Advancing Innovation and Convergence In Cancer Research

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Office of the Director, National Cancer Institute, NIH

Meeting Global Challenges: German-US Innovation Policy

National Academy of Science and DIW Berlin

Berlin, Germany
May 25, 2011

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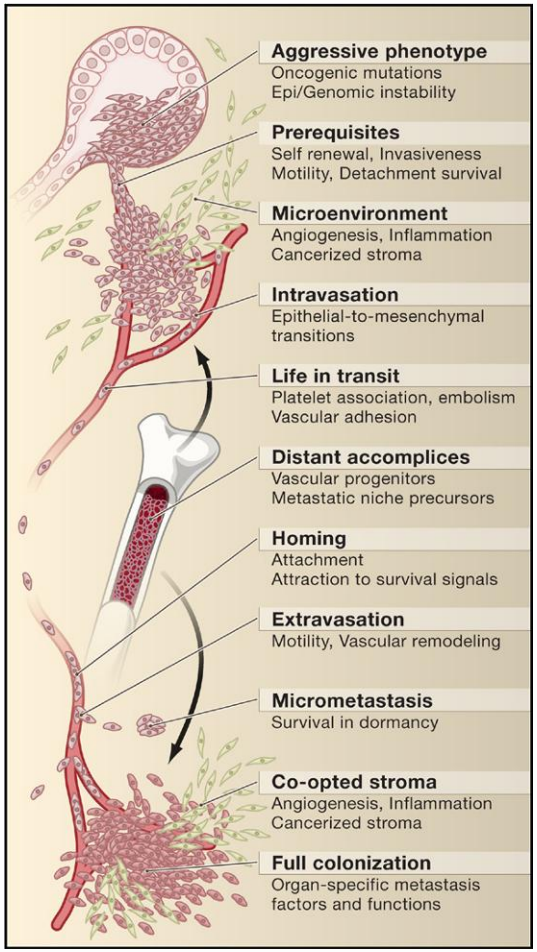
Advisers to the Nation on Science, Engineering, and Medicine

DIW BERLIN

NCI Alliance for Nanotechnology in Cancer | OBBR Office of Biorepositories and Biospecimen Research | PHYSICAL SCIENCES in ONCOLOGY | Office of Cancer Genomics | CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER | The Cancer Genome Atlas

What is It?
Tumor, Cancer, and Metastasis

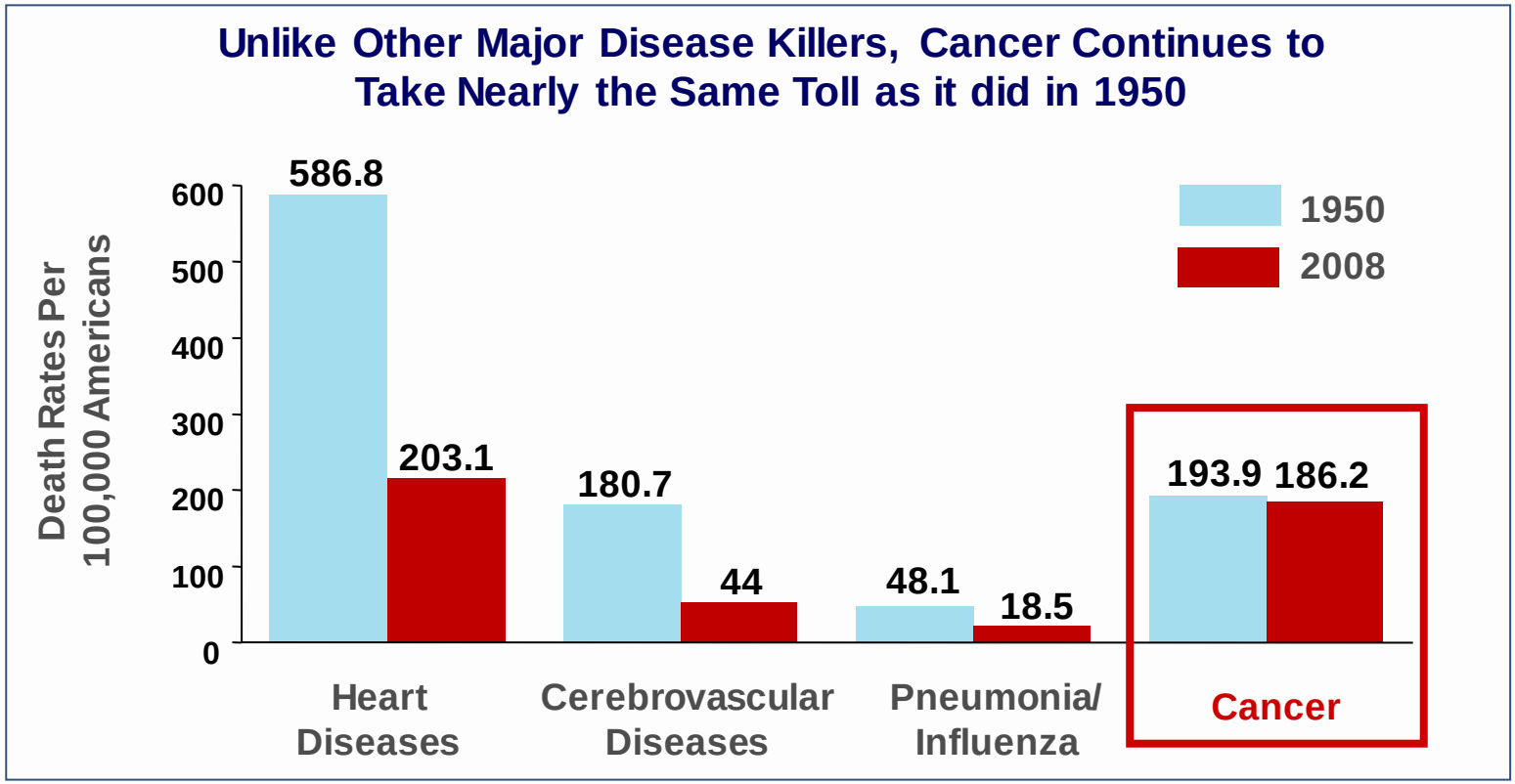


Site	All stages	Local	Regional	Distant
Breast (female)	86.6	97.0	78.7	23.3
Colon and rectum	62.3	90.1	65.5	9.2
Liver	6.9	16.3	6.0	1.9
Lung and bronchus	14.9	48.7	16.0	2.1
Melanoma	89.6	96.7	60.1	13.8
Ovary	53.0	94.7	72.0	30.7
Pancreas	4.4	16.6	6.8	1.6
Prostate	97.5	100.0	--	34.0
Testis	95.5	99.1	95.0	73.1

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

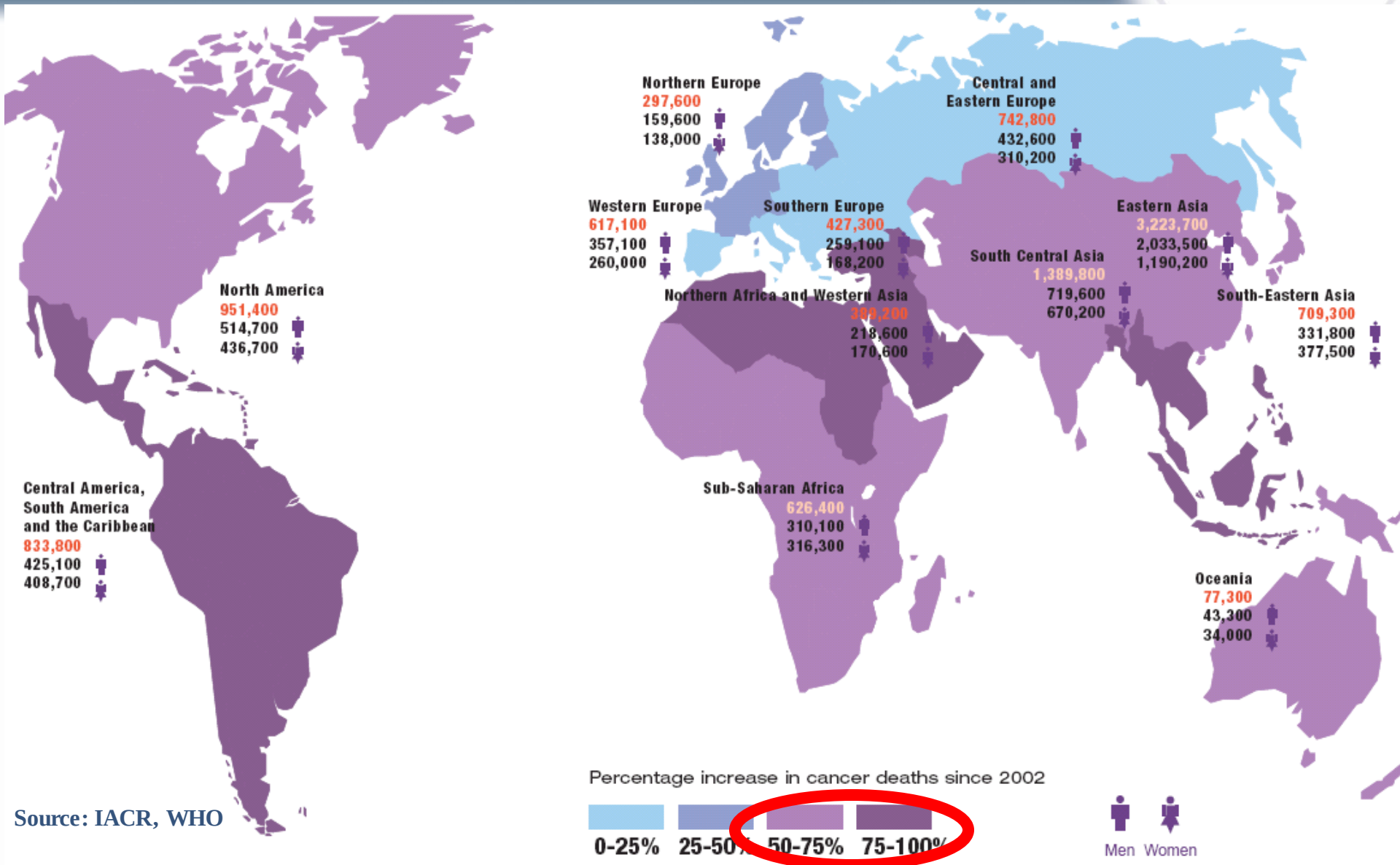
Reality: In the U.S., Cancer Continues to Represent an Enormous Burden

- **569,490** Americans died of cancer in 2010
- **1,529,560** Americans will be diagnosed with cancer this year
- **$124.6 billion** in 2010 for cancer healthcare costs



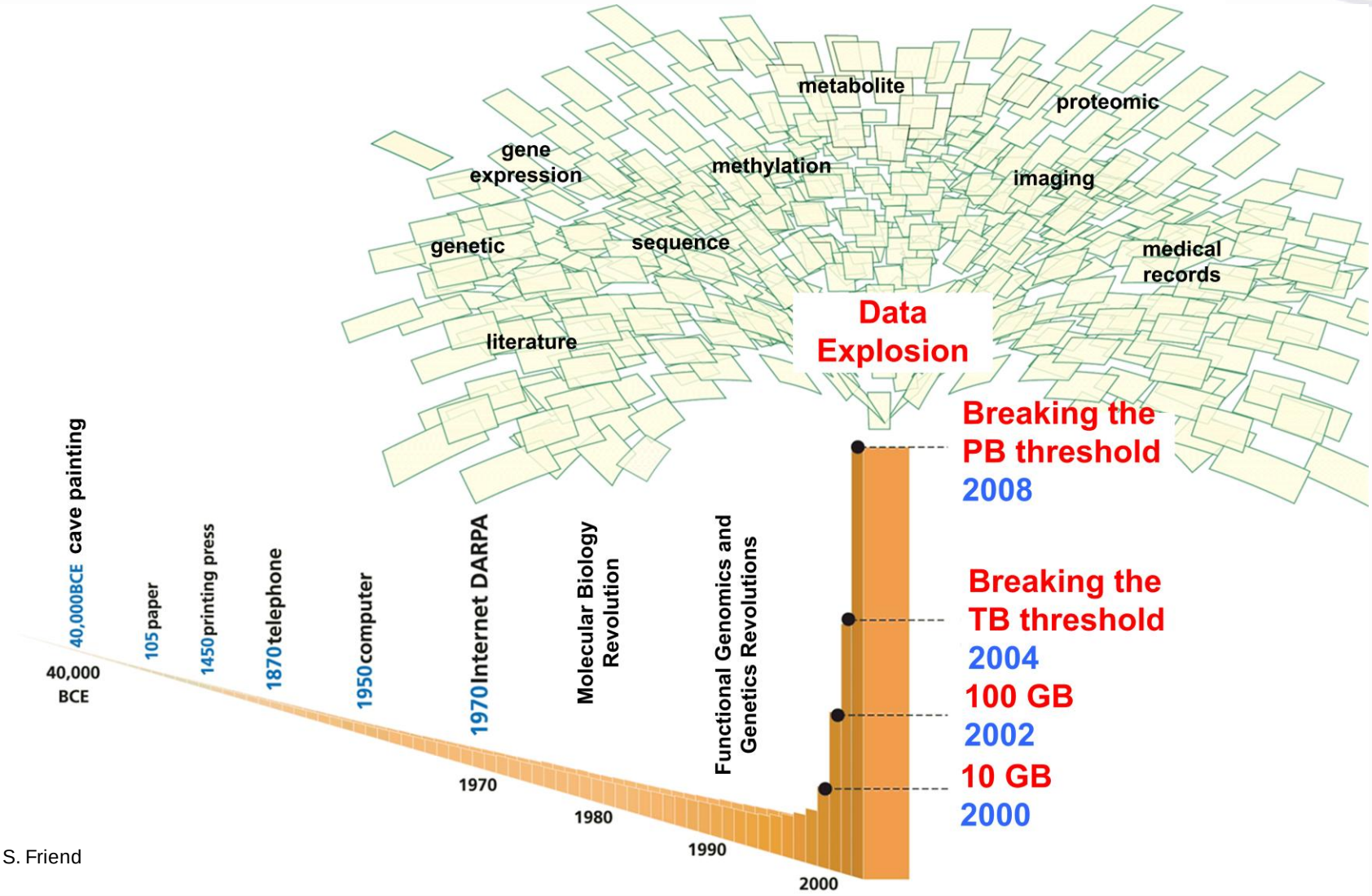
Source for 2010 deaths and diagnoses: American Cancer Society (ACS) 2010 Cancer Facts & Figures; Atlanta, Georgia
Source for 2008 age-adjusted death rate: National Center for Health Statistics, NCHS Public-use file for 2008 deaths.

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



Source: IACR, WHO

Unprecedented Amount of Scientific Knowledge: Omics(ssss)



S. Friend

Is More Knowledge Yielding More Solutions for Patients?

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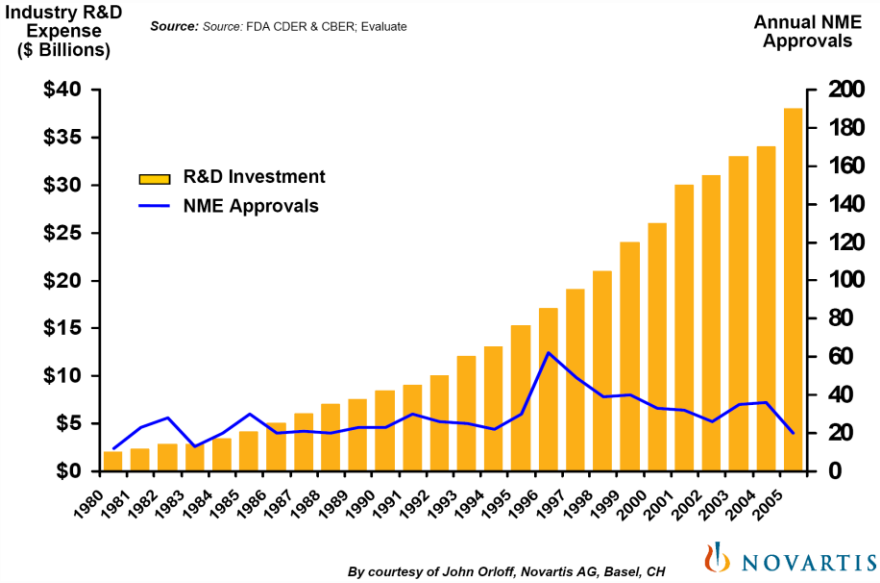
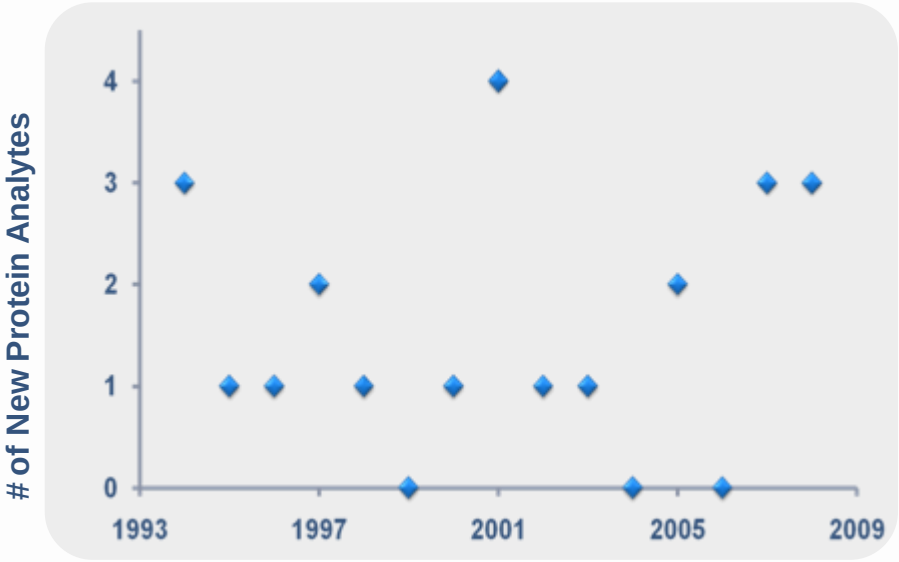
Drugs



Start to Finish

- 10 – 15 years (1,000 – 6,000 volunteers)
- ~ $1 billion

Diagnostic Biomarkers



- Averaging 1.5 FDA approvals per year
- 1000's of samples

Maybe…but can it be more efficient?

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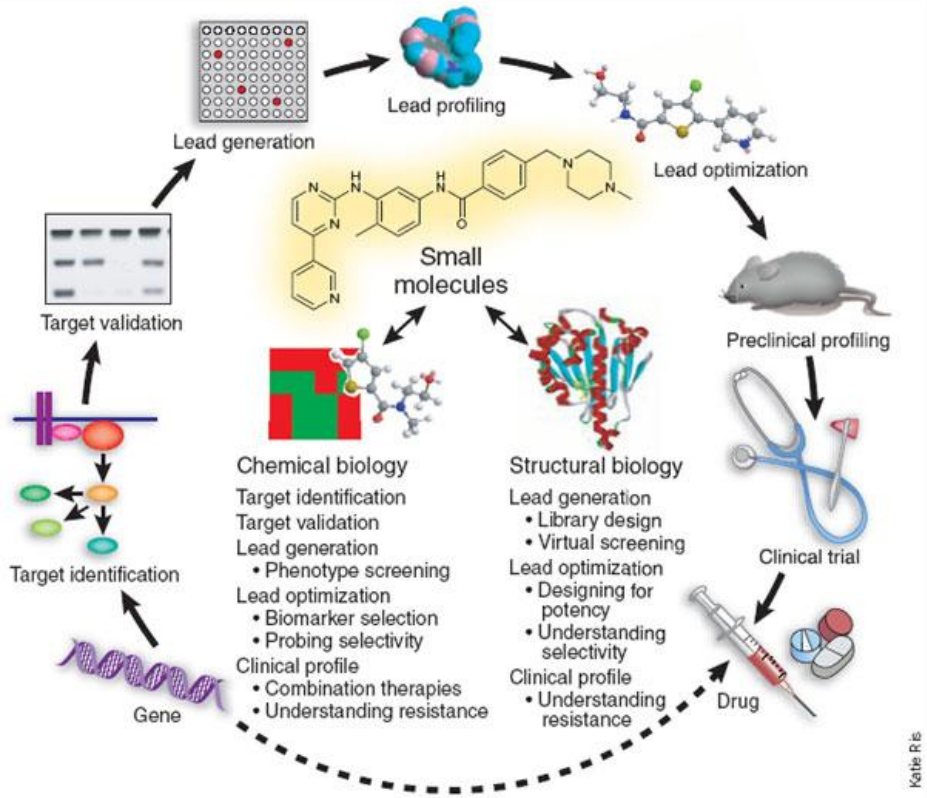
Leigh Anderson, Clin Chem (2010) 56: 177-185

Translation Pace: How To Break Out of Current Paradigm?



Turning the Crank…

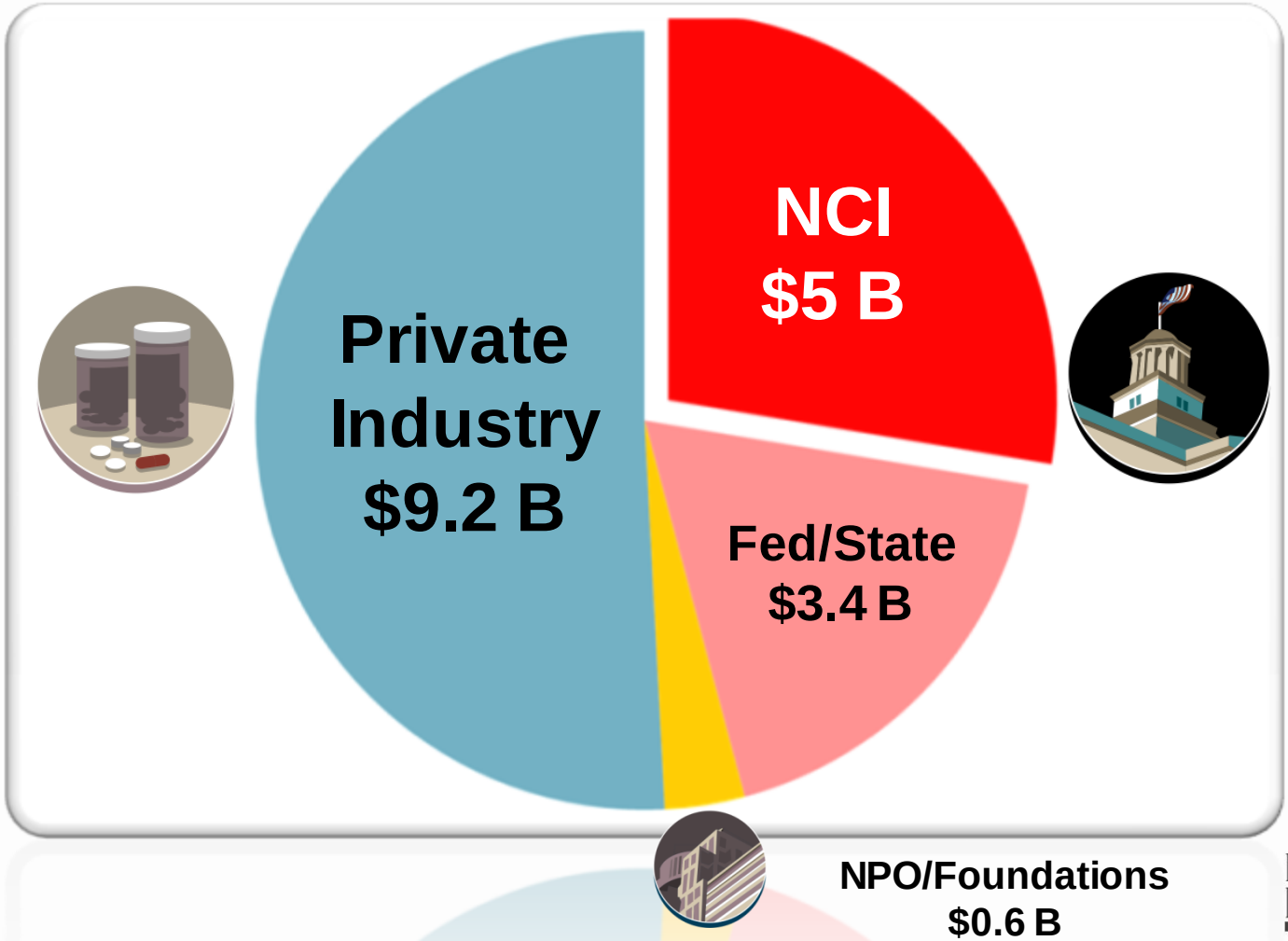
Key Needs (from community)

- Standards and protocols
- Real-time, public release of data
- Multi-disciplinary teams and environment
- Team members with multi-disciplinary **training**

The potential to transform cancer drug discovery and diagnostics

National Cancer Program: Stakeholders

~$18 B per year



NCAB Working Group Report, 2010

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

Acting Director
Douglas Lowy, MD

CENTER *for* STRATEGIC SCIENTIFIC INITIATIVES

Deputy Director
Jerry S.H. Lee, PhD

PHYSICAL SCIENCES in ONCOLOGY

Cancer Target Discovery & Development (CTD²)

CLINICAL PROTEOMIC TECHNOLOGIES for CANCER

IMAT Innovative Molecular Analysis Technologies

THE CANCER GENOME ATLAS

NCI Alliance for Nanotechnology in Cancer

caHUB The Cancer Human Biobank

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**…"

Good Idea + **Unique Good Idea Implementation** ⇒ **Innovation** ⇑⇑ **Potential**

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First Step (-back): Cancer & Genes- Take a Page from Engineers?

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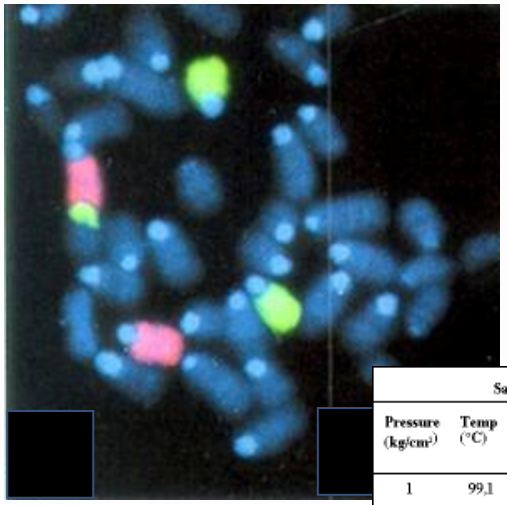
Disease of Genomic Alterations

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



Pressure (kg/cm²)	Temp (°C)	Saturated steam: Vapour enthalpy (kcal/kg)	Saturated steam: Specific volume (m³/kg)	Superheated 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

- **Systematic identification of all genomic chang**
- **Repeat for all cancers**
- **Make it publically available**

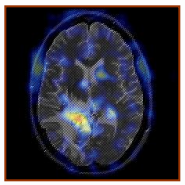
TCGA: Connecting Multiple Sources, Experiments, and Data Types

Center for Strategic Scientific Initiatives

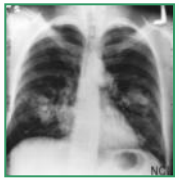
The Cancer Genome Atlas

Three Cancers- Pilot

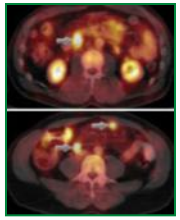
glioblastoma multiforme (brain)



squamous carcinoma (lung)



serous cystadenocarcinoma (ovarian)



Biospecimen Core Resource with more than 13 Tissue Source Sites

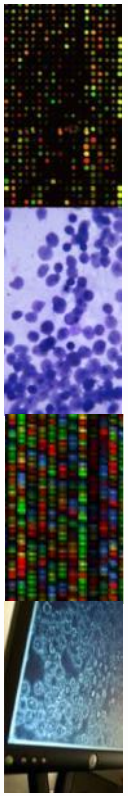
7 Cancer Genomic Characterization Centers

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



National Cancer Institute

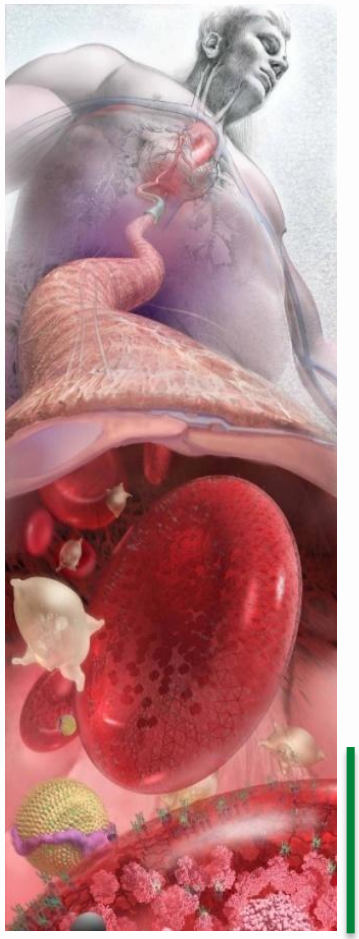
National Cancer Institute | National Human Genome Research Institute

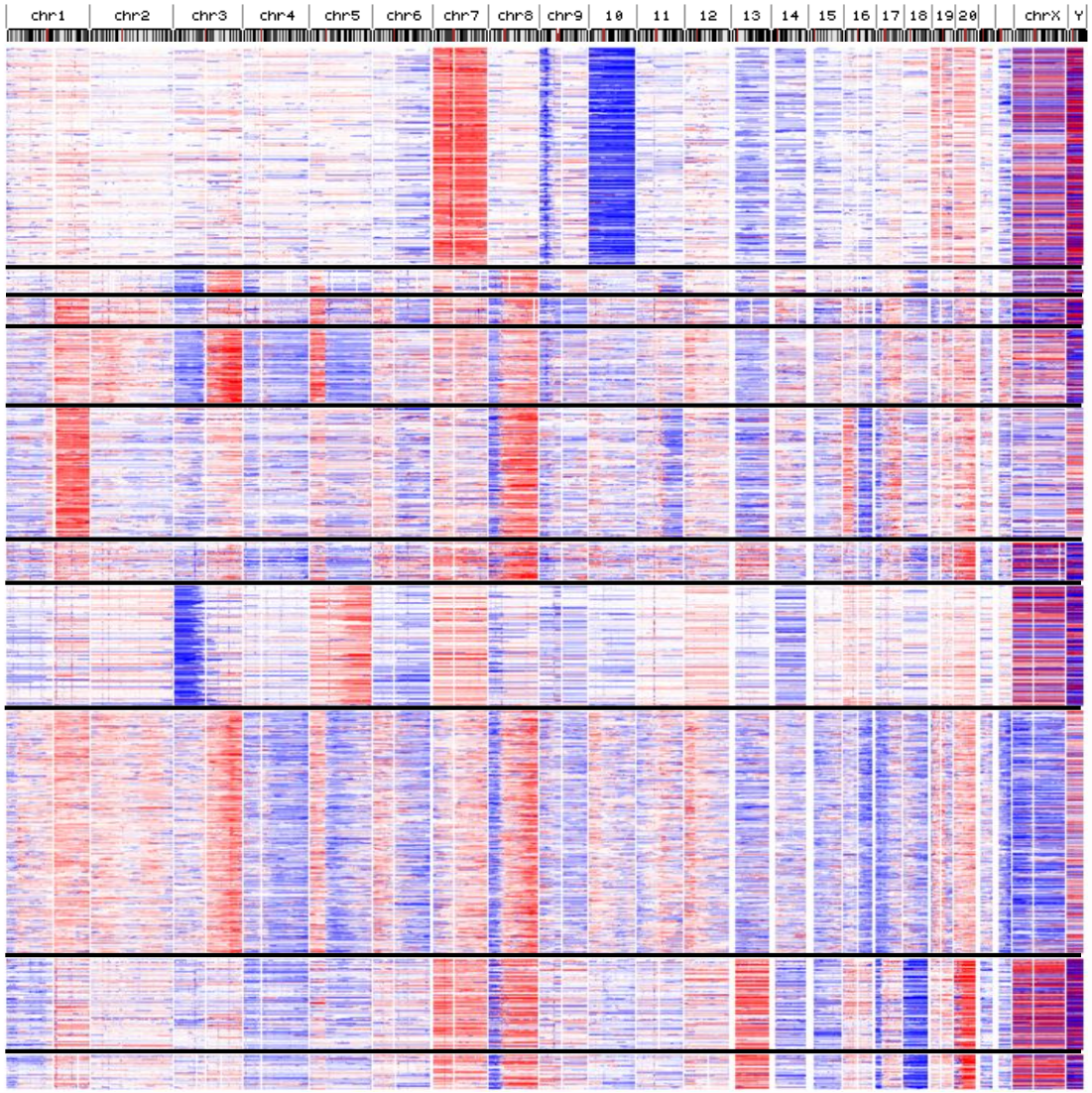
The Cancer Genome Atlas Data Portal

Understanding genomics to improve cancer care

TCGA Home | Contact Us | For the Media

Center for Strategic Scientific Initiatives





Glioblastoma:	470
Head & neck:	51
Lung adeno:	57
Lung squamous:	159
Breast carcinoma:	180
Stomach adeno:	84
Kidney clear carc:	260
Ovarian serous:	525
Colon adeno:	198
Rectum carcinoma:	74

Source: UCSC Cancer Genomic Heatmaps (CopyNumber SNP6). May 2011

Unanticipated Innovations of TCGA: Human Interactions

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Mid- 2008

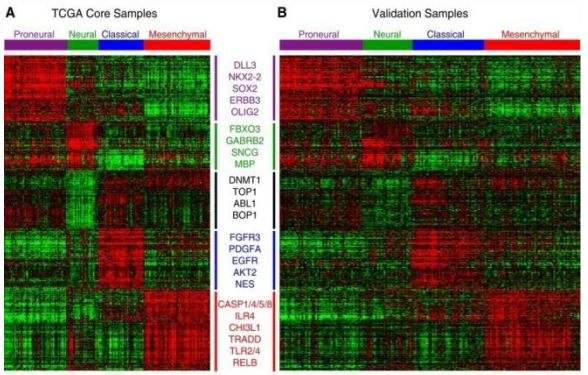
- Reference cancer genome for GBM
- Single author paper (TCGA Network)
  - 300+ authors
- Unanticipated Scientific Discoveries
  - Hypothesis on a possible resistance mechanism to temozolomide (TMZ)

Comprehensive genomic characterization defines human glioblastoma genes and core pathways

The Cancer Genome Atlas Research Network*

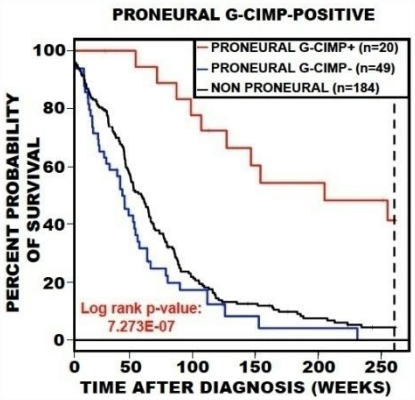
2009

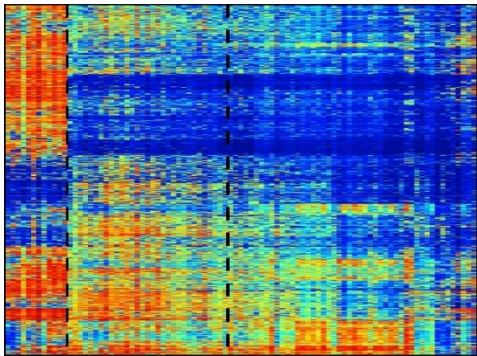
- Gene expression-based classification of GBM
- Response to aggressive therapy differs by subtype- **exclude non-responders**



2010

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

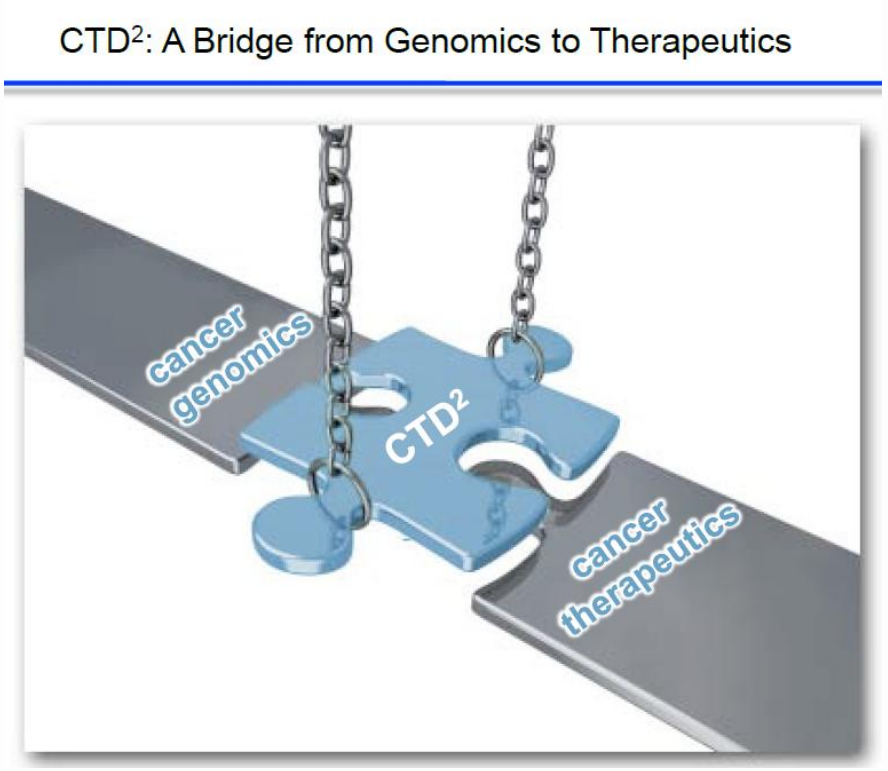




Launching Soon: Cancer Target Discovery and Development Network (CTD²)

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**



Solicitation for U01 will be released summer of 2011

http://grants.nih.gov/grants/guide/notice-files/NOT-CA-11-010.html

National Cancer Institute

Could We Do the Same for Cancer Proteomics: Not Yet…

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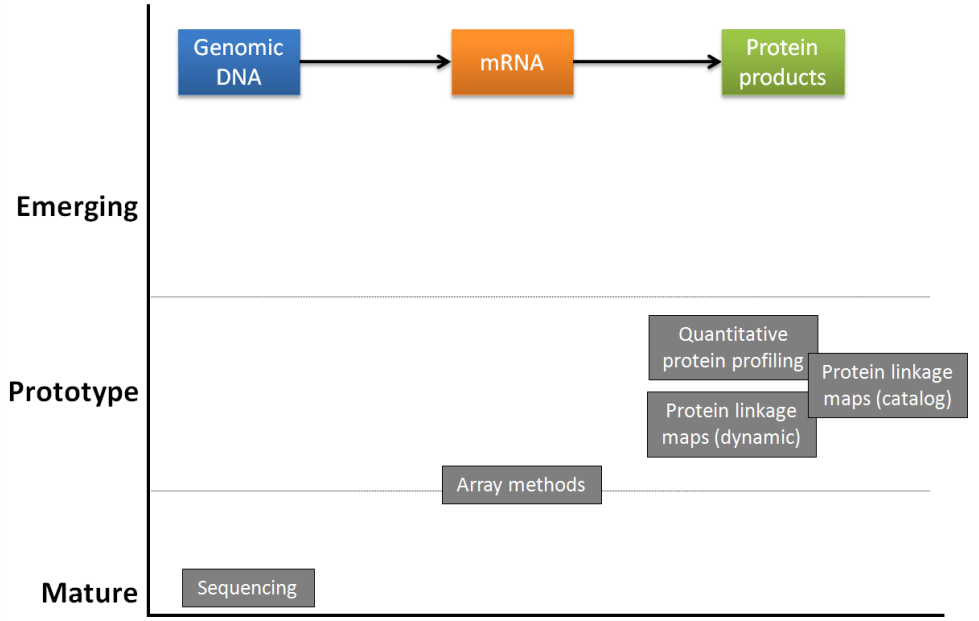
Technologies for Quantitative Analysis



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

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

Clinical Proteomic Technologies for Cancer (CPTAC) Pilot

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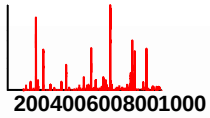
CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

nature biotechnology

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



caTranche

FDA

U.S. National Institutes of Health | www.cancer.gov

ANTIBODY CHARACTERIZATION LABORATORY

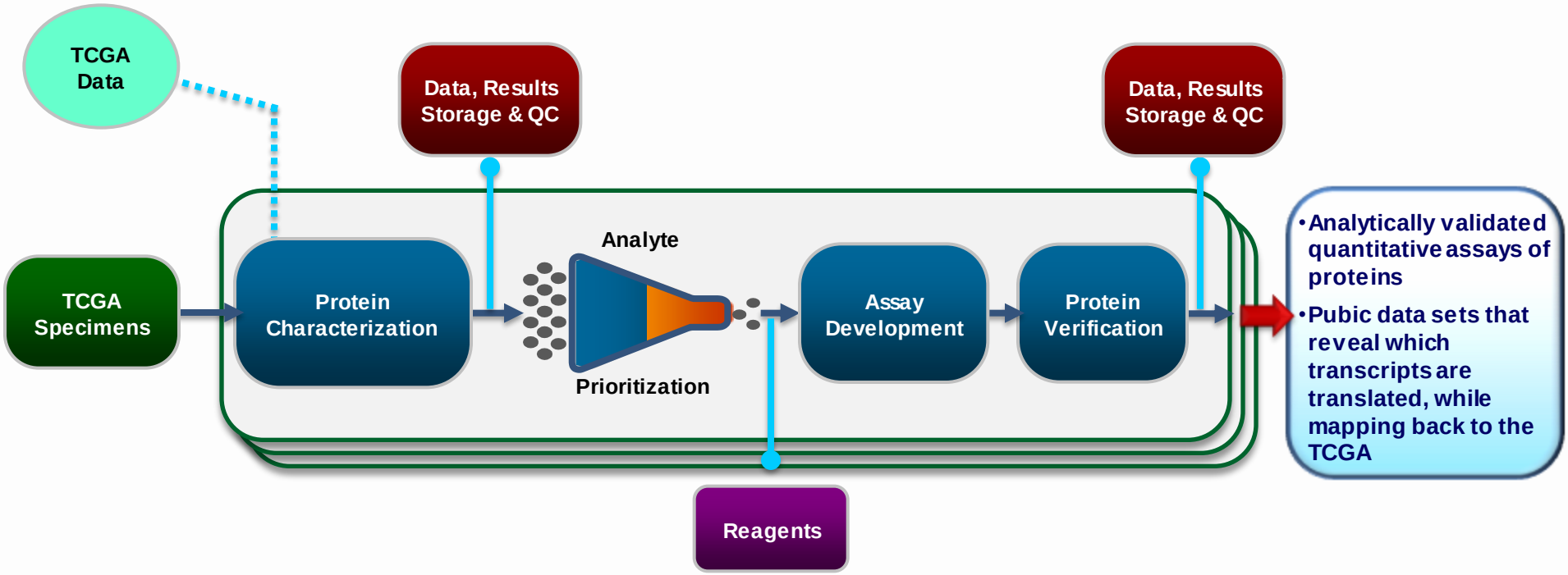
Accomplishments (Highlights)

- First demonstration that MRM is highly reproducible across multiple laboratories and technology platforms
- Development of public data portal of raw mass spec data

Unanticipated Innovations

- **Joint development with FDA of mock 510(k) pre-submission for proteomic platforms**
  - Educate new generation of developers
- **Established Antibody Characterization Laboratory**
  - Provides high quality reagents at minimum cost to community
  - All characterization data posted on public database
  - Industry partners and collaborations

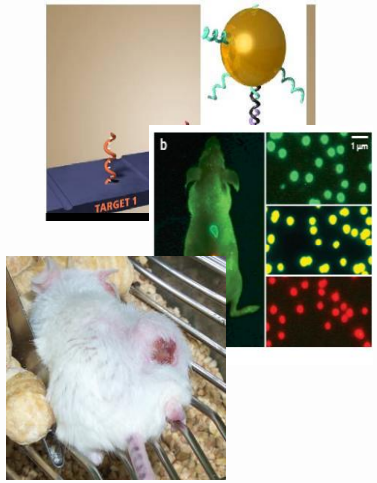
Full Steam Ahead: CPTC Phase 2 Pipeline (Summer '11)

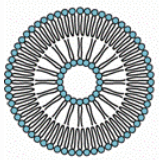


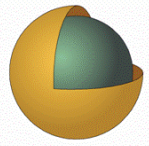
Nanotechnology: Disruptive Innovation for Clinical Oncology?

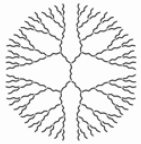
Center for Strategic Scientific Initiatives

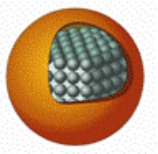
- Combine power of innovation in nano-materials and cancer biology to develop new solutions in cancer
  - Detect Disease *Before* Health Has Deteriorated
    - Sensors
    - Imaging
  - Deliver Therapeutics
    - Local delivery
    - Improved efficacy
    - Post-therapy monitoring
  - Develop Research Tools to Enhance Understanding of the Disease




Liposome


Gold nanoshell


Dendrimer


Quantum Dot

National Cancer Institute

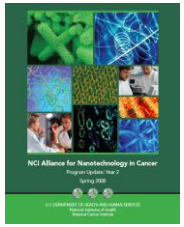
Bringing Nanotechnology to Cancer Research & Oncology: ANC Network

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

Cancer Nanotechnology Plan Published

NCI Alliance for Nanotechnology in Cancer

Phase I (Pilot) Awarded



Evaluation and Update

- Scientific Output
  - Over 600 pubs
- Clinical Translation
  - 50 companies
  - Over 200 patents
  - 8-10 clinical trials

NCI Alliance for Nanotechnology in Cancer

Program Renewed

RFA Released

NCI Alliance for Nanotechnology in Cancer

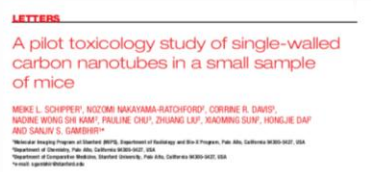
Phase II (Clinical) Kick-Off

NANOTECHNOLOGY CHARACTERIZATION LABORATORY

NCL Launches

2004 2005 2006 2007 2008 2009 2010 2011

Nano Imaging


LETTERS

A pilot toxicology study of single-walled carbon nanotubes in a small sample of mice

MEIKE L. SCHIPPER[1], NOZOMI NAKAYAMA-RATCHFORD[1], CORRINE R. DAVIS[2], NADINE WONG SHI KAM[1], PAULINE CHU[1], ZHUANG LIU[1], XIAOMING SUN[1], HONGJIE DAI[1] AND SANJIV S. GAMBHIR[1,2]*

Nano Diagnostics

Nano Therapy


Vol 464|15 April 2010|doi:10.1038/nature08956 nature

LETTERS

Evidence of RNAi in humans from systemically administered siRNA via targeted nanoparticles

Mark E. Davis[1], Jonathan E. Zuckerman[1], Chung Hang J. Choi[1], David Seligson[2,3], Anthony Tolcher[5], Christopher A. Alabi[1†], Yun Yen[6], Jeremy D. Heidel[7] & Antoni Ribas[2,4]

Basic **Translational** **Pre-Clinical** **Clinical**

Now What? How to Interpret It All? (Who?)

CENTER for STRATEGIC SCIENTIFIC INITIATIVES

LOTS of Quantitative and Reproducible Data (Macro, Micro, and Nano!)

	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

Harness Understanding

"Simple"

"Complex"

Bringing In New Perspectives: Brainstorming with Experts

~300 extramural participants

Consensus Scientific Themes

- Understanding the Physics of Cancer
- Evolution and Evolutionary Theory in Cancer
- Coding, Decoding and Transfer of Information in Cancer
- "De-convoluting" the Complexity of Cancer

Consensus Needs

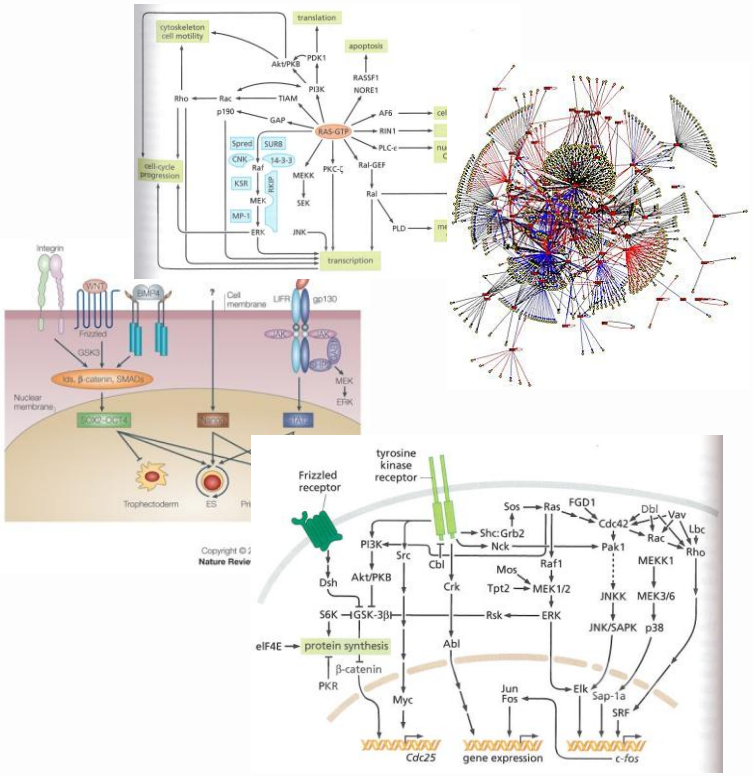
- Establish trans-disciplinary physical sciences-oncology centers
- Centers composed of integrated physical sciences-oncology teams
- Focus on theme(s) for center framework
- Centers led by physical scientists with co-investigator(s) from cancer biology/oncology

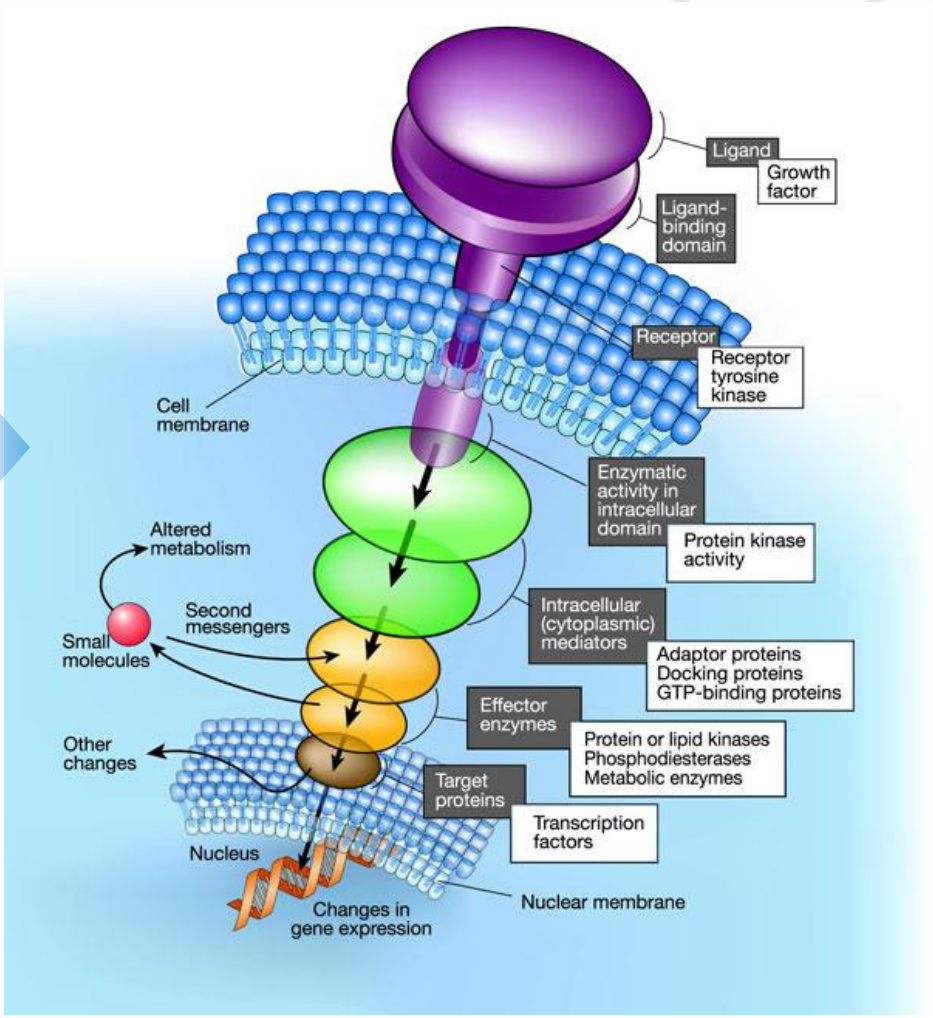
Center for Strategic Scientific Initiatives

National Cancer Institute

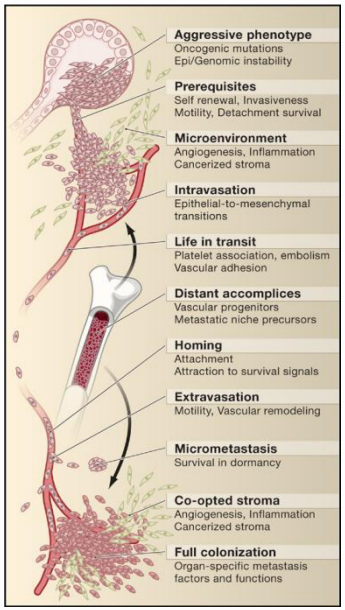
Critical to Think in Terms of Space and Time

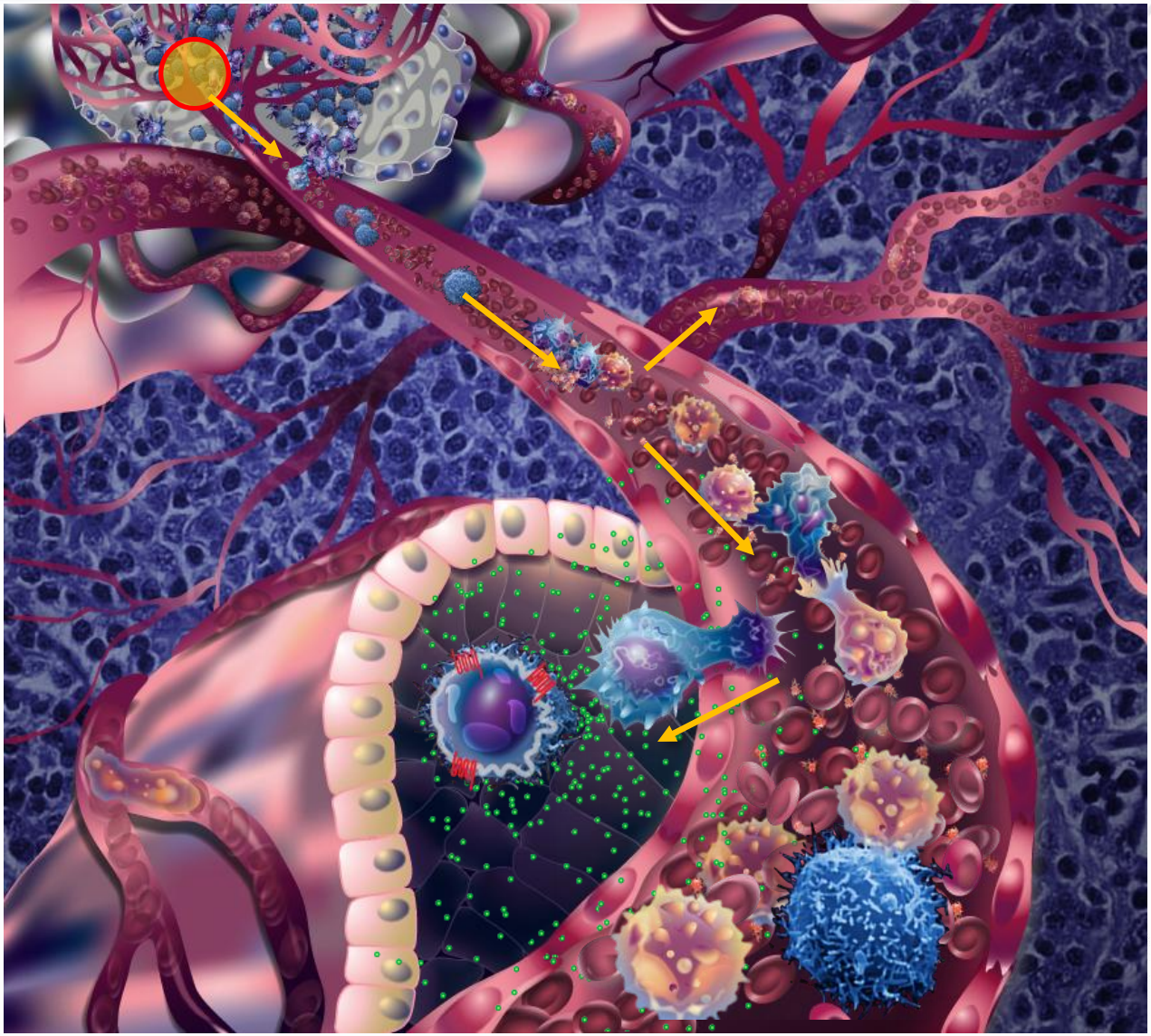
CENTER for STRATEGIC SCIENTIFIC INITIATIVES





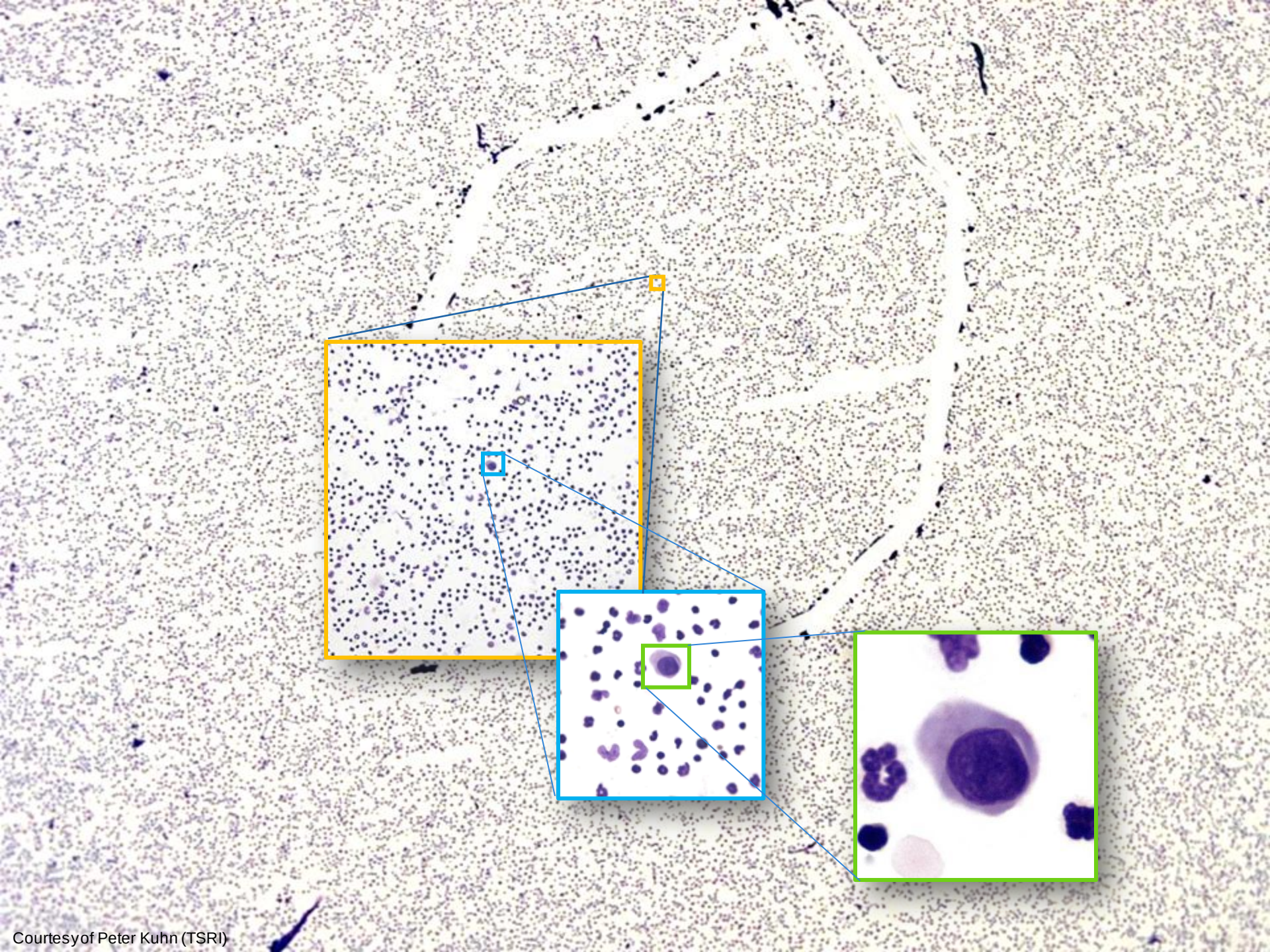
Metastasis: Deleterious but also Rare and Random!





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

Courtesy of Peter Kuhn (TSRI)



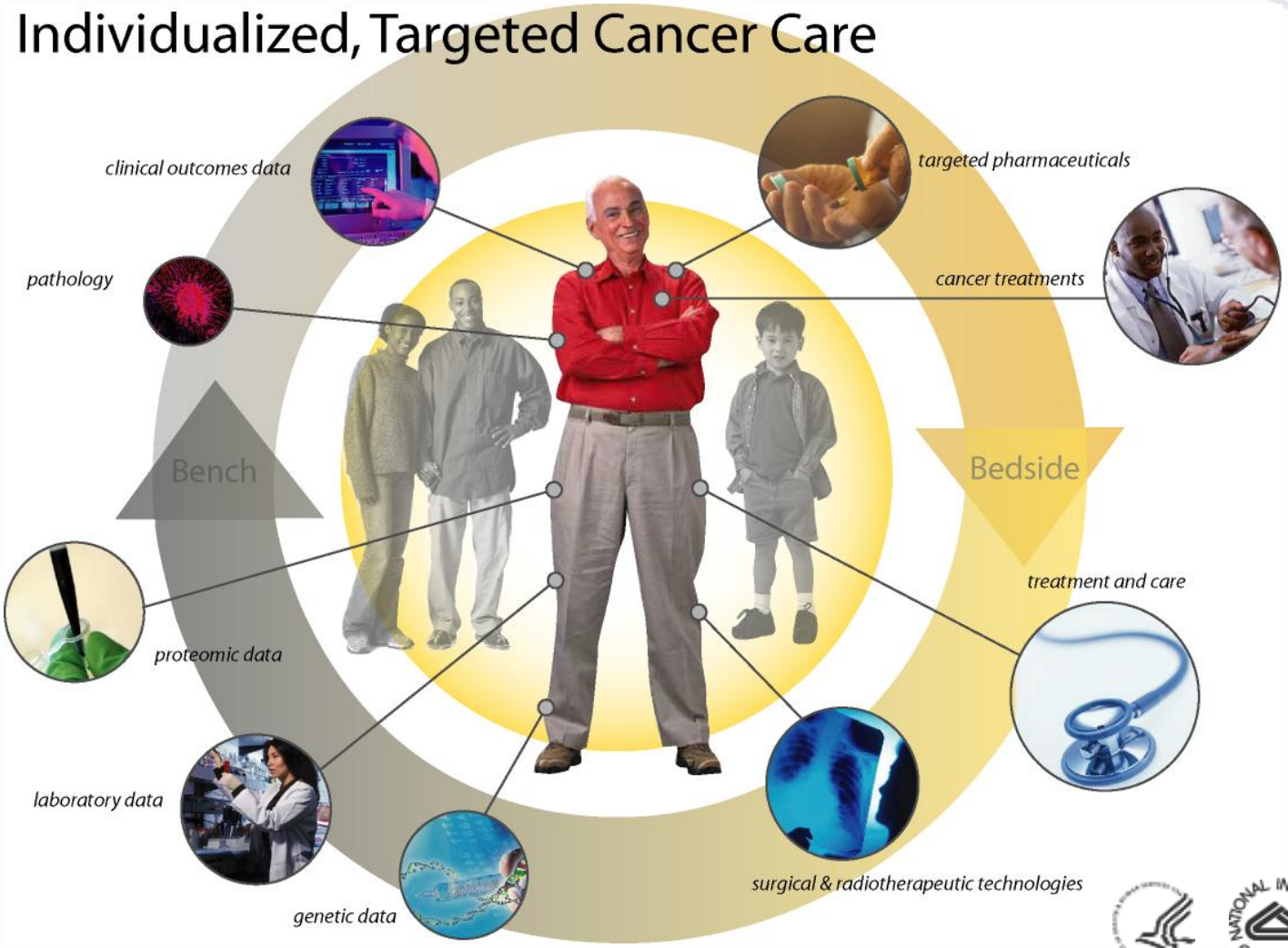
Courtesy of Peter Kuhn (TSRI)

Physical Sciences-Oncology Centers Program Goal and Vision

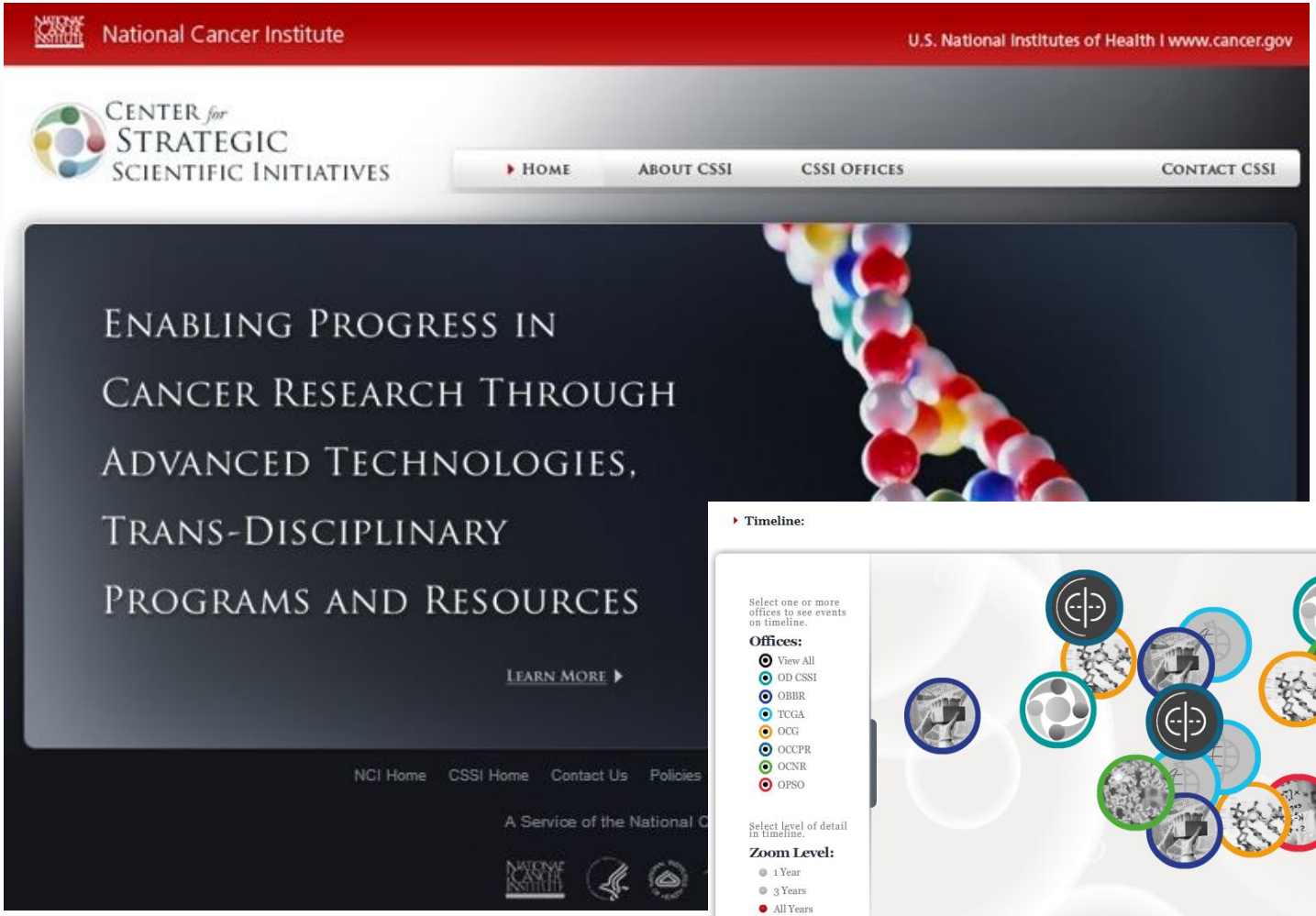
- To generate ***new knowledge*** and catalyze ***new fields of study*** in cancer research by utilizing physical sciences/engineering principles to enable a better understanding of cancer and its behavior at all scales.
- Not looking for new tools to do "better" science, but new perspectives and approaches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

A Future Where Individualized Medicine Becomes Reality



Learn More About CSSI…



http://cssi.cancer.gov