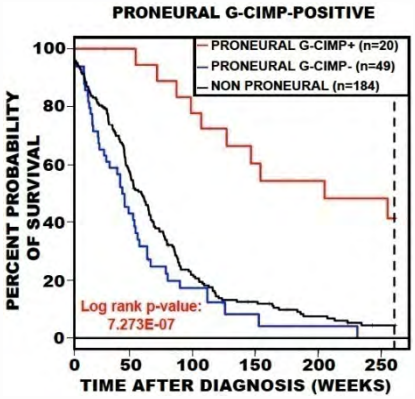


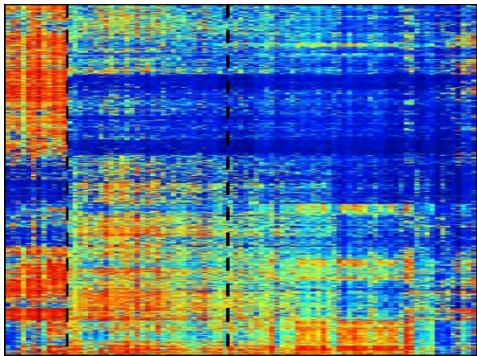

## 2009

- Gene expression-based classification of GBM
- Response to aggressive therapy differs by subtype- **exclude non-responders**

## 2010

- Identification of new subset of GBM
- Occurs in younger patients
- Evidence of **better prediction of outcomes**



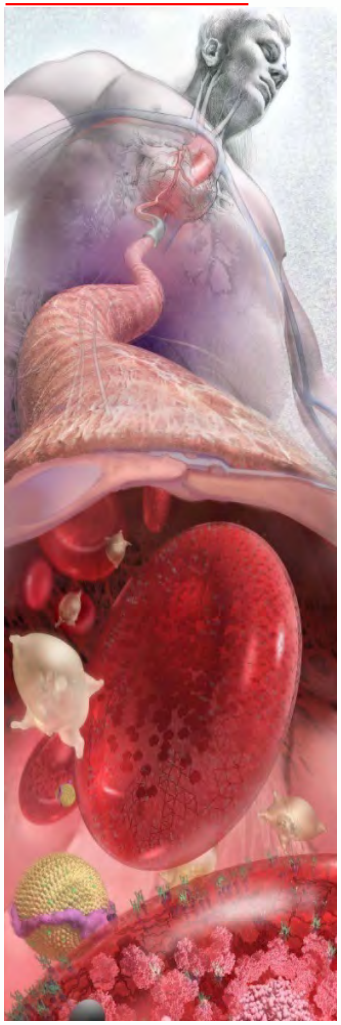



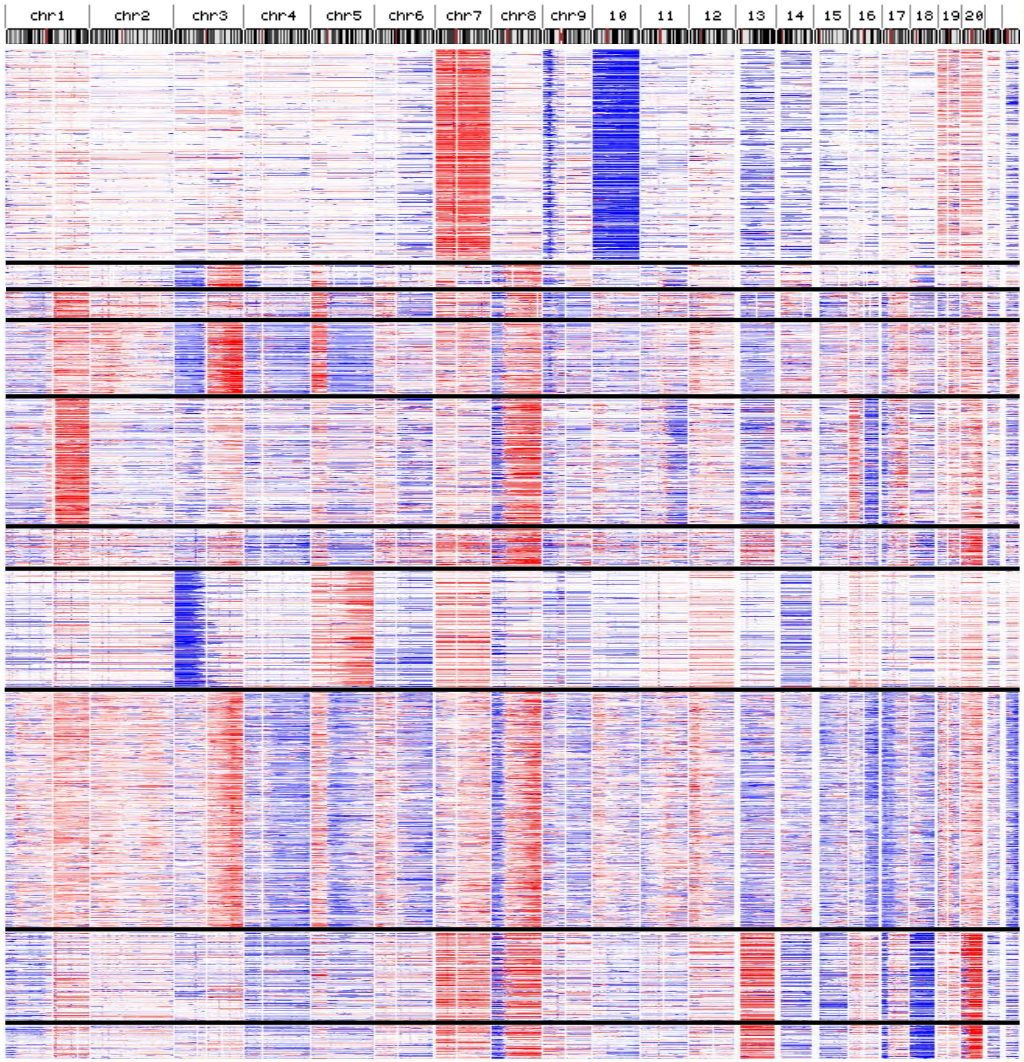
# Genomic "Steam Table"

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

Center for Strategic Scientific Initiatives

***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** |

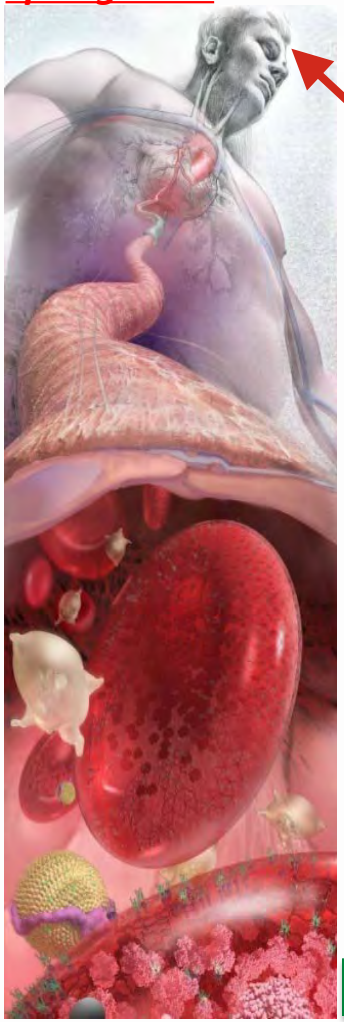
Source: UCSC Cancer Genomic Heatmaps (CopyNumber SNP6)
[https://genome-cancer.ucsc.edu/] Compiled by Jerry S.H. Lee, PhD, May 2011

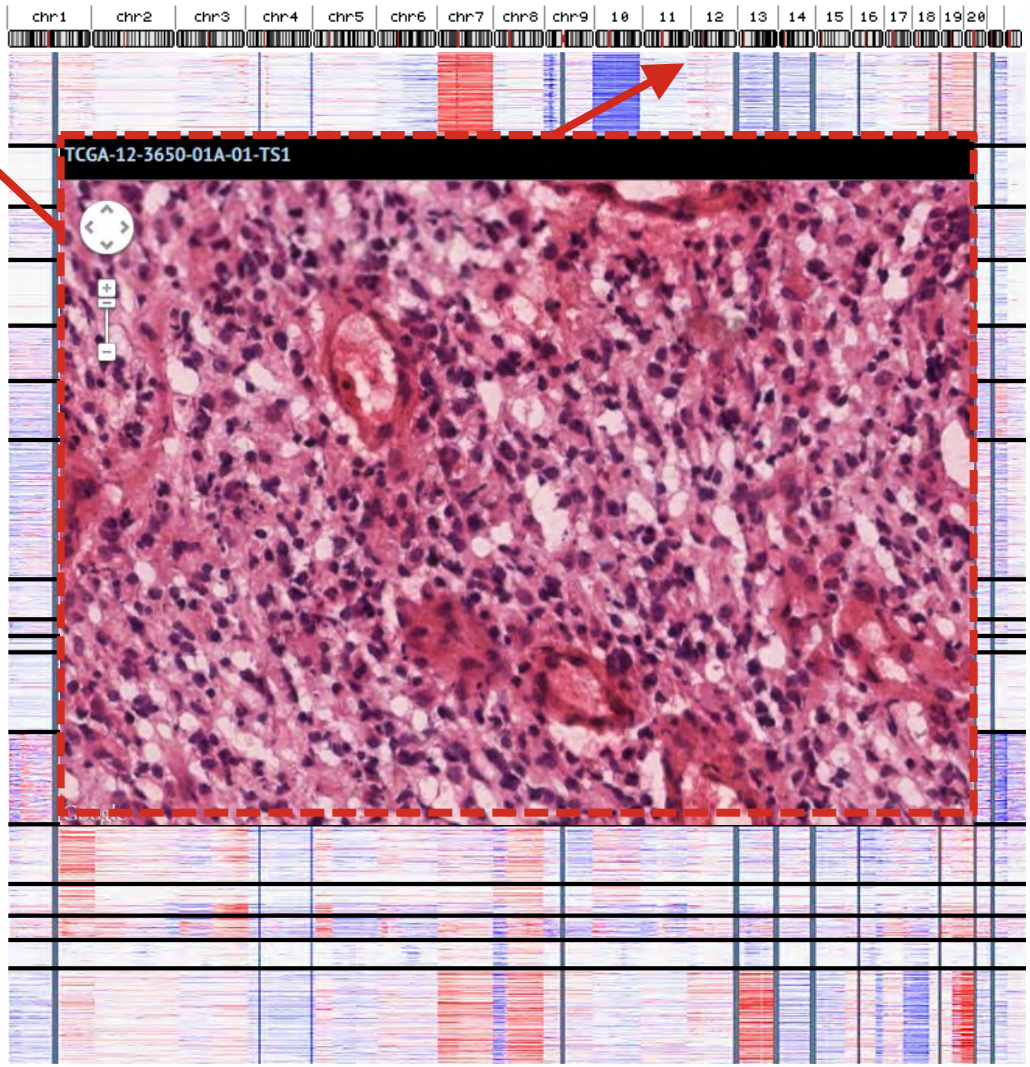
# Genomic "Steam Table"

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

Center for Strategic Scientific Initiatives

***Spring 2013***





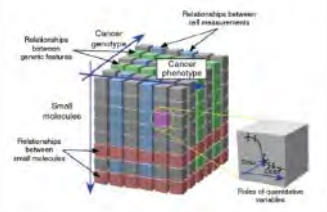

| | |
|---|---|
| Glioblastoma: | 563 |
| Brain lower grade glioma: | 180 |
| Head & neck: | 306 |
| Thyroid carc: | 401 |
| Lung adeno: | 356 |
| Lung squamous: | 343 |
| Breast carc: | 866 |
| Stomach adeno: | 237 |
| Liver hep. carc: | 97 |
| Kidney pap. cell carc: | 103 |
| Kidney clear cell carc: | 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

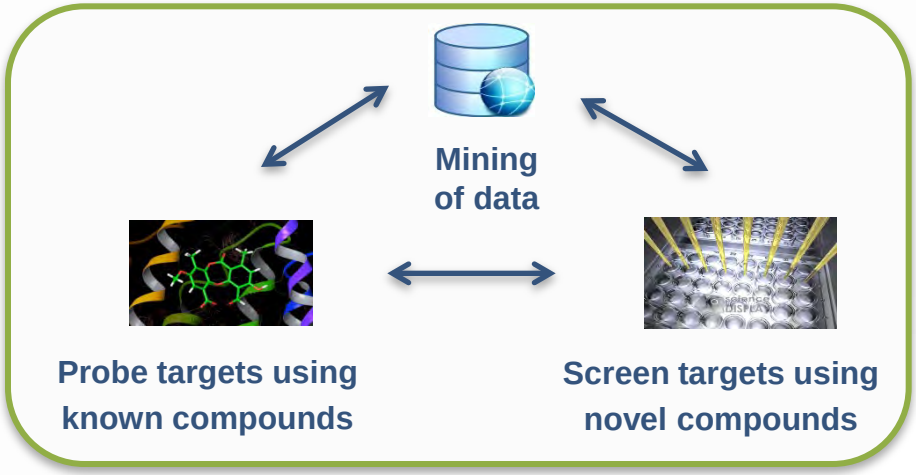
# Cancer Target Discovery & Dev. Network ($CTD^2$)

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

- **Accelerate the translation of patient genomic data into clinical application**
  - Innovate integration of computational mining of large-scale genomic data analysis
  - Identify and confirm new therapeutic target candidates
    - Existing therapeutics and /or orphan drugs
  - Identify and confirm novel modulators
    - Small molecules
    - siRNAs
- **Share models, reagents, analysis tools, and data with scientific community**

NATURE BIOTECHNOLOGY
Towards patient-based cancer therapeutics
The Cancer Target Discovery and Development Network*



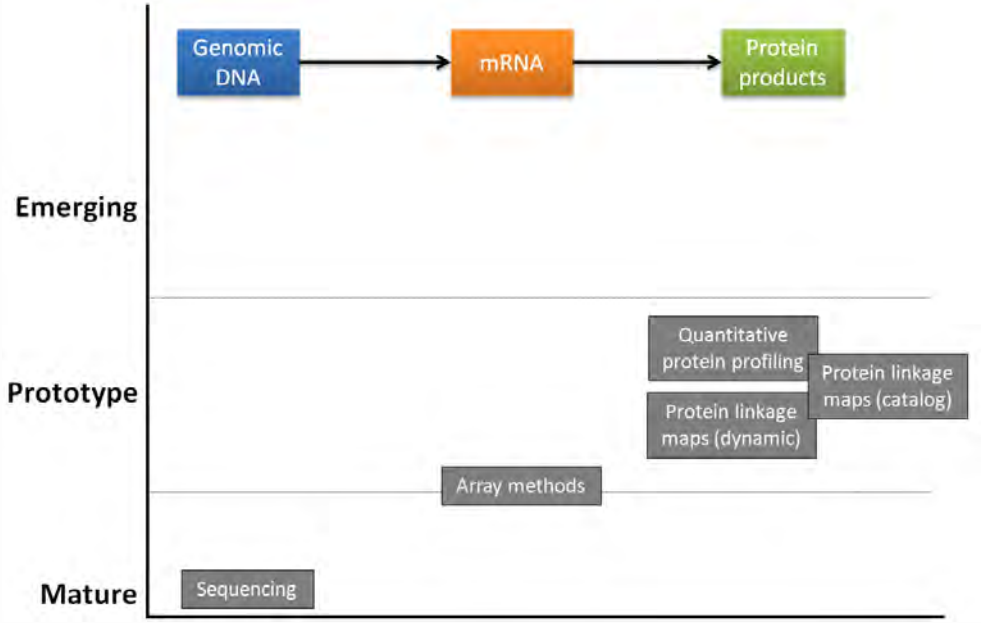

*Nature Biotechnology*, Sept 2010

# What about Biomarkers? Step 1.5- Cancer Proteomics

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

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

## Technologies for Quantitative Analysis




## Major Challenges

- Analytical variability in platforms
- Lack of standards, protocols, and reference data
- No consensus on data acquisition, analysis, and open access reporting of raw data

**Unlike genomic technologies, proteomic technologies were not yet fully mature**

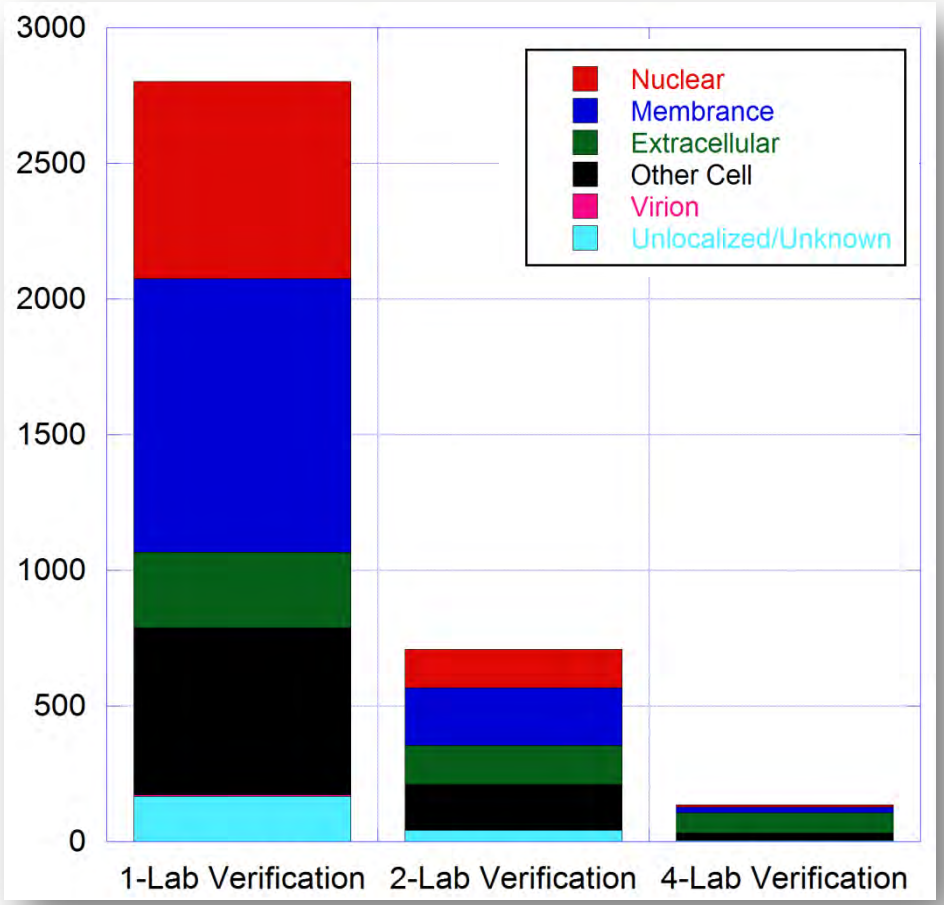
Source: Adopted from "Defining the Mandate of Proteomics in the Post-Genomics Era: Workshop Report." *National Academy of Sciences.* 2002.

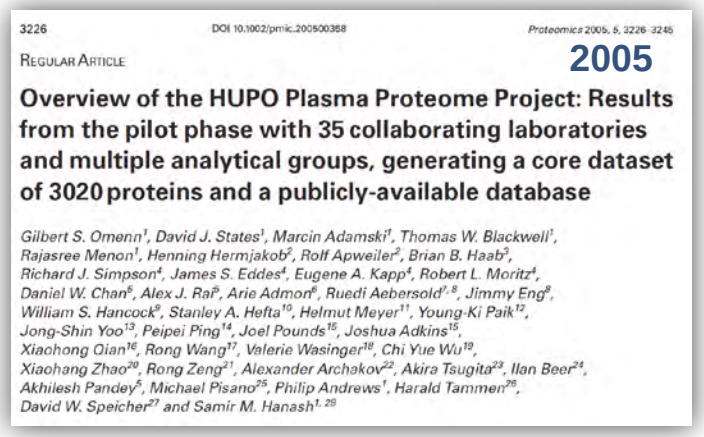
# Heterogeneity of Platforms and Reproducibility Challenges

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

# Reproducibility of Clinical Proteomics in 2005

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

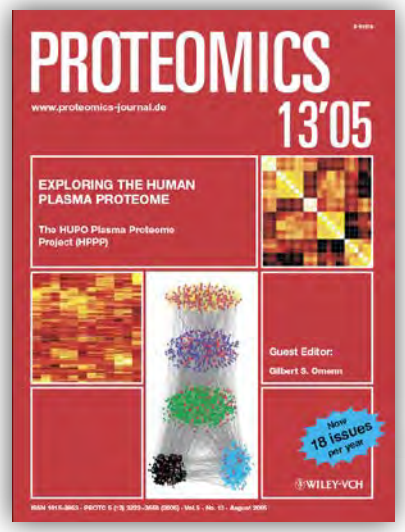




3226 DOI 10.1002/pmic.200500358 *Proteomics* 2005, 5, 3226–3245

REGULAR ARTICLE **2005**

**Overview of the HUPO Plasma Proteome Project: Results from the pilot phase with 35 collaborating laboratories and multiple analytical groups, generating a core dataset of 3020 proteins and a publicly-available database**

*Gilbert S. Omenn[1], David J. States[1], Marcin Adamski[1], Thomas W. Blackwell[1], Rajasree Menon[1], Henning Hermjakob[2], Rolf Apweiler[2], Brian B. Haab[3], Richard J. Simpson[4], James S. Eddes[4], Eugene A. Kapp[4], Robert L. Moritz[4], Daniel W. Chan[5], Alex J. Rai[5], Arie Admon[6], Ruedi Aebersold[7, 8], Jimmy Eng[8], William S. Hancock[9], Stanley A. Hefta[10], Helmut Meyer[11], Young-Ki Paik[12], Jong-Shin Yoo[13], Peipei Ping[14], Joel Pounds[15], Joshua Adkins[15], Xiaohong Qian[16], Rong Wang[17], Valerie Wasinger[18], Chi Yue Wu[19], Xiaohang Zhao[20], Rong Zeng[21], Alexander Archakov[22], Akira Tsugita[23], Ilan Beer[24], Akhilesh Pandey[5], Michael Pisano[25], Philip Andrews[1], Harald Tammen[26], David W. Speicher[27] and Samir M. Hanash[1, 28]*




*Courtesy of Gil Omenn*

# Clinical Proteomic Technologies for Cancer (CPTAC) Pilot

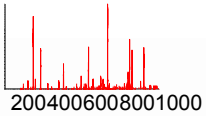
CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

nature biotechnology

June 2009

Multi-site assessment of the precision and reproducibility of multiple reaction monitoring–based measurements of proteins in plasma




## Reproducibility

- **First demonstration** that MRM is highly reproducible **across multiple laboratories** and technology platforms
- **Community Resource**: Antibody Characterization Laboratory Launched

## Data Sharing ("Amsterdam Principles")

- **Timing**
  - Data generated by individual investigators should **be released into the public domain at the latest upon publication while data generated by community resource projects should be released upon generation** following appropriate QA/QC procedures
- **Comprehensiveness**
  - High quality raw data (e.g., mass spectral, protein/affinity array data) be released to the public. They should be well annotated with metadata, information on data quality, and identification quality control data
- **Format**
  - Open access to proteomic data requires community-supported standardized formats, controlled vocabularies, reasonable reporting requirements, and publicly available central repositories

research articles Journal of proteome research

May 2009

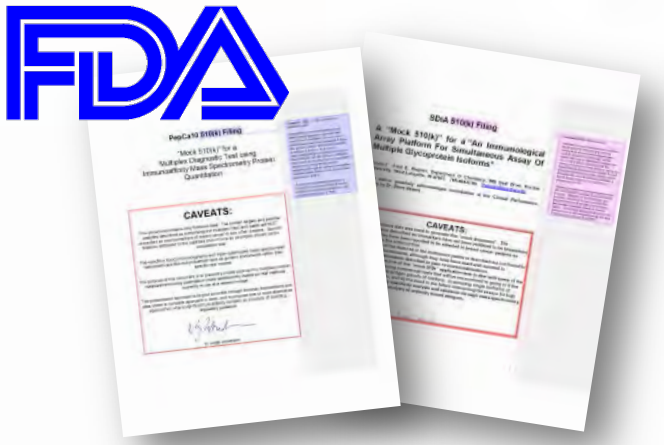
**Recommendations from the 2008 International Meeting on Proteomics Data Release and Sharing Policy: The Amsterdam Principles**

Henry Rodriguez,*,† Mike Snyder,‡ Mathias Uhlén,§ Phil Andrews,∥ Ronald Beavis,⊥ Christoph Borchers,# Robert J. Chalkley,∇ Sang Yun Cho,○ Katie Cottingham,◆ Michael Dunn,¶ Tomasz Dylag,† Ron Edgar,□ Peter Hare,■ Albert J. R. Heck,● Roland F. Hirsch,▼ Karen Kennedy,○ Patrik Kolar,† Hans-Joachim Kraus,● Parag Mallick,□ Alexey Nesvizhskii,● Peipei Ping,▽ Fredrik Pontén,▼ Liming Yang,◐ John R. Yates,▽ Stephen E. Stein,▭ Henning Hermjakob,# Christopher R. Kinsinger,† and Rolf Apweiler#

*Center for Strategic Scientific Initiatives, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, 20892, Department of Molecular, Cellular, and Developmental Biology, Yale University, New Haven, Connecticut 06520, KTH Biotechnology, KTH - AlbaNova University Center, Stockholm, Sweden, Department of Biological Chemistry, University of Michigan Medical School, Ann Arbor, Michigan 48109, Department of Medical Genetics, University of British Columbia, Vancouver, British Columbia, Canada, University of Victoria Proteomics Centre, Victoria, British Columbia, Canada, Department of Pharmaceutical Chemistry, University of California, San Francisco, San Francisco, California, 94158, Yonsei Proteome Research Center, Yonsei*

# CPTAC Pilot: Crosstalk with FDA and Educating Community

- **Analytical Validation Review Documents**
  - CPTAC/FDA Workshop - identify analytical validation needs for clinical proteomic technologies in the context of intended use

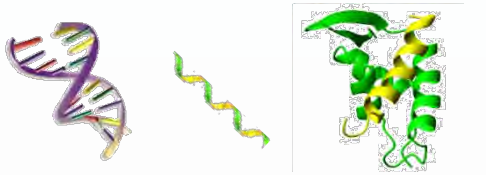



- **Outputs:**
  - Public mock 510(k) pre-applications that serve as review documents on:
    - multiplex MRM-MS assay
    - multiplex affinity-based assay
  - Published in special issue of *Clinical Chemistry* (by AACC), that informs research community and FDA to technology platforms that will likely be part of future 510k submissions

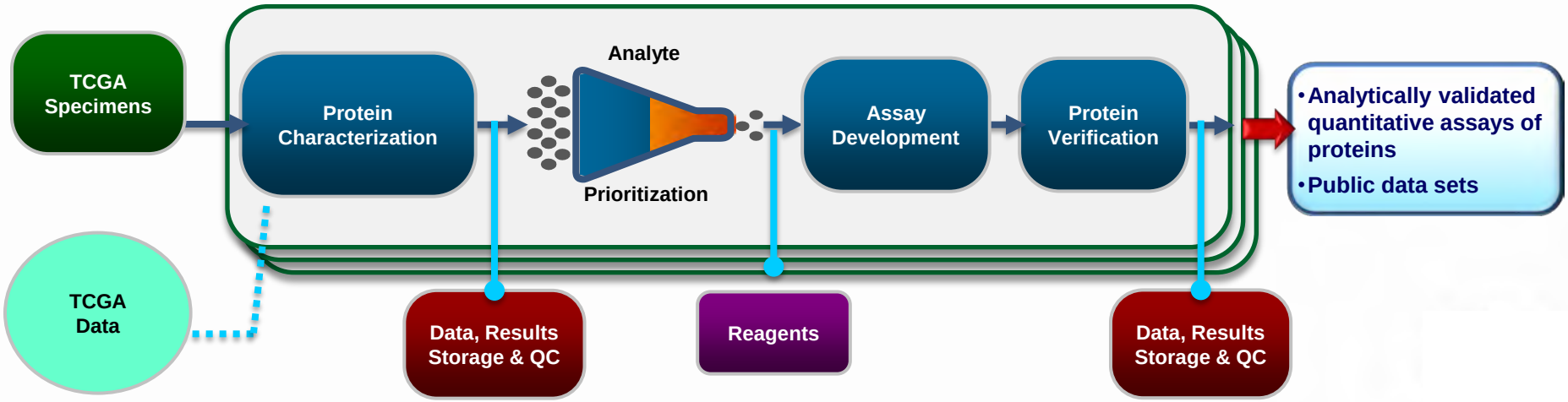
# Phase II: Clinical Proteomic Tumor Analysis Consortium

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

***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

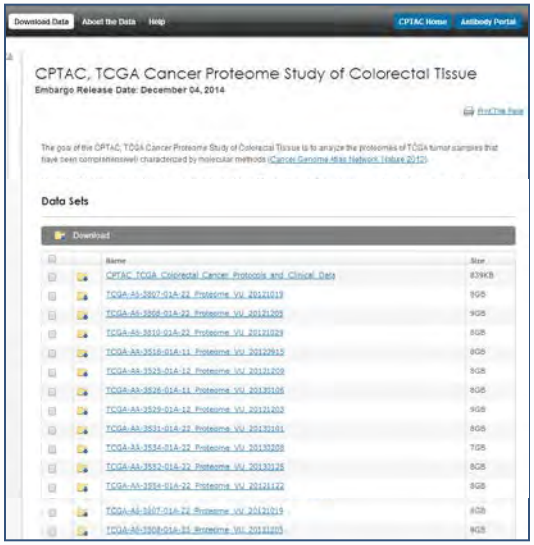
# CPTAC Public Resources: http://proteomics.cancer.gov

Center for Strategic Scientific Initiatives

LIVE

CPTAC Data Portal

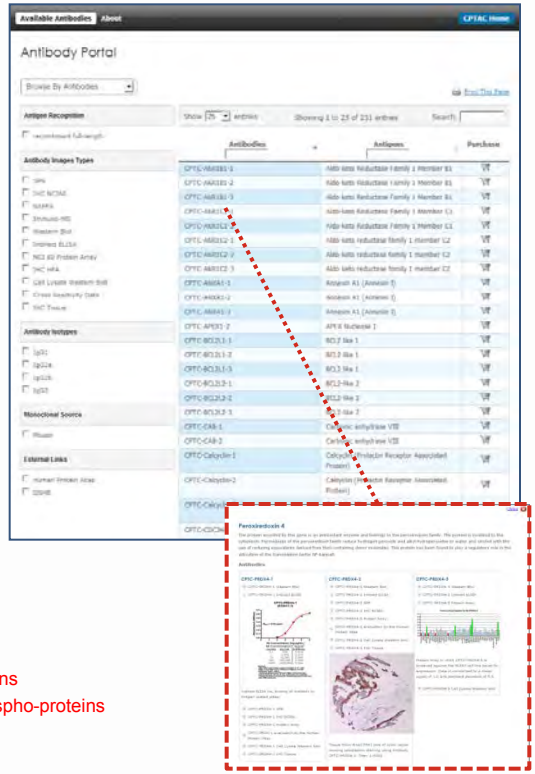
**11,419 files (2.2 TB)**




LIVE

NCI Antibody Portal

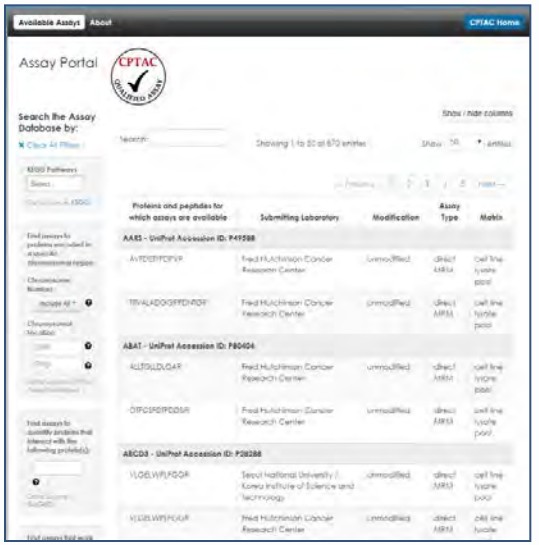
**280 mAbs (~$35)**




COMING SOON

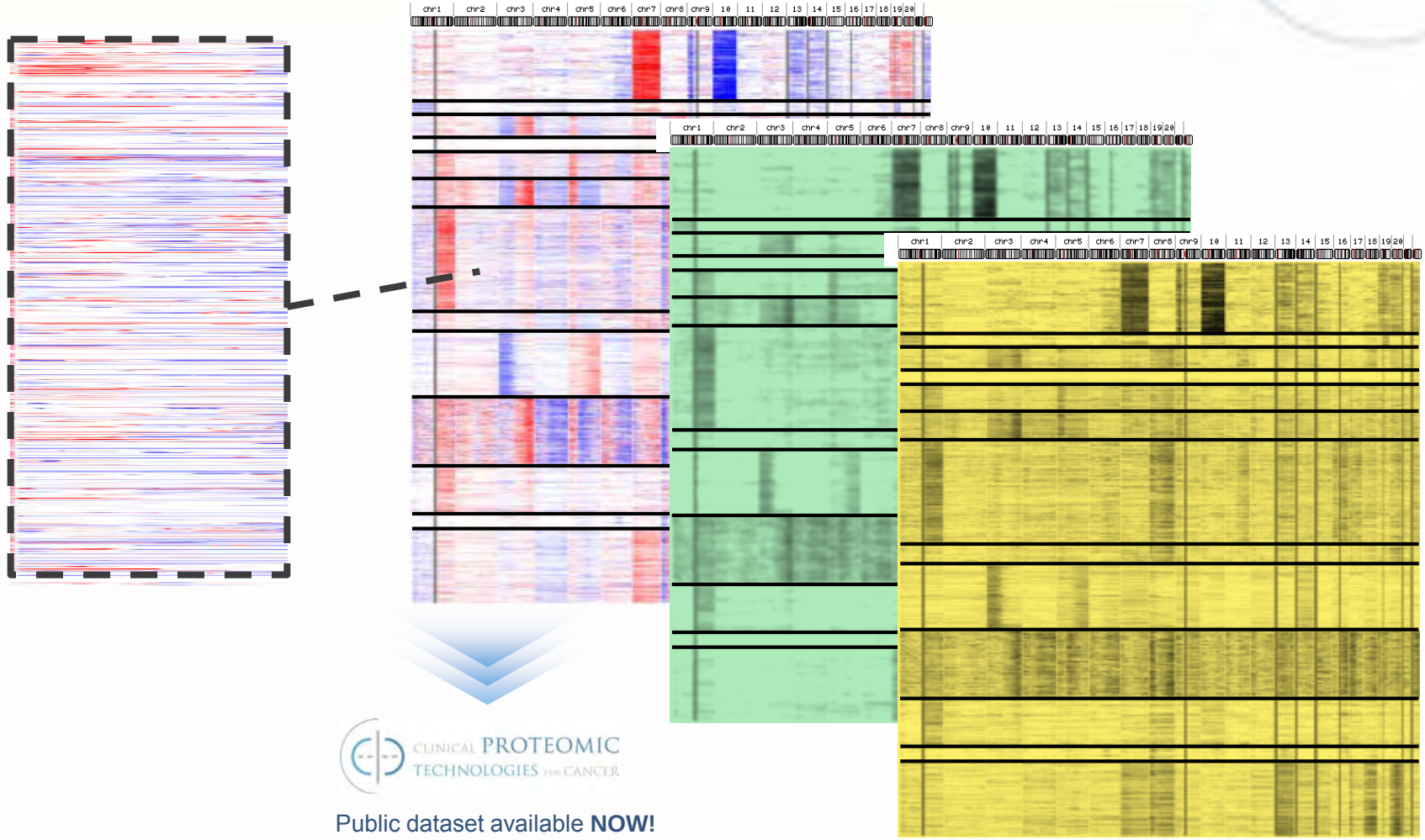
CPTAC Assay Portal

**542 assays**




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

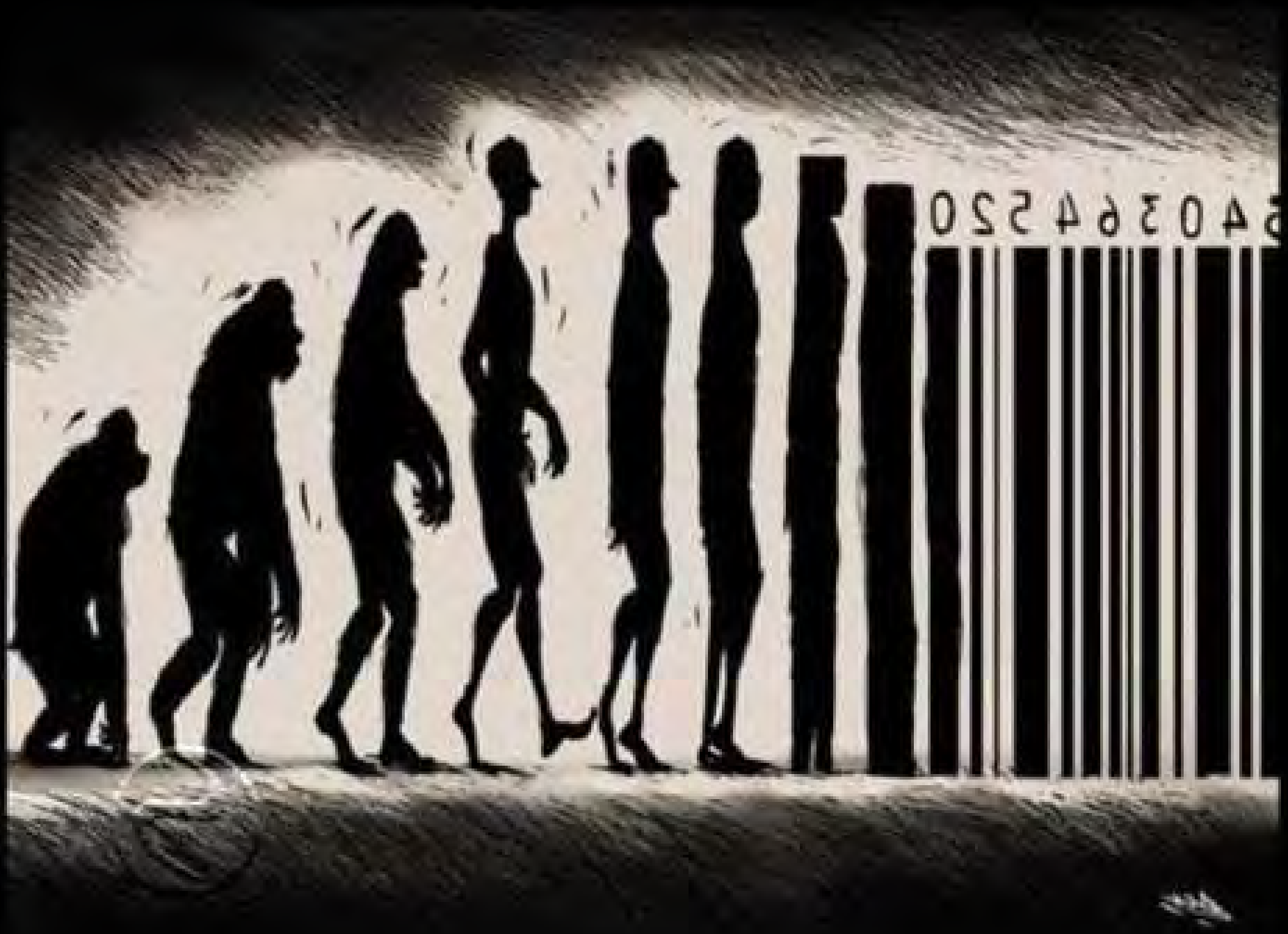
# Where Do We Go From Here?
# Is it JUST More Data?




CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

Public dataset available **NOW!**

**Time? (Evolution)**



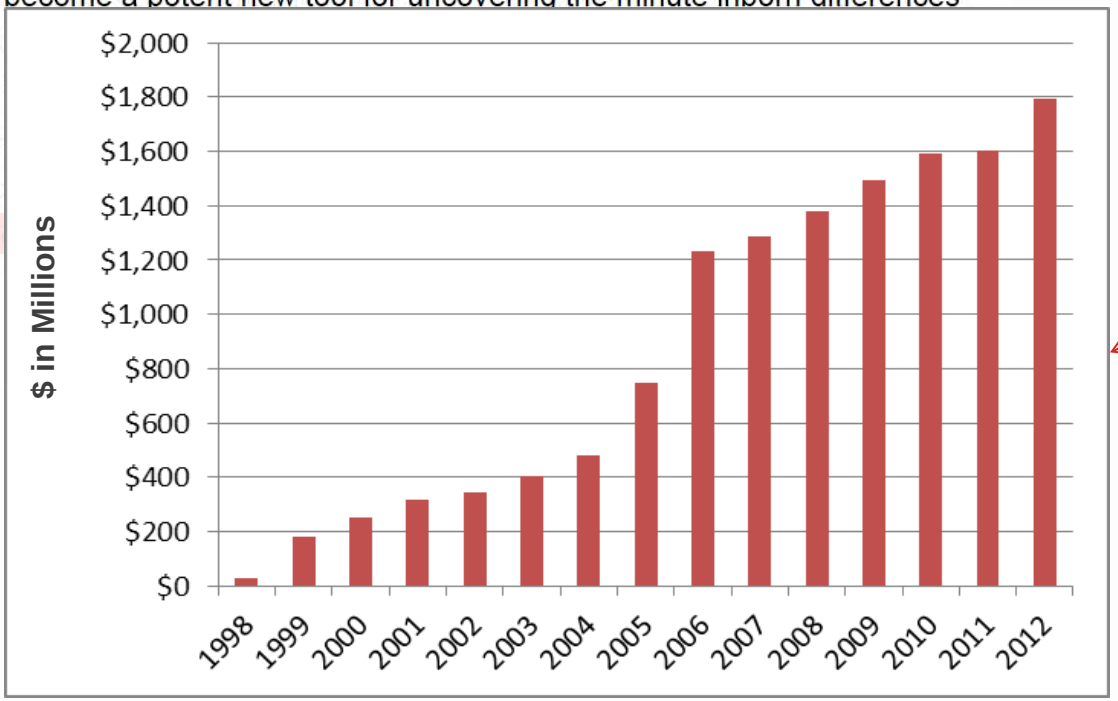
# Personalized Medicine

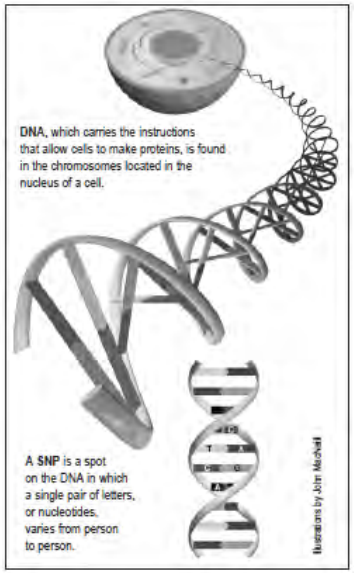
CENTER for STRATEGIC SCIENTIFIC INITIATIVES

THE WALL STREET JOURNAL.
Friday, April 16, 1999

The pharmaceutical industry makes billions of dollars a year selling one-size-fits-all medicines. But now the race is on to come up with tailor-made drugs that will treat people based on their individual genetic makeup.

Drug companies hope to create a map of genetic landmarks that will become a potent new tool for uncovering the minute inborn differences




## How Fine-Tuning By Drug Makers Will Work

- **Herceptin from Genentech Inc.**
  Breast-cancer drug developed specifically to treat a minority of patients whose tumors have elevated levels of a protein, her-2.
- **Xeloda from Roche Holding Ltd.**
  Some patients may respond better to this breast-cancer drug than others because of differences in enzymes that process it.
- **Clozaril from Novartis AG**
  Old schizophrenia drug that causes rare blood disorder in a small number of patients; researchers hope to use gene-map data to develop test to predict who will get the disorder.
- **Orzel from Bristol-Myers Squibb Co.**
  Colorectal cancer drug currently under FDA re[illegible] company is performing studies to identify which patients to develop diarrhea and other side-effects fron

Compiled from www.gene.com and www.roche.com

# 2012: Cancer Treatment and Survivorship Statistics

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

An estimated 13.7 million Americans with a history of cancer were alive on January 1, 2012.

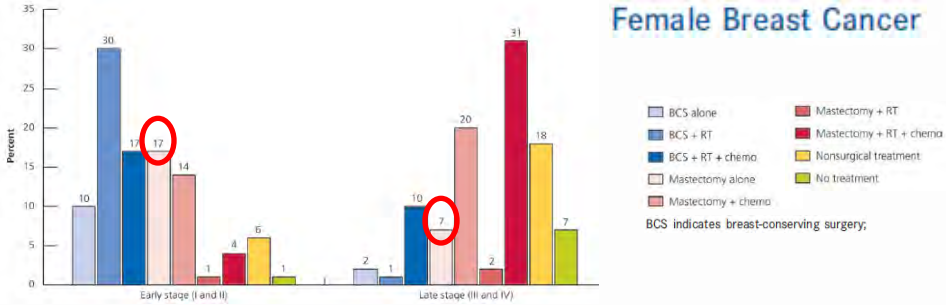
**As of January 1, 2012**

| Male | Female |
|---|---|
| Prostate 2,778,630 (43%) | Breast 2,971,610 (41%) |
| Colon & rectum 595,210 (9%) | Uterine corpus 606,910 (8%) |
| Melanoma 481,040 (7%) | Colon & rectum 603,530 (8%) |
| Urinary bladder 437,180 (7%) | Melanoma 496,210 (7%) |
| Non-Hodgkin lymphoma 279,500 (4%) | Thyroid 436,590 (6%) |
| Testis 230,910 (4%) | Non-Hodgkin lymphoma 255,450 (4%) |
| Kidney & renal pelvis 213,000 (3%) | Uterine cervix 245,020 (3%) |
| Lung & bronchus 189,080 (3%) | Lung & bronchus 223,150 (3%) |
| Oral cavity & pharynx 185,240 (3%) | Ovary 192,750 (3%) |
| Leukemia 167,740 (3%) | Urinary bladder 148,210 (2%) |
| **All sites 6,442,280** | **All sites 7,241,570** |

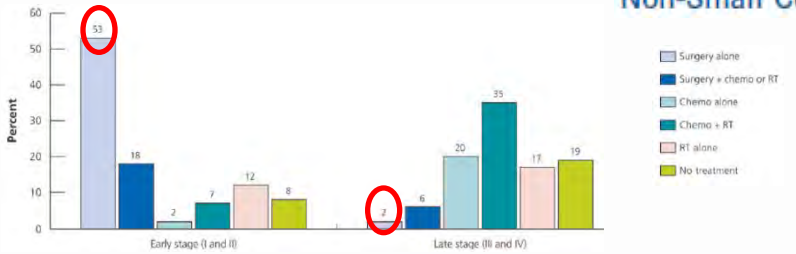
Estimated Numbers of US Cancer Survivors by Site.

## Cancer Treatment Patterns by Stage, 2008.

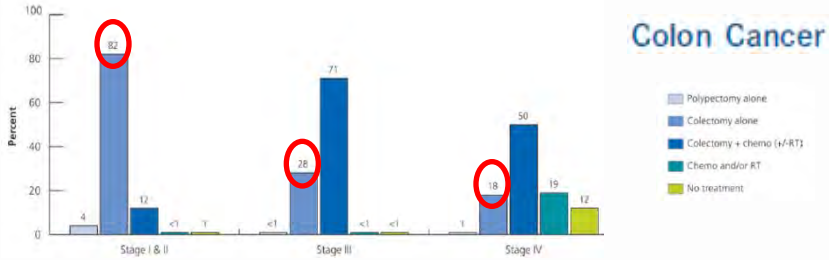
### Female Breast Cancer




### Non-Small Cell Lung Cancer

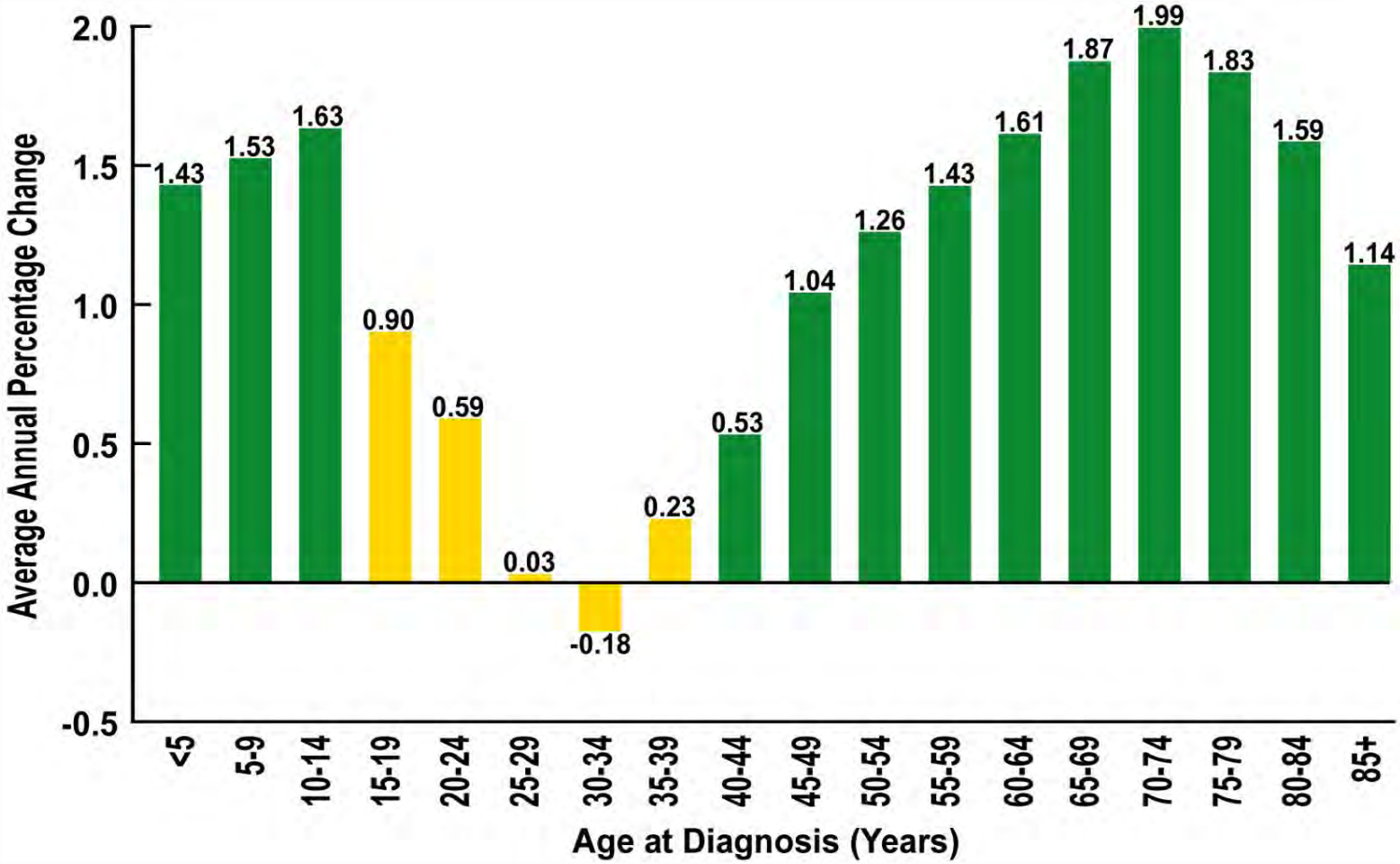



### Colon Cancer



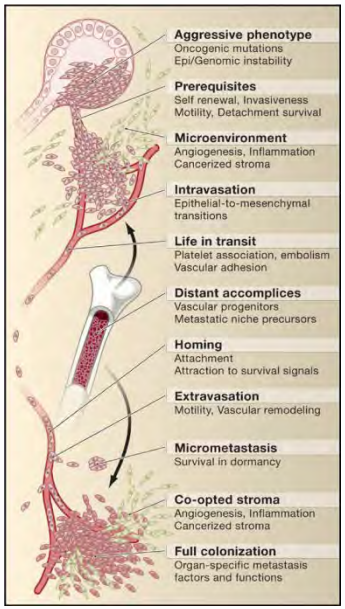

Modified from Siegel et. al. *CA Cancer J Clin*, June 2012

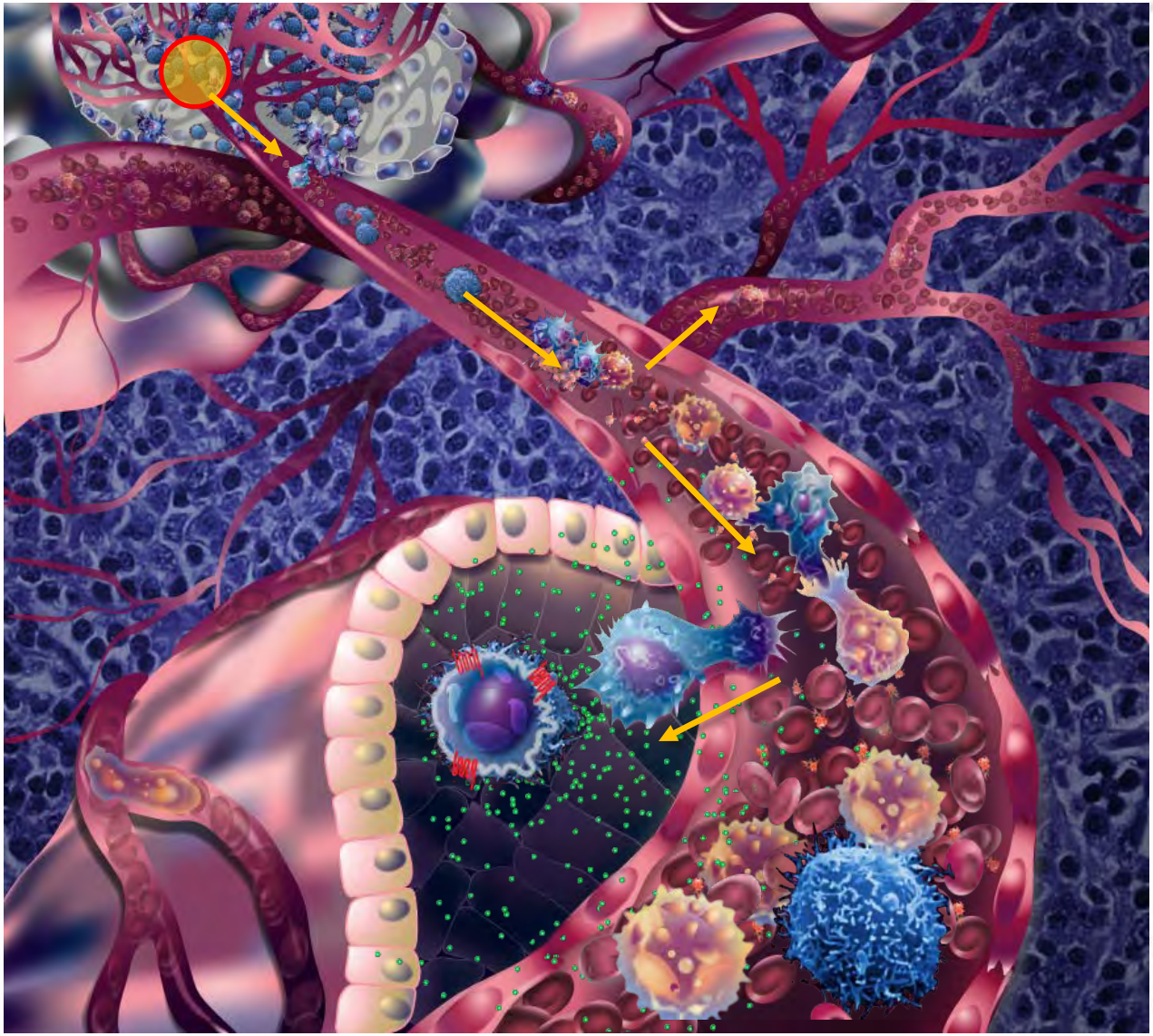
# Survival Improvement Gap: Improvement in 5-Year Relative Survival, Invasive Cancer, 1975 – 1997




http://seer.cancer.gov/

# Metastasis: Deleterious but also Rare and Random- Why?



**Well-known to be an inefficient process (0.01%)**

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

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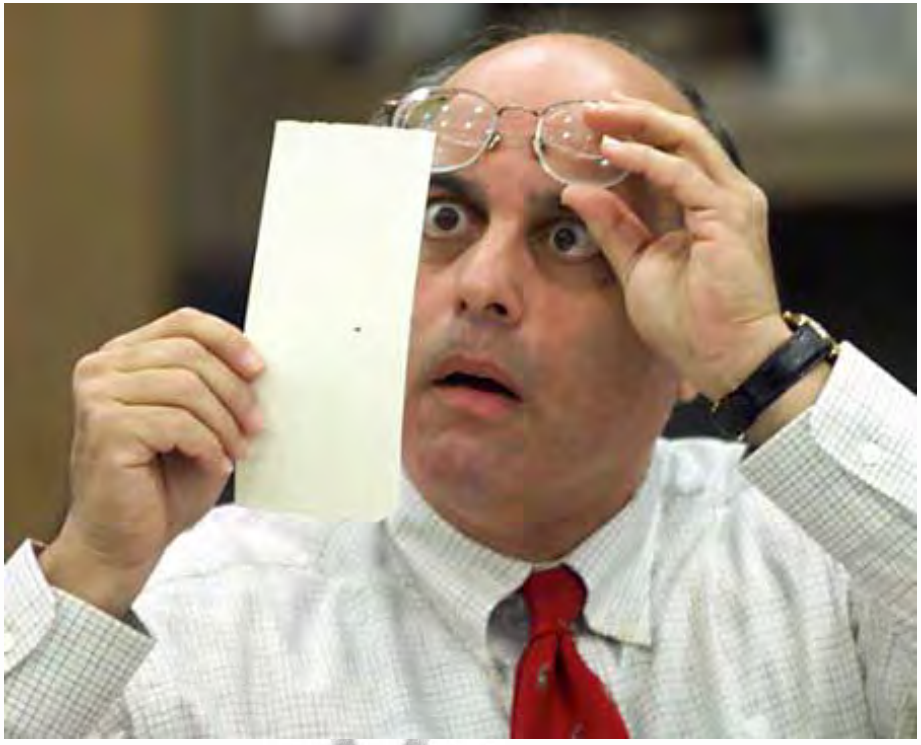
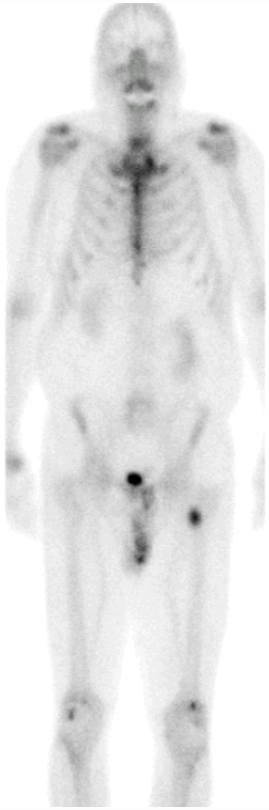
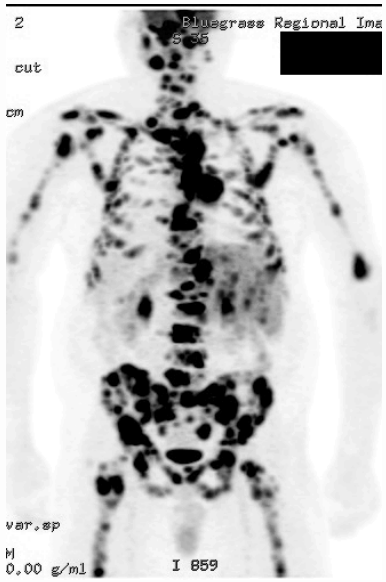
**M0**



**M1**



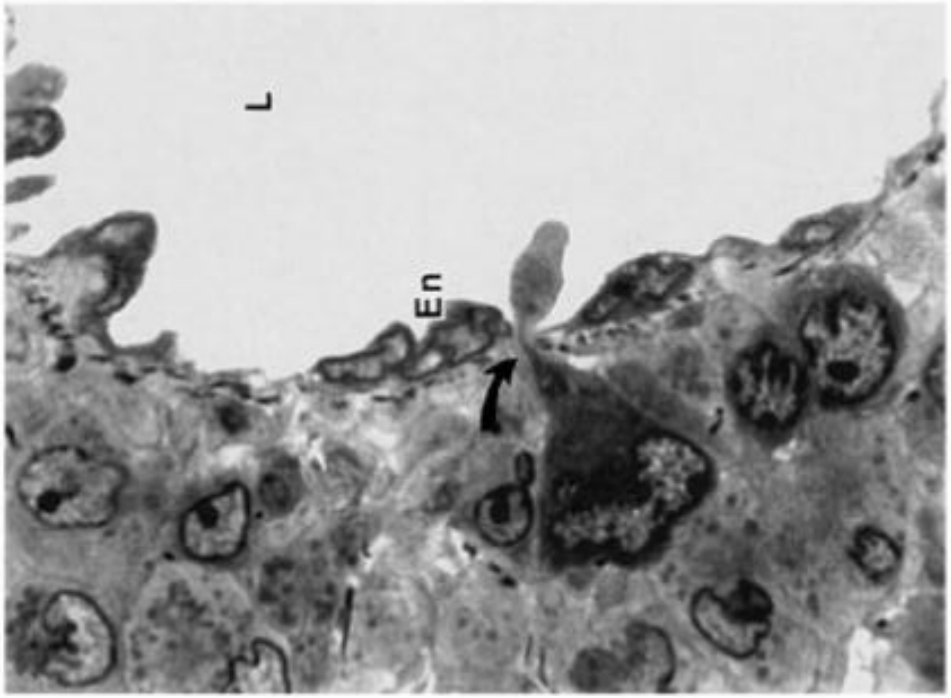
**M1**




| Distant metastasis (M)§ | |
|---|---|
| M0 | No distant metastasis |
| M1 | Distant metastasis |

Adapted from and courtesy of Jacob Scott, M.D., Moffitt PS-OC

# Cancer:
# A Disease of…Cell Mechanics?




"…metastatic cells must overcome numerous physical obstacles barring metastasis…in this way, cancer may progress as a disease of genetically heterogeneous cell populations driven to evolve by sequential environmental pressures…"

*Cancer Metastasis: Building a Framework, Gupta et. al.* Cell 2006

# Winter 2007: Cell As A Machine, ASCB sessions, and IMAT

CENTER for STRATEGIC SCIENTIFIC INITIATIVES


**Organizers**

**Professor K. Jimmy Hsia**
Department of Mechanical Science and Engineering
University of Illinois at Urbana-Champaign

**Professor Roger D. Kamm**
Department of Mechanical Engineering and Department of Biological Engineering
Massachusetts Institute of Technology

**Professor Michael P. Sheetz**
Department of Biological Sciences
Columbia University

**Professor Subra Suresh**
Dean of Engineering and Department of Materials Science and Engineering
Massachusetts Institute of Technology

**The American Society for Cell Biology**

**Dec 1-5, 2007**

**Force and Form in Cell Biology**

*Dennis Discher,* University of Pennsylvania, *Thomas Pollard (Chair),* Yale University, *Michael P. Sheetz,* Columbia University, *Valerie M. Weaver,* University of California, San Francisco

Introduction
Stem Cell Force Generation and Differentiation. *D. Discher;* Molecular/Cell Biophysics Lab, University of Pennsylvania, Philadelphia, PA
Transformation: A Force to Resist. *V. M. Weaver;* Department of Surgery, University of California, San Francisco, San Francisco, CA
Shaping Cells by Force and Rigidity through Protein Stretching. *M. P. Sheetz;* Department of Biological Sciences, Columbia University, New York, NY

**Creating Next Generation Nano Tools for Cell Biology**

*Jerry S.H. Lee (Chair)*

*Speakers*

- *Milan Mrksich,* University of Chicago
- *David Sept,* Washington University in St. Louis
- *Zong Ling Wang,* Georgia Institute of Technology
- *Muhammad Yousaf,* University of North Carolina at Chapel Hill
- *Raoul Kopelman,* University of Michigan
- *Leland WK Chung,* Emory School of Medicine
- *Douglas Hanahan,* University of California, San Francisco

**Announced release of RFAs and inclusion of cell motility and mechanics as topics**

# 2009 Bringing In New Perspectives: PS-OC Program

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

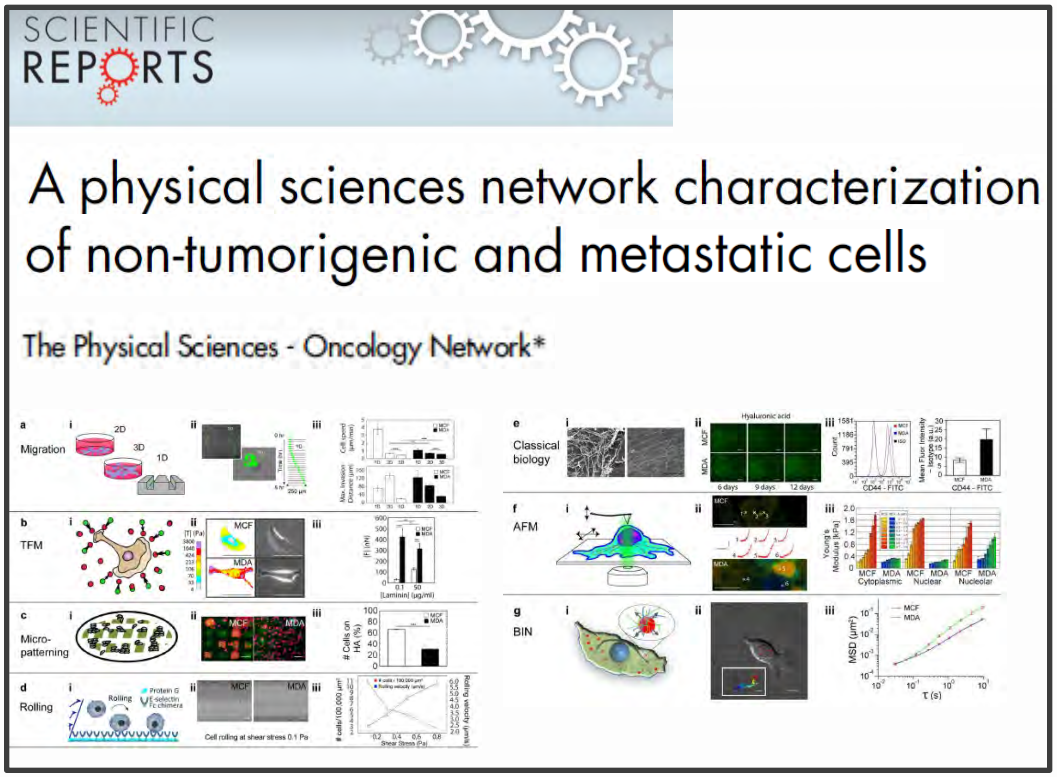
- To generate ***new knowledge*** and catalyze ***new fields of study*** in cancer research by utilizing physical sciences/engineering principles to enable a better understanding of cancer and its behavior at all scales.
- Not looking for new tools to do "better" science, but new perspectives and approaches 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 in ONCOLOGY

***New – "Schools of Thought"***

# New Collective Insights of Physical Science Parameters: Living Project

CENTER for STRATEGIC SCIENTIFIC INITIATIVES




- **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)

PS-OC → D C C

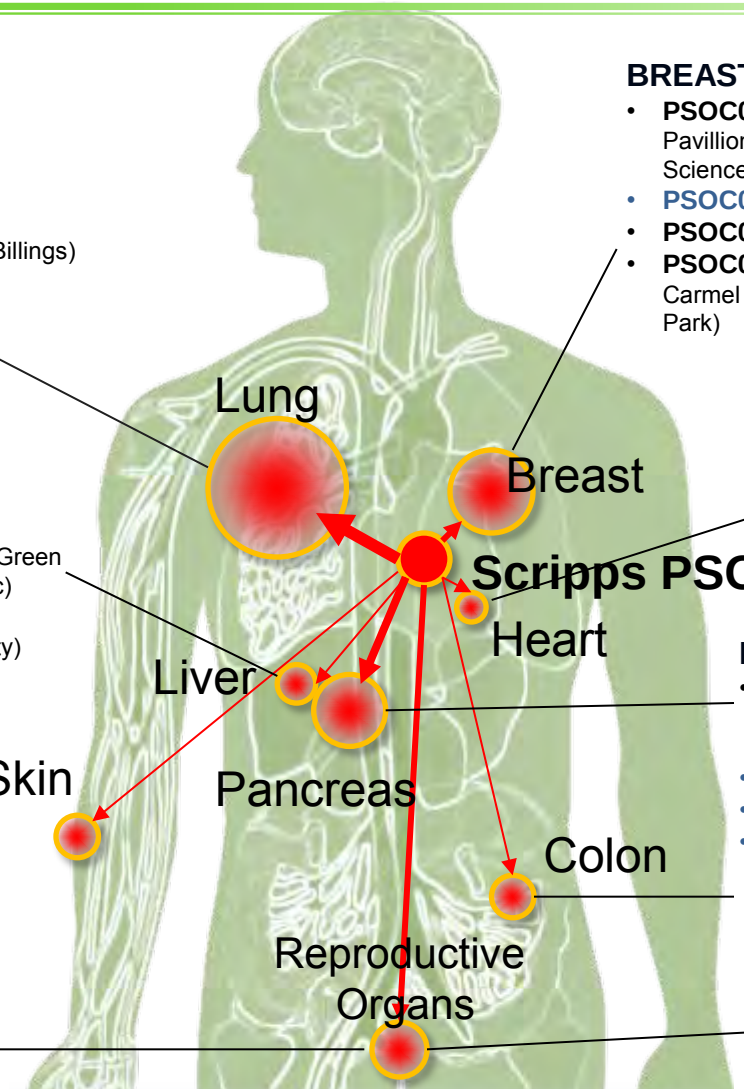
http://opso.cancer.gov/data/

PS-OC Network Bioresource Core Facility

**Cells**

*Scientific Reports*, April 2013

# 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 Pavillion, Carmel Valley, Rancho Bernardo, Torrey Pines Science Park)
- **PSOC0051** (USC)
- **PSOC0058** (USC)
- **PSOC0060** (Scripps Health)
- **PSOC0063** (NorthShore)

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

**HEART:**
- **PSOC0057** (Scripps Health)

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

**COLON:**
- **PSOC0066** (Scripps Clinic)

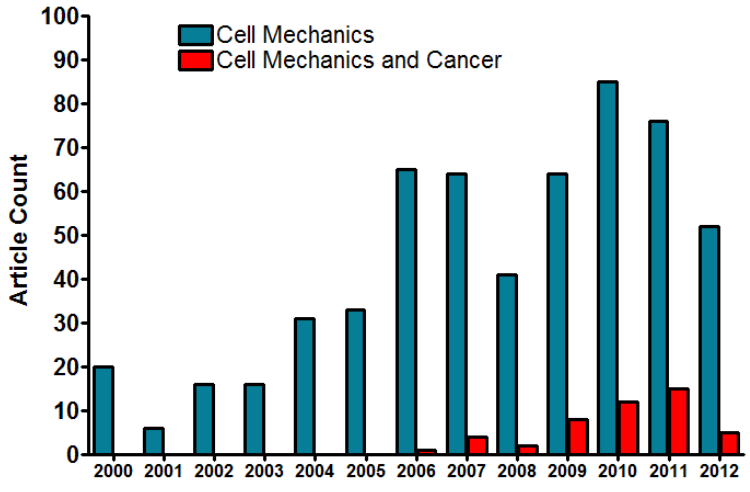
**OVARIAN:**
- **PSOC0052** (Scripps Memorial Hospital, South Coast Gynecologic Oncology)

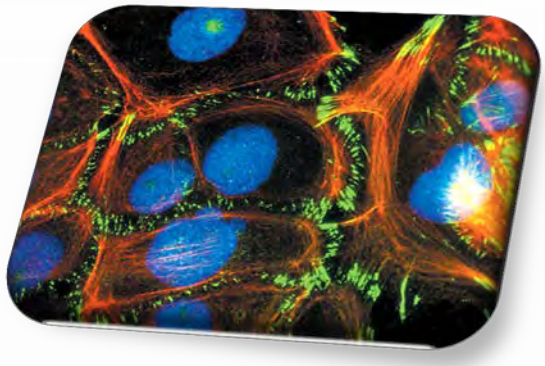
Courtesy of Peter Kuhn (TSRI)

# Cell Mechanics: A Continuing Growing Community

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

## Papers

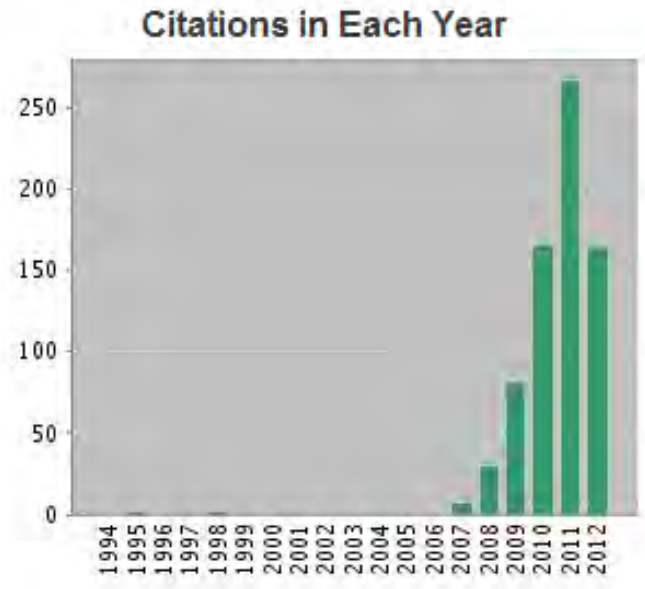


## Citations

Use the checkboxes to remove individual items from this Citation Report or restrict to items published between 1898 and 2012 Go

| | 2008 | 2009 | 2010 | 2011 | 2012 | Total | Average Citations per Year |
|---|---|---|---|---|---|---|---|
| | 31 | 82 | 166 | 267 | 165 | 726 | 38.21 |
| 1. Title: **Biomechanics and biophysics of cancer cells** Author(s): Suresh, Subra Source: ACTA BIOMATERIALIA Volume: 3 Issue: 4 Pages: 413-438 DOI: 10.1016/j.actbio.2007.04.002 Published: JUL 2( | 15 | 33 | 35 | 46 | 24 | 155 | 25.83 |
| 2. Title: **Mechanics, malignancy, and metastasis: The force journey of a tumor cell** Author(s): Kumar, Sanjay; Weaver, Valerie M. Source: CANCER AND METASTASIS REVIEWS Volume: 28 Issue: 1-2 Pages: 113-127 DOI: 10.1007/s10555-008-9173-4 | 0 | 5 | 31 | 45 | 21 | 102 | 25.50 |
| 3. Title: **AFM indentation study of breast cancer cells** Author(s): Li, Q. S.; Lee, G. Y. H.; Ong, C. N.; et al. Source: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS Volume: 374 Issue: 4 Pages: 609-613 DOI: | 0 | 12 | 28 | 27 | 16 | 83 | 16.60 |
| 4. Title: **Cell mechanics using atomic force microscopy-based single-cell compression** Author(s): Lulevich, Valentin; Zink, Tiffany; Chen, Huan-Yuan; et al. Source: LANGMUIR Volume: 22 Issue: 19 Pages: 8151-8155 DOI: 10.1021/la060561p Published: SEP 12 2006 | 3 | 10 | 11 | 13 | 10 | 49 | 7.00 |




**Statistics generated using *Web of Science* with keywords "cell mechanics" and "cancer"**

# But is it clinically relevant? Perhaps…

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

**2010**

| Clinical Indication | Physical Property | Mechanism of Action | Development Status (Agent Example) |
|---|---|---|---|
| Anesthesiology | **Shape Motility** | Membrane Fluidity Intracellular Calcium | FDA Approved (Tetracaine) |
| Cardiovascular | **Shape Motility Contraction** | ERK Kinase Rho-Rho-Kinase Intracellular Calcium | Preclinical (Thyroid hormone) Clinical Phase II (Resveratrol) FDA Approved (Atorvastatin) |
| Diabetes | **Contraction** | Rho-Rho-Kinase PI3 Kinase | FDA Approved (Insulin) |
| Endocrinology | **Contraction** | Rho-Rho-Kinase | Preclinical (Somatostatin) |
| Glaucoma | **Shape** | Ion Co-transport Inhibition | FDA-Approved (Edecrin) |
| Immunology | **Shape** | DP2 Receptor | Clinical Phase II (AM211) |
| Nephrology | **Elasticity** | ERK1/2 Kinase | Preclinical (Aldosterone) |
| Neurology | **Shape Size Elasticity** | Dopamine Receptor Serotonin Receptor | Preclinical (TIMP-1) Clinical Phase II (Epothilone D) FDA Approved (Imipramine) |
| Oncology | **Shape Size Motility Elasticity** | Somatostatin agonist Microtubule Microfilament Anti-mitotic Tyrosine Kinase | Preclinical (Octreotide) Clinical Phase II (Vinflunine) Clinical Phase II (AEE788) Clinical Phase III (Xyotax) FDA Approved (Abraxane) FDA Approved (Nexavar) |
| Orthopedic | **Shape Elasticity** | Metalloproteinase | FDA Approved (IL-1β) |
| Pulmonary Disease | **Contraction** | E-Cadherin Vimentin | Preclinical (TGF-β1) |
| Regenerative Medicine | **Shape Size** | Rho-Rho-Kinase | Marketed (Vitamin D3) |

| | 2010 | 2012 | 2014 |
|---|---|---|---|
| Preclinical | 12 | 16 | |
| Phase I/II | 7 | 10 | |
| Phase III | 0 | 0 | |
| FDA Approved | 15 | 15 | |

**Industry Dev.**

Novartis, Roche, Bayer, Kosan Pharma, etc.

Abraxis, GSK, Janssen, Merck, Pfizer,etc.

Independent analysis conducted by CCS Associates

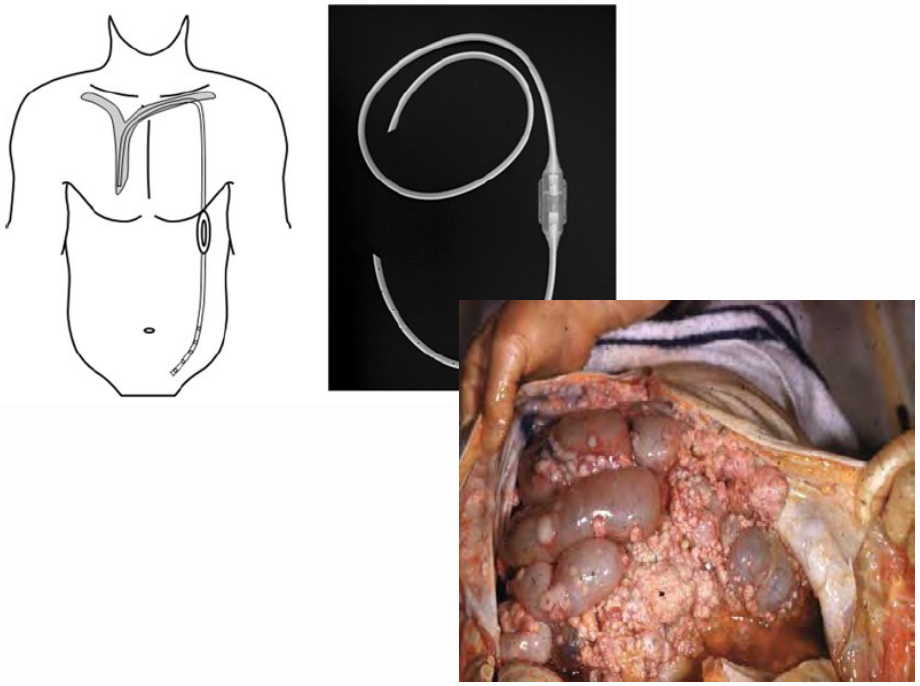
# Exceptions…The Only Sure Thing in Cancer…

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

## Mechanisms of Metastasis in Patients with Peritoneovenous Shunts (PVS)

- Performed peritoneovenous shunting on **29 patients** to alleviate abdominal pain and distension in malignant ascites due to **inoperable cancer.**

- **15** that were autopsied **did not** develop metastases even after 27 months of survival.



***"The findings in female patient D. J. are particularly interesting in this regard, because the cells of her tumor had already shown capability to form blood-borne metastases (in the liver and vertebrae) before the shunt was inserted, yet did not form any elsewhere even after the cells were directly infused into the systemic veins."-***

Tarin et. al. *Cancer Research*, 1984

# 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?**

**PQD4: What are the mechanistic bases for differences in cancer drug metabolism and toxicity at various stages of life?**

# Then…(2002)




Drew Sheneman, The Star-Ledger, Newark, NJ

# Now…(2014): Moore's Law of Analysts?

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~100

Cancer genome characterization centres: Broad Institute/Dana-Farber Cancer Institute Gad Getz[38], Wendy Winckler[38,72,73], Roel G. W. Verhaak[38,72,73], Michael S. Lawrence[38], Michael O'Kelly[38], Jim Robinson[38], Gabriele Alexe[38], Rameen Beroukhim[38,39,73], Scott Carter[38], Derek Chiang[38,72], Josh Gould[38], Supriya Gupta[38], Josh Korn[38], Craig Mermel[38,72], Jill Mesirov[38], Stefano Monti[38], Huy Nguyen[38], Melissa Parkin[38], Michael Reich[38], Nicolas Stransky[38], Barbara A. Weir[38,72,73], Levi Garraway[38,39,73], Todd Golub[38,72,73], Matthew Meyerson[38,39,73]. **Harvard Medical School/Dana-Farber Cancer Institute** Lynda Chin[22,24,25], Alexei Protopopov[24], Jianhua Zhang[24], Ilana Perna[24], Sandy Aronson[25], Narayanan Sathiamoorthy[25], Georgia Ren[24], Jun Yao[24], W. Ruprecht Wiedemeyer[72], Hyunsoo Kim[26], Sek Won Kong[27,28], Yonghong Xiao[29], Isaac S. Kohane[26,27,29], Jon Seidman[10], Peter J. Park[26,27,29], Raju Kucherlapati[26]. **Johns Hopkins/University of Southern California** Peter W. Laird[30], Leslie Cope[30], James G. Herman[31], Daniel J. Weisenberger[21], Fei Pan[31], David Van Den Berg[30], Leander Van Neste[34], Joo Mi Yi[33], Kornel E. Schuebel[33], Stephen B. Baylin[31]. **HudsonAlpha Institute/Stanford University** Devin M. Absher[35], Jun Z. Li[35], Audrey Southwick[35], Shannon Brady[37], Amita Aggarwal[35], Tisha Chung[35], Gavin Sherlock[37], James D. Brooks[36], Richard M. Myers[35]. **Lawrence Berkeley National Laboratory** Paul T. Spellman[39], Elizabeth Purdom[40], Lakshmi R. Jakkula[39], Anna V. Lapuk[39], Henry Marr[39], Shannon Dorton[39], Yoon Gi Choi[41], Ju Han[39], Aparna Ray[39], Victoria Wang[40], Steffen Durinck[39], Mark Robinson[42], Nicholas J. Wang[39], Karen Vranizan[41], Vivian Peng[41], Eric Van Name[41], Gerald V. Fontenay[39], John Ngai[43], John G. Conboy[39], Bahram Parvin[39], Heidi S. Feiler[39], Terence P. Speed[40,42], Joe W. Gray[39]. **Memorial Sloan-Kettering Cancer Center** Cameron Brennan[44], Nicholas D. Socci[44], Adam Olshen[45], Barry S. Taylor[44,46], Alex Lash[44], Nikolaus Schultz[44], Boris Reva[44], Yevgeniy Antipin[44], Alexey Stukalov[44], Benjamin Gross[44], Ethan Cerami[44], Wei Qing Wang[44], Li-Xuan Qin[45], Venkatraman E. Seshan[45], Liliana Villafania[47], Magali Cavatore[47], Laetitia Borsu[48], Agnes Viale[47], William Gerald[48], Chris Sander[44], Marc Ladanyi[48]. **University of North Carolina, Chapel Hill** Charles M. Perou[49,50], D. Neil Hayes[49], Michael D. Topal[50,52], Katherine A. Hoadley[49], Yuan Qi[51], Sai Balu[52], Yan Shi[52], Junyuan Wu[52]

**Comprehensive genomic characterization defines human glioblastoma genes and core pathways**

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Cancer genome characterization centres: Broad Institute/Dana-Farber Cancer Institute M. Meyerson[35,47,48], W. Winckler[47], G. Getz[37], R. G. W. Verhaak[35,47], S. L. Carter[35,47], C. H. Mermel[35,47], G. Saksena[35], H. Nguyen[35], R. C. Onofrio[35], M. S. Lawrence[35], D. Hubbard[35,47,48], S. Gupta[35], A. Crenshaw[35], A. H. Ramos[35,47,48], K. Ardlie[35], **Harvard Medical School** L. Chin[49,50], A. Protopopov[49], Jianhua Zhang[49], T. M. Kim[51], I. Perna[49], Y. Xiao[49], H. Zhang[49], G. Ren[49], N. Sathiamoorthy[50], R. W. Park[49], E. Lee[51], P. J. Park[51,53], R. Kucherlapati[54]. **HudsonAlpha Institute/Stanford University** D. M. Absher[55], L. Waite[55], G. Sherlock[56], J. D. Brooks[57], J. Z. Li[58], J. Xu[58], R. M. Myers[55]. **University of Southern California/Johns Hopkins University** P. W. Laird[59], L. Cope[60], J. G. Herman[61], H. Shen[59], D. J. Weisenberger[59], H. Noushmehr[59], F. Pan[59], T. Triche Jr[59], B. P. Berman[59], D. J. Van Den Berg[59], J. Buckley[59], S. B. Baylin[61]; **Lawrence Berkeley National Laboratory** P. T. Spellman[62], E. Purdom[63], P. Neuvial[62], H. Bengtsson[62], L. R. Jakkula[62], S. Durinck[62], J. Han[62], S. Dorton[62], H. Marr[62], Y. G. Choi[64], V. Wang[65], N. J. Wang[62], J. Ngai[64], J. G. Conboy[62], B. Parvin[62], H. S. Feiler[62], T. P. Speed[62,66], J. W. Gray[62]. **Memorial Sloan-Kettering Cancer Center** D. A. Levine[8], N. D. Socci[67], Y. Liang[67], B. S. Taylor[67], N. Schultz[67], J. Borsu[68], A. E. Lash[67], C. Brennan[69], A. Viale[67], C. Sander[67], M. Ladanyi[68]; **University of North Carolina at Chapel Hill** K. A. Hoadley[70,72,73], S. Meng[73], Y. Du[73], Y. Shi[73], L. Li[73], Y. J. Turman[73], D. Zang[73], E. B. Helms[73], S. Balu[73], X. Zhou[75], J. Wu[73], M. D. Topal[72,73], D. N. Hayes[73,74], C. M. Perou[71,72,73]

Genome data analysis centres: Broad Institute G. Getz[35], D. Voet[35], G. Saksena[35], Junihua Zhang[35], H. Zhang[35], C. J. Wu[35], S. Shukla[35], K. Cibulskis[35,36], M. S. Lawrence[35], A. Sivachenko[35], R. Jing[35], R. W. Park[34,51], Y. Liu[35], P. J. Park[51], M. Noble[35], L. Chin[35,49,50]. **Johns Hopkins University** H. Carter[76], D. Kim[76], R. Karchin[76]. **Lawrence Berkeley National Laboratory** P. T. Spellman[62], E. Purdom[63], P. Neuvial[62], H. Bengtsson[62], S. Durinck[62], J. Han[62], J. C. Korkola[62], L. M. Heiser[62], R. J. Cho[62], Z. Hu[62], B. Parvin[62], T. P. Speed[62,66], J. W. Gray[62]. **Memorial Sloan-Kettering Cancer Center** N. Schultz[67], E. Cerami[67], B. S. Taylor[67], A. Olshen[76], B. Reva[67], Y. Antipin[67], R. Shen[76], P. Mankoo[67], R. Sheridan[67], G. Cinello[67], W. K. Chang[67,77], J. A. Bernanke[78], L. Borsu[68], D. A. Levine[8], M. Ladanyi[68]. **C. Sander[67]; University of California Santa Cruz/Buck Institute** D. Haussler[79,80], C. C. Benz[81], J. M. Stuart[79], S. C. Benz[79], J. Z. Sanborn[79], C. J. Vaske[79,82], J. Zhu[79], C. Szeto[79], G. K. Scott[81], C. Yau[81]; **University of North Carolina at Chapel Hill** K. A. Hoadley[71,72,73], Y. Du[73], S. Balu[73], D. N. Hayes[72,74], C. M. Perou[71,72,73], M. D. Wilkerson[73]; **The University of Texas MD Anderson Cancer Center** N. Zhang[83], R. Akbani[83], K. A. Baggerly[83], W. K. Yung[84], G. B. Mills[20,83], J. N. Weinstein[20,83]

**Integrated genomic analyses of ovarian carcinoma**

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**Disease working group** Matthew Meyerson[1,2,6], Stephen B. Baylin[29], Ramaswamy Govindan[30], Rehan Akbani[83], Ijeoma Azodo[58], David Beer[54], Ron Bose[30], Lauren A. Byers[30], David Carbone[30], Li-Wei Chang[75], Derek Chiang[1,3,5], Andy Chu[1], Elizabeth Chun[1], Eric Collisson[28], Leslie Cope[29], Chad J. Creighton[41], Ludmila Danilova[29], Li Ding[32], Gad Getz[1,5], Peter S. Hammerman[1,2], D. Neil Hayes[23,28], Bryan Hernandez[1], James G. Herman[29], John Heymach[30], Cristiane Ida[43], Marcin Imielinski[1,6], Bruce Johnson[2], Igor Jurisica[57], Jacob Kaufman[56], Farhad Kosari[53], Raju Kucherlapati[11,12], David Kwiatkowski[2], Marc Ladanyi[17,18], Michael S. Lawrence[1], Christopher A. Maher[32], Andy Mungall[7], Sam Ng[58], William Pao[59], Martin Peifer[28,29], Robert Penny[31], Gordon Robertson[7], Valerie Rusch[60], Chris Sander[16], Nikolaus Schultz[16], Ronglai Shen[61], Jiil Siegfried[61], Aileen Sinha[16], Andrey Sivachenko[1], Carrie Sougnez[4], Dominik Stoll[7], Joshua Stuart[36], Roman K. Thomas[58,59,62], Sandra Tomaszek[58], Ming-Sound Tsao[56], William D. Travis[62], Charles Vaske[36], John N. Weinstein[42,55], Daniel Weisenberger[40], David Wheeler[63], Dennis A. Wigle[54], Matthew D. Wilkerson[74], Christopher Wilks[36], Ping Yang[53], Jianjua John Zhang[2,10]

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**Comprehensive genomic characterization of squamous cell lung cancers**

The Cancer Genome Atlas Network*

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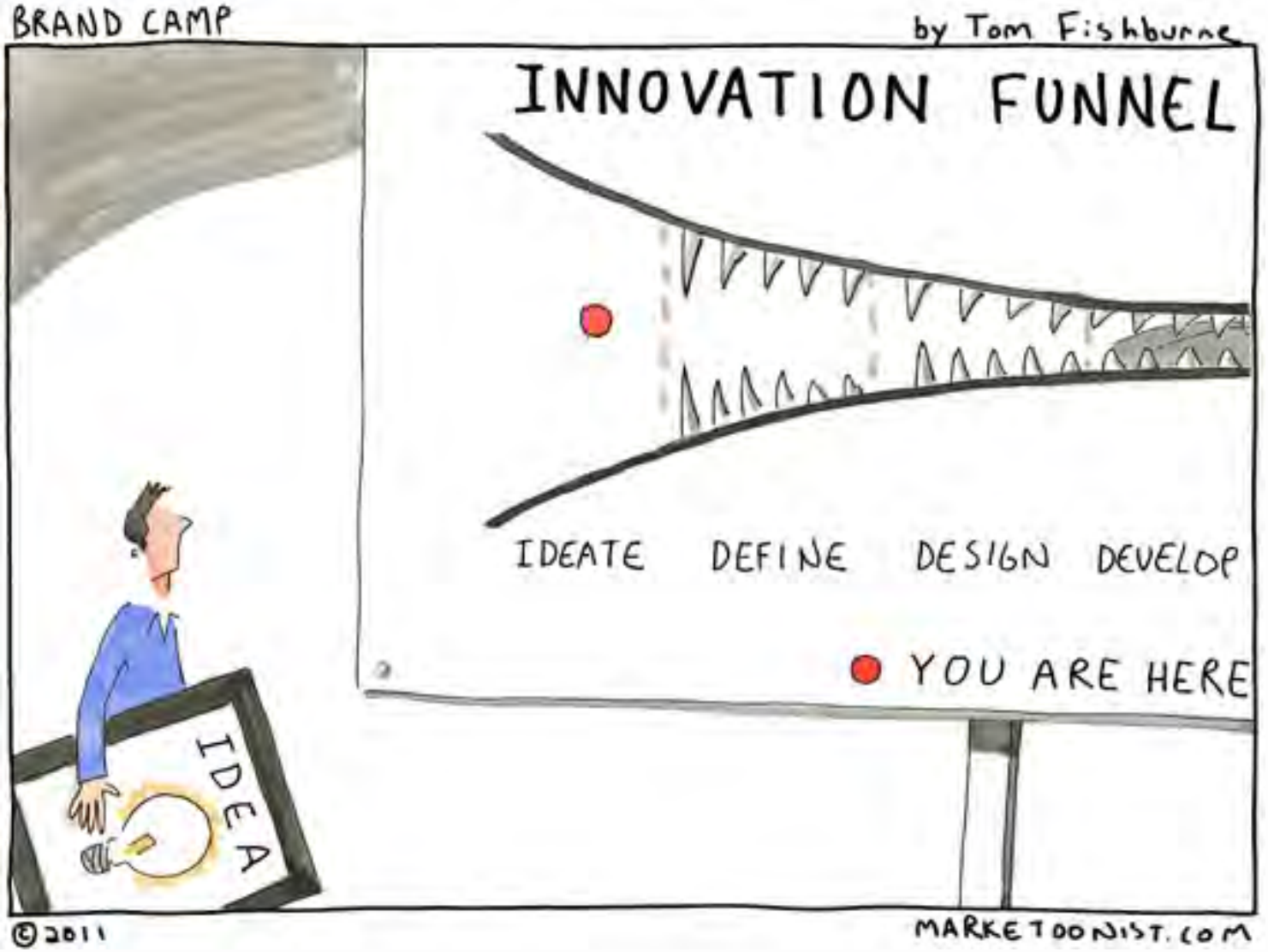
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# Upcoming Funding Opportunities

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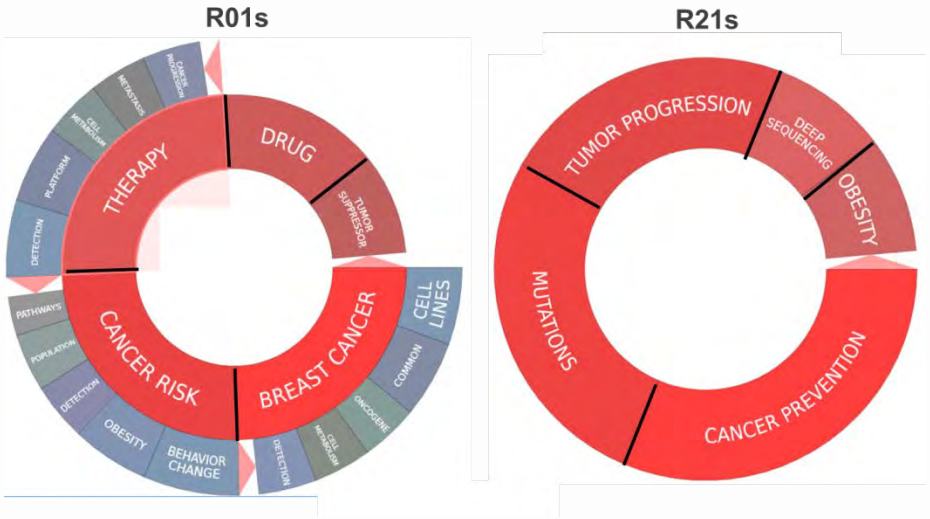


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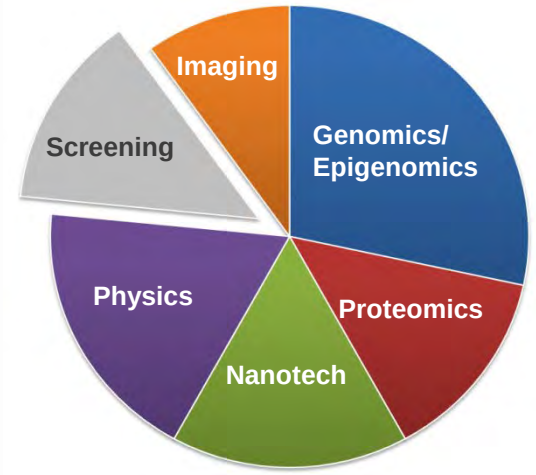
## *Provocative Questions ($30M)*

**Due Date 06/20/14**

*PQ Program Director*
emily.greenspan@nih.gov

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**Due Dates 05/20 and 9/18/14**

*IMAT Program Director*
anthony.dickherber@nih.gov

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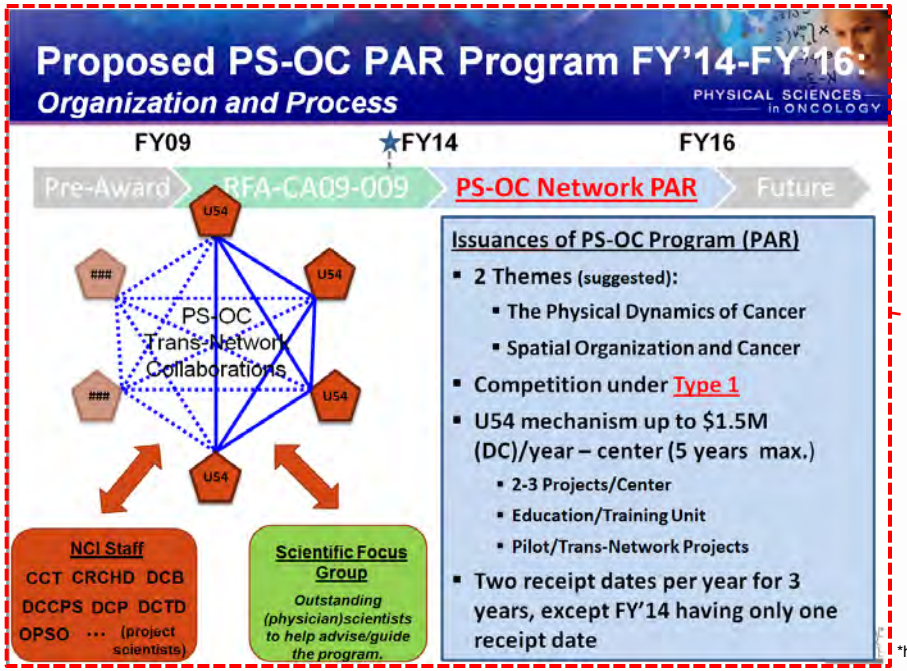
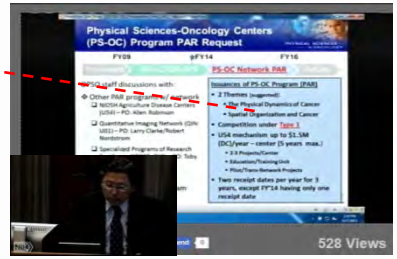
larry.nagahara@nih.gov




Discussion from NCI Board of Scientific Advisors (Nov 2013)

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## NCI Alliance for Nano Program (Approved 3/2014)


NCI Alliance for Nanotechnology in Cancer

Piotr Grodzinski, PhD
piotr.grodzinski@nih.gov

Stephanie Morris, PhD
stephanie.morris@nih.gov

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- **Research Answers to NCIs Provocative Questions- Group A-E (R01)**
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- **Research Answers to NCIs Provocative Questions- Group A-E (R21)**
  - Due Date: 06/20/2014 RFA-CA-13-017, 019, 021, 023, 025 ($0.5-1M each RFA, $2.5M - $5M total)
- **Early-Stage Innovative Molecular Analysis Technology Development (R21)**
  - Due Date: 05/20/2014 and 09/18/2014 RFA-CA-14-003 ($5M)
- **Validation and Advanced Development of Emerging Molecular Analysis Technologies (R33)**
  - Due Date: 05/20/2014 and 09/18/2014 RFA-CA-14-004 ($4M)
- **Early-Stage Development of Innovative Technologies for Biospecimen Science (R21)**
  - Due Date: 05/20/2014 and 09/18/2014 RFA-CA-14-005 ($0.8M)
- **Validation and Advanced Development of Emerging Technologies for Biospecimen Science (R33)**
  - Due Date: 05/20/2014 and 09/18/2014 RFA-CA-14-006 ($0.7M)

# Relevant NCI Funding Opportunities

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

- **Innovative Molecular Analysis Technology Development for Cancer Research and Clinical Care (R43/R44)**
  - Due Date: 5/28/2014 and 11/4/2014 PAR-13-327
- **Early-Stage Development of Informatics Technology (U01)**
  - Due Date: 6/18/2014 and 11/18/2014 PAR-12-288
- **Advanced Development of Informatics Technology (U24)**
  - Due Date: 6/18/2014 and 11/18/2014 PAR-13-294
- **Imaging and Biomarkers for Early Cancer Detection (R01)**
  - Due Date: 7/10/2014 and 12/11/2014 PAR-13-189
- **Image-guided Drug Delivery in Cancer (R01)**
  - Due Date: 6/19/2014 and 11/19/14 PAR-13-185
- **Biomarkers for Early Detection of Hematopoietic Malignancies (R21/R01)**
  - Due Date: 6/16/2014 (R21) & 7/5/2014 (R01) [Standard] PA-12-220 (R21) & PA-12-221 (R01)

# Acknowledgements/Thanks to the "Secret Ingredients"

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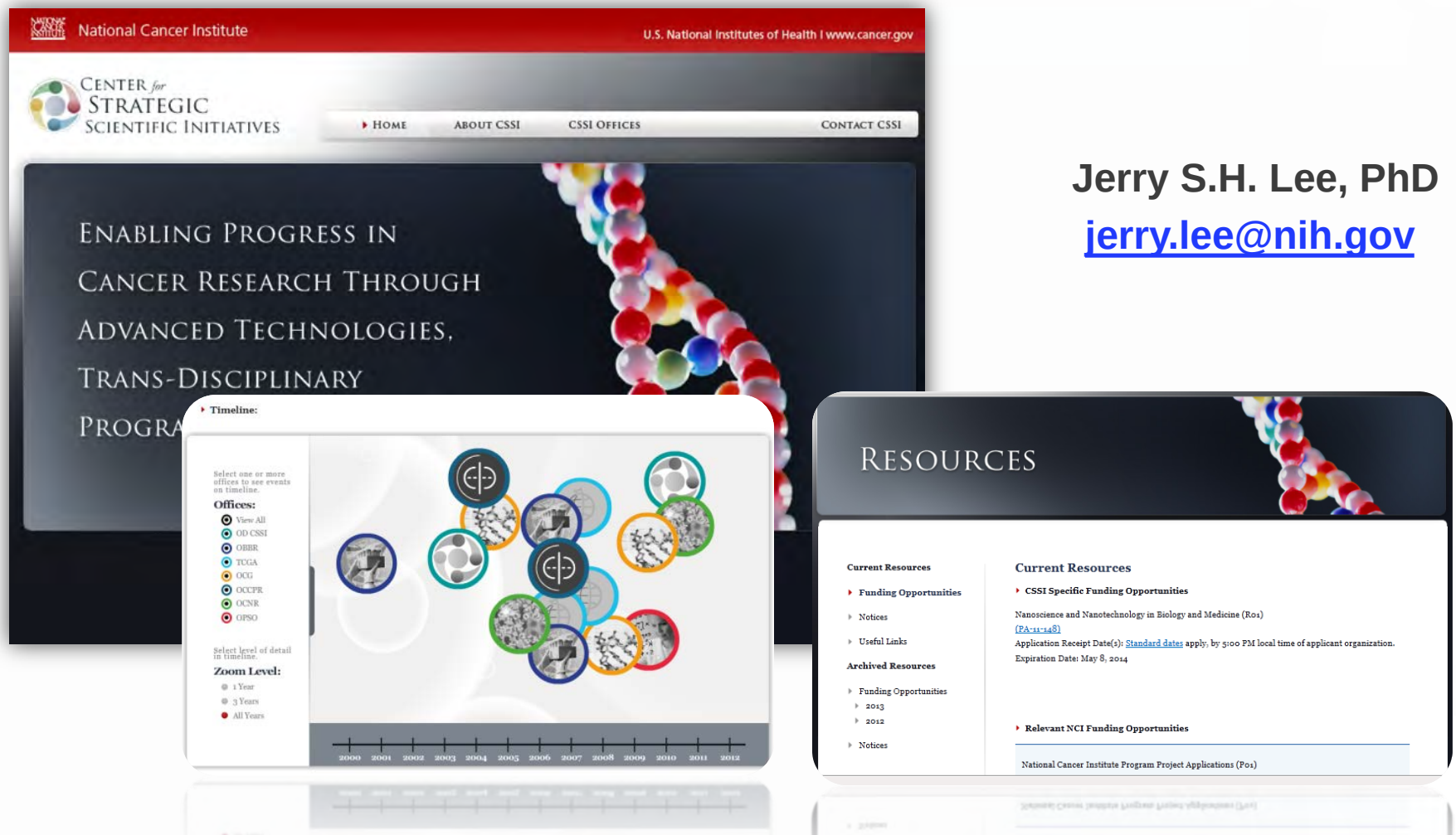


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