Advancing Innovation and Convergence In Cancer Research

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Deputy Director

Center for Strategic Scientific Initiatives (CSSI)

Office of the Director, National Cancer Institute, NIH

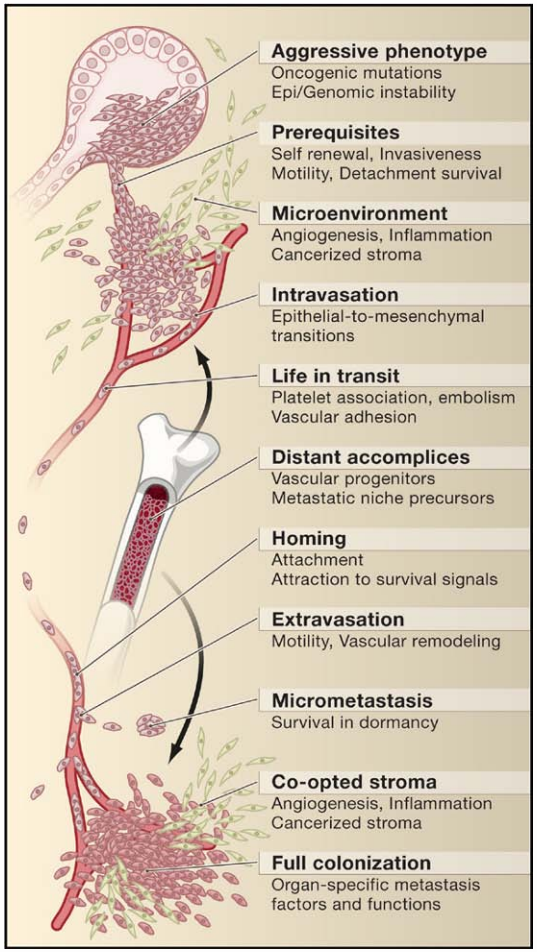
E Kamakani Noi`I: *Wind that Seeks Knowledge*

Waikiki, Hawai'i

January 14th, 2011

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

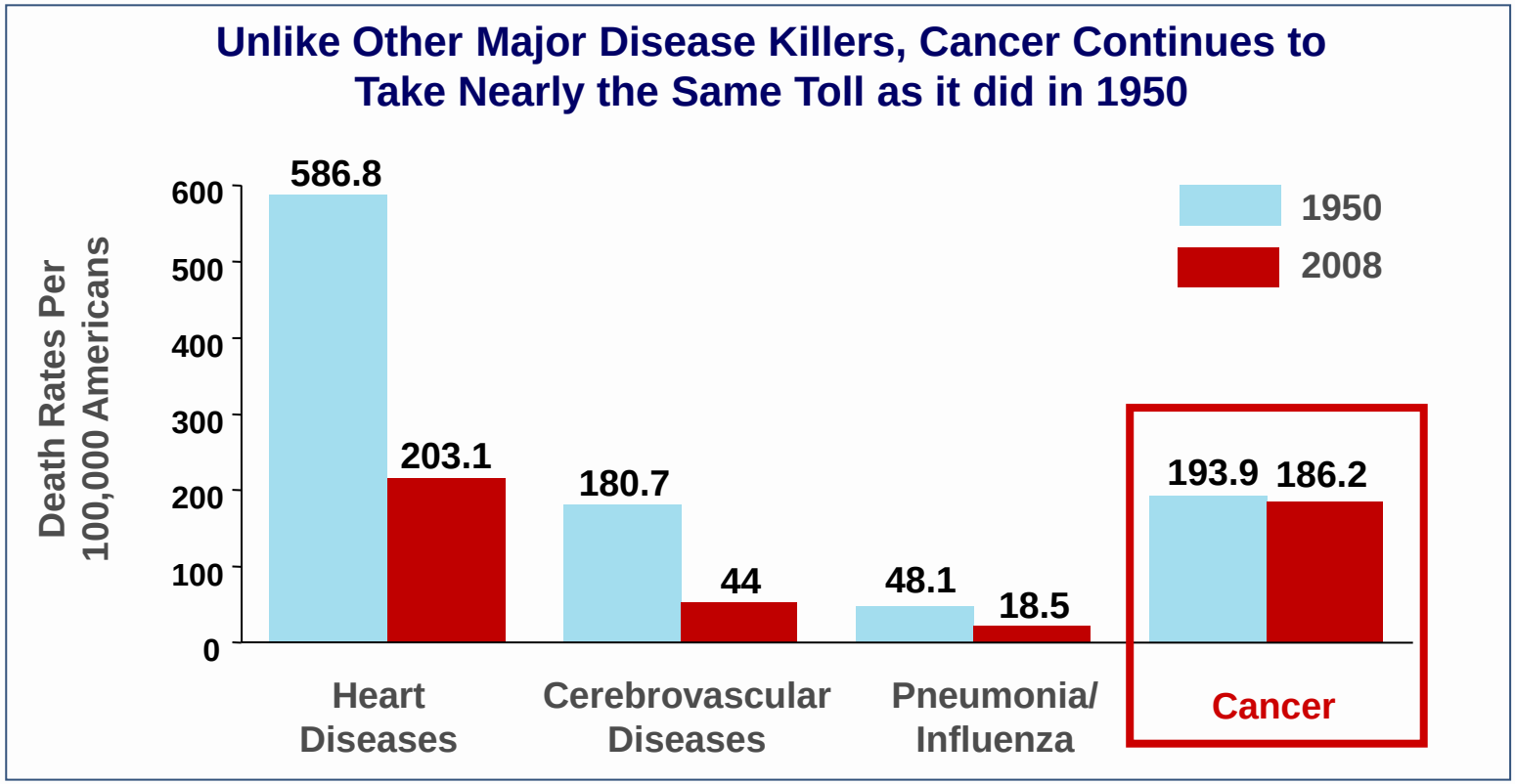


Site	All stages	Local	Regional	Distant
Breast (female)	86.6	97.0	78.7	23.3
Colon and rectum	62.3	90.1	65.5	9.2
Liver	6.9	16.3	6.0	1.9
Lung and bronchus	14.9	48.7	16.0	2.1
Melanoma	89.6	96.7	60.1	13.8
Ovary	53.0	94.7	72.0	30.7
Pancreas	4.4	16.6	6.8	1.6
Prostate	97.5	100.0	--	34.0
Testis	95.5	99.1	95.0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

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

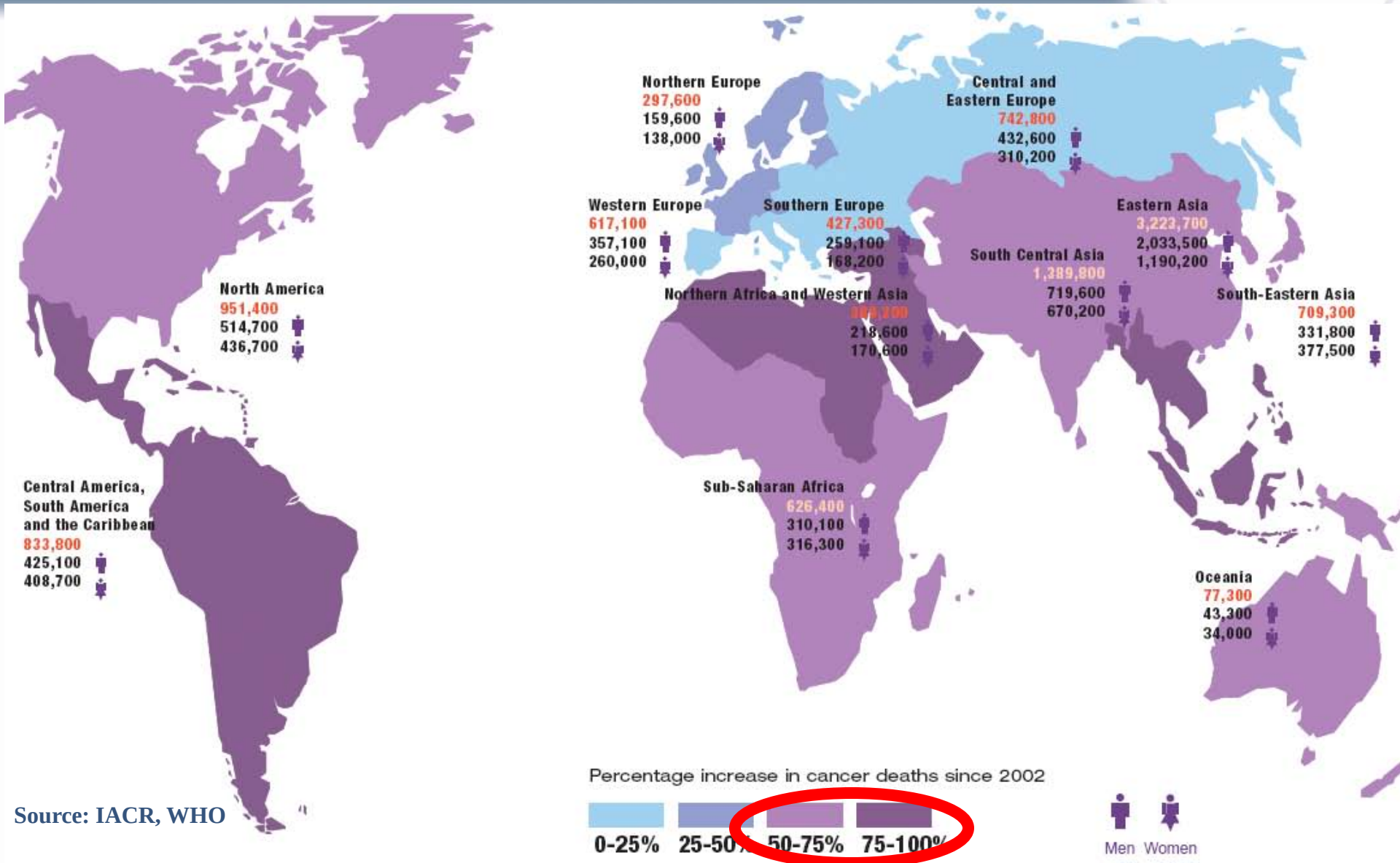
Reality: In the U.S., Cancer Continues to be Represent an Enormous Burden

- **569,490** Americans died of cancer in 2010
- **1,529,560** Americans will be diagnosed with cancer this year
- **$228.1 billion** in 2008 for cancer healthcare costs



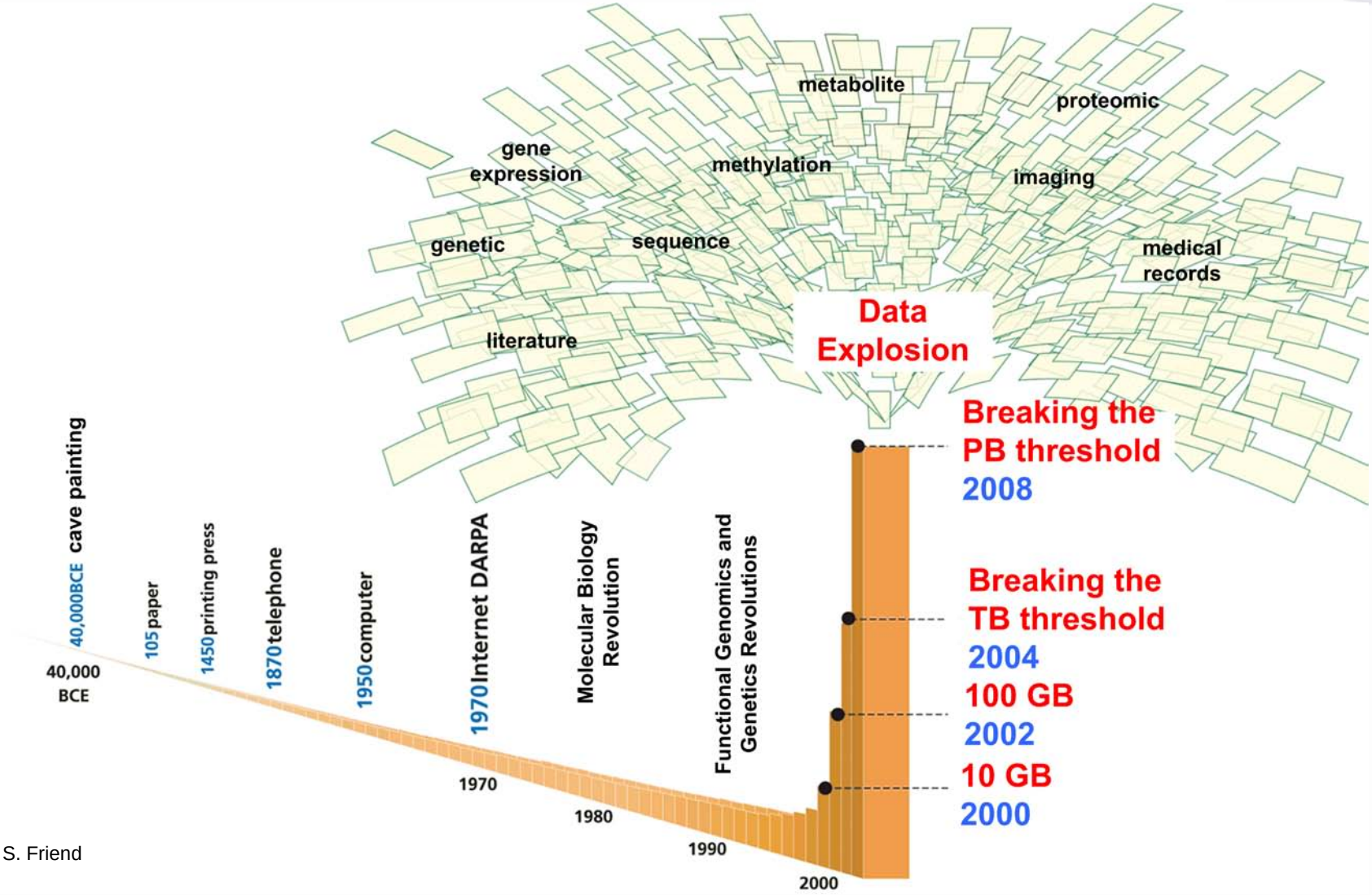
Source for 2010 deaths and diagnoses: American Cancer Society (ACS) 2010 Cancer Facts & Figures; Atlanta, Georgia
Source for 2008 age-adjusted death rate: National Center for Health Statistics, NCHS Public-use file for 2008 deaths.

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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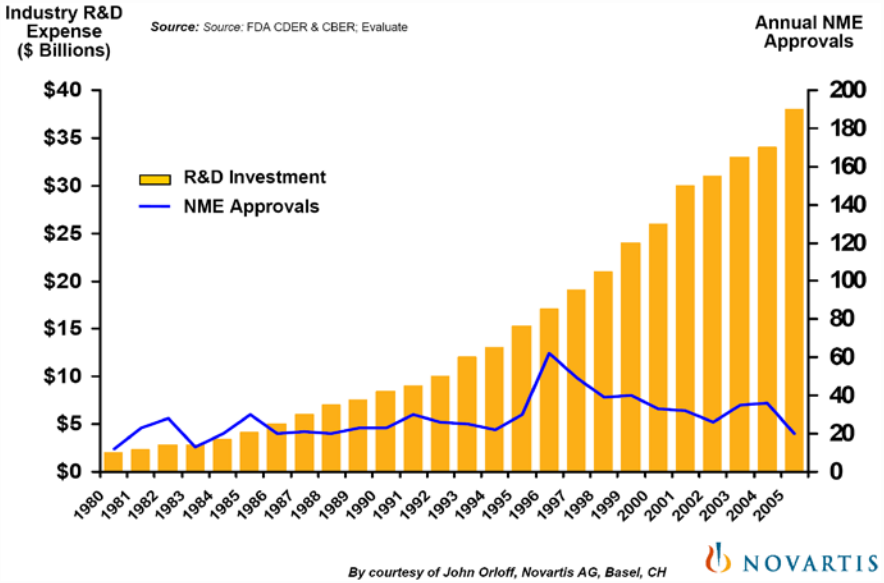
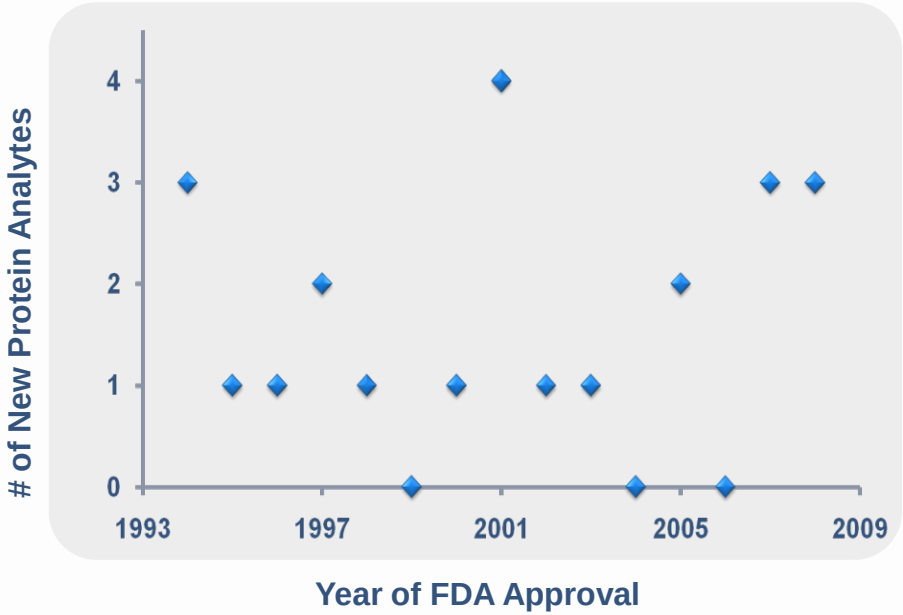
Drugs



Start to Finish

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

Diagnostic Biomarkers



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

Maybe…but can it be more efficient?

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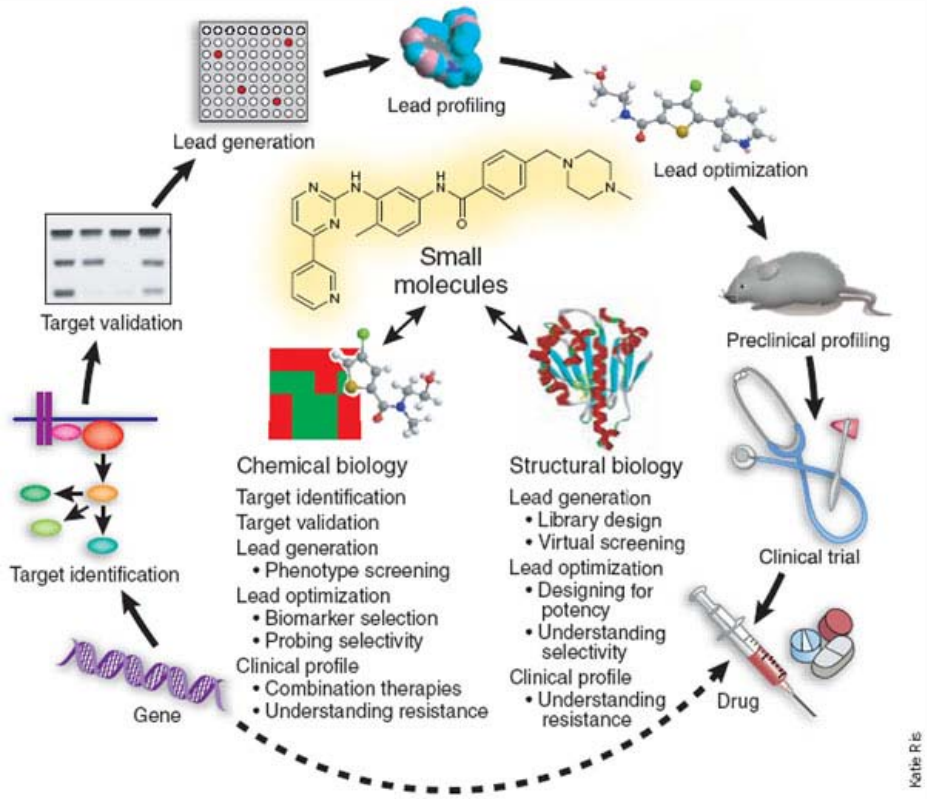
Leigh Anderson, Clin Chem (2010) 56: 177-185

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

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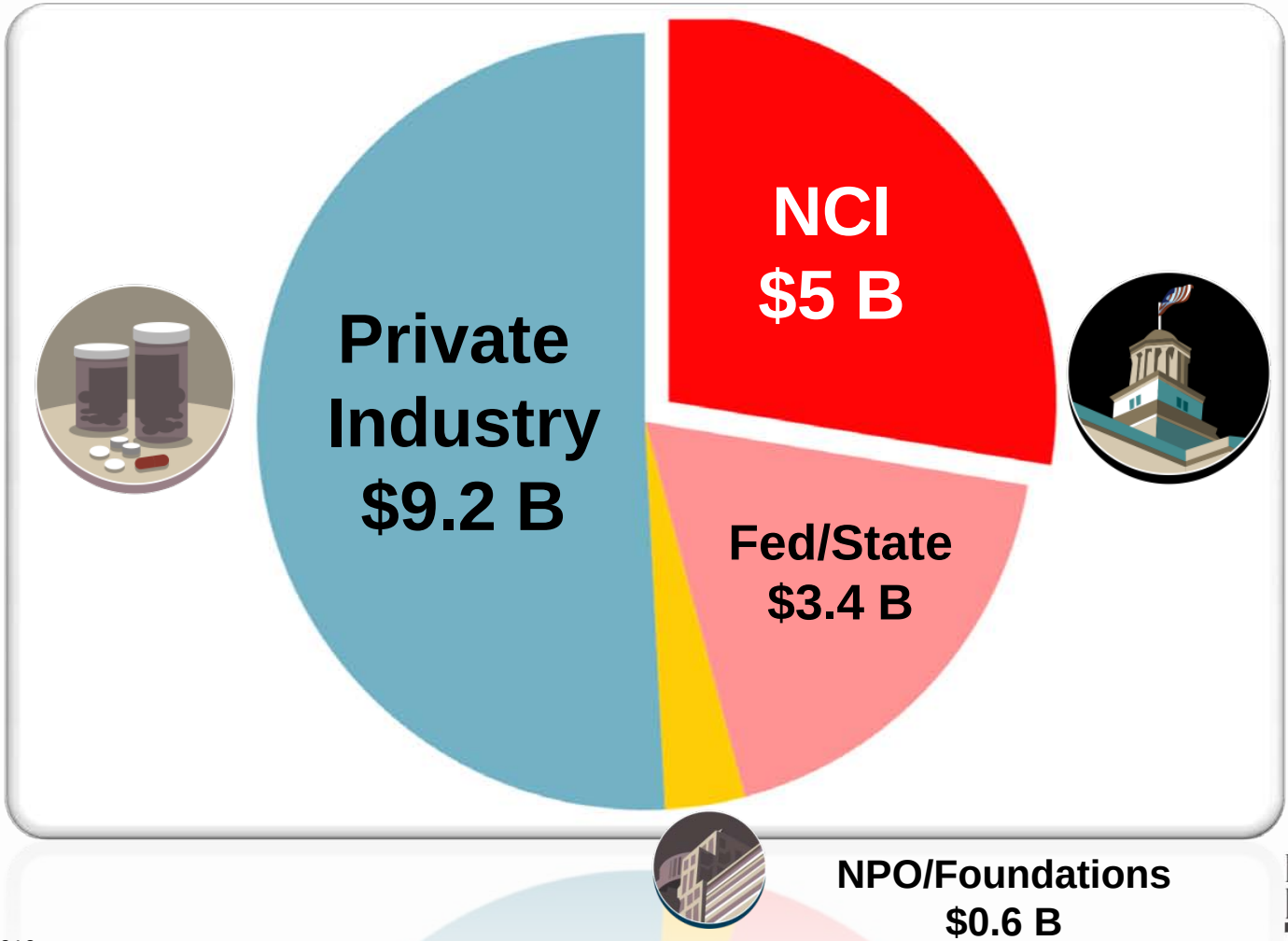
~$18 B per year



NCAB Working Group Report, 2010

National Cancer Institute

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: Cancer & Genes- Take a Page from Engineers?

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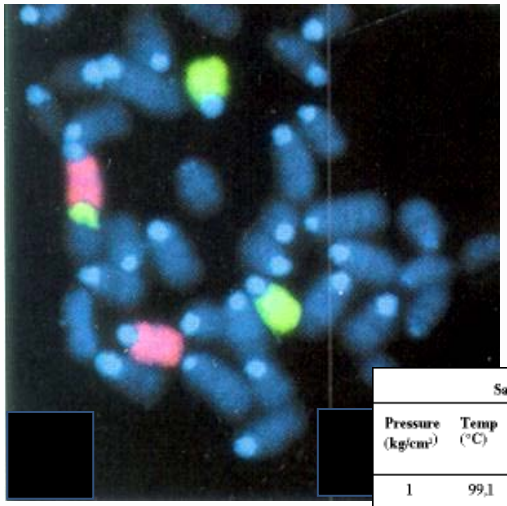
Disease of Genomic Alterations

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



	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
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 changes**
- **Repeat for all cancers**
- **Make it publically available**

TCGA: Connecting Multiple Sources, Experiments, and Data Types

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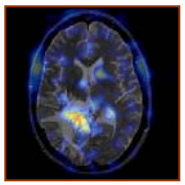
The Cancer Genome Atlas

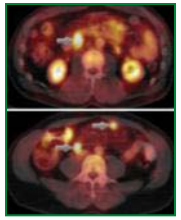
Three Cancers- Pilot

glioblastoma multiforme (brain)



squamous carcinoma (lung)

serous cystadenocarcinoma (ovarian)



Biospecimen Core Resource with more than 13 Tissue Source Sites

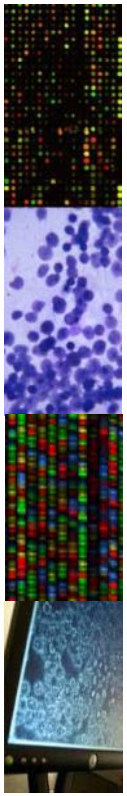
7 Cancer Genomic Characterization Centers

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



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Unanitcipated Innovation: Cancer Human Biobank (caHUB)

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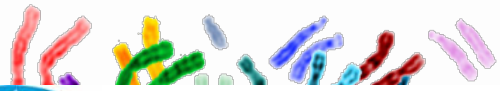
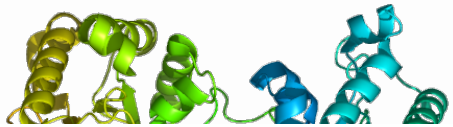
Genomics **Proteomics**





caHUB The Cancer Human Biobank

All Depend On High-Quality, Annotated Human Biospecimens

"Garbage In…Garbage Out"

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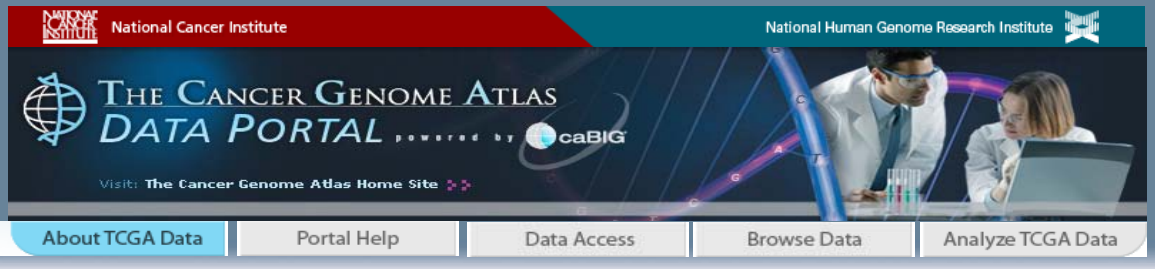

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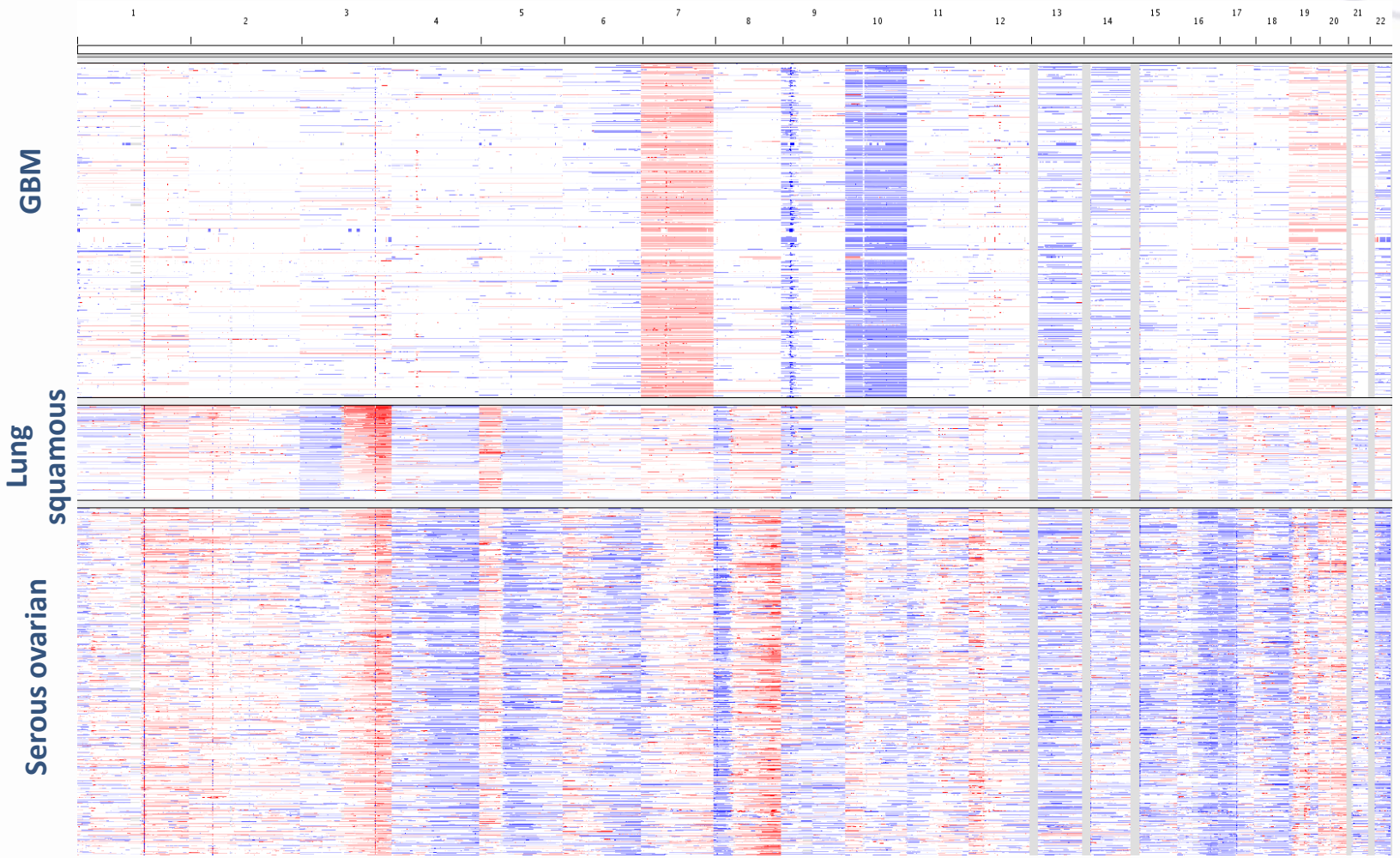

GBM: 400 cases, Lung squamous: 113 cases, Serous ovarian : 486 cases

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Unanticipated Innovations…

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Mid- 2008

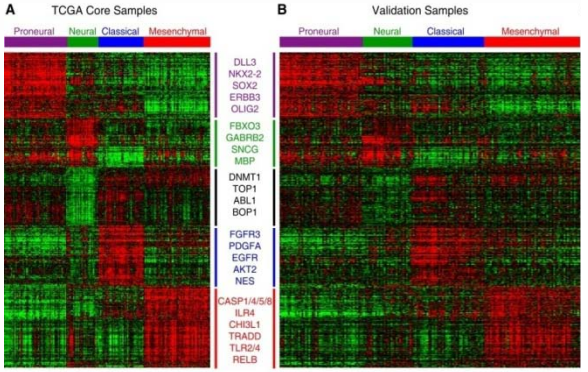
- Reference cancer genome for GBM
- Single author paper (TCGA Network)
  - 300+ authors
- Unanticipated Scientific Discoveries
  - Hypothesis on a possible resistance mechanism to temozolomide (TMZ)

Comprehensive genomic characterization defines human glioblastoma genes and core pathways

The Cancer Genome Atlas Research Network*

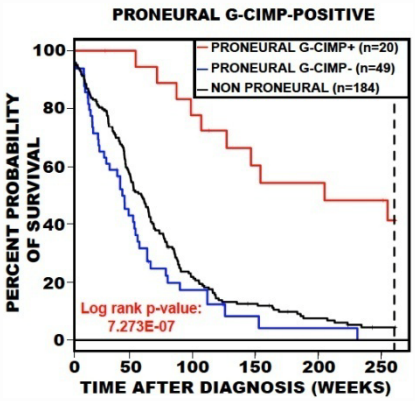
2009

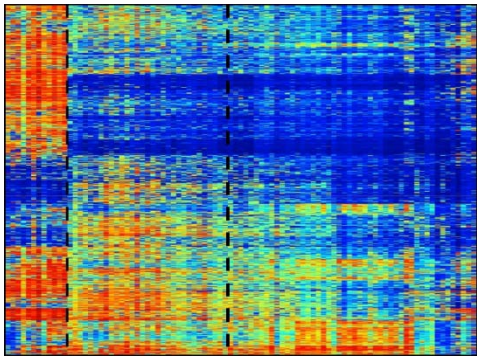
- Gene expression-based classification of GBM
- Response to aggressive therapy differs by subtype- **exclude non-responders**



2010

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





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

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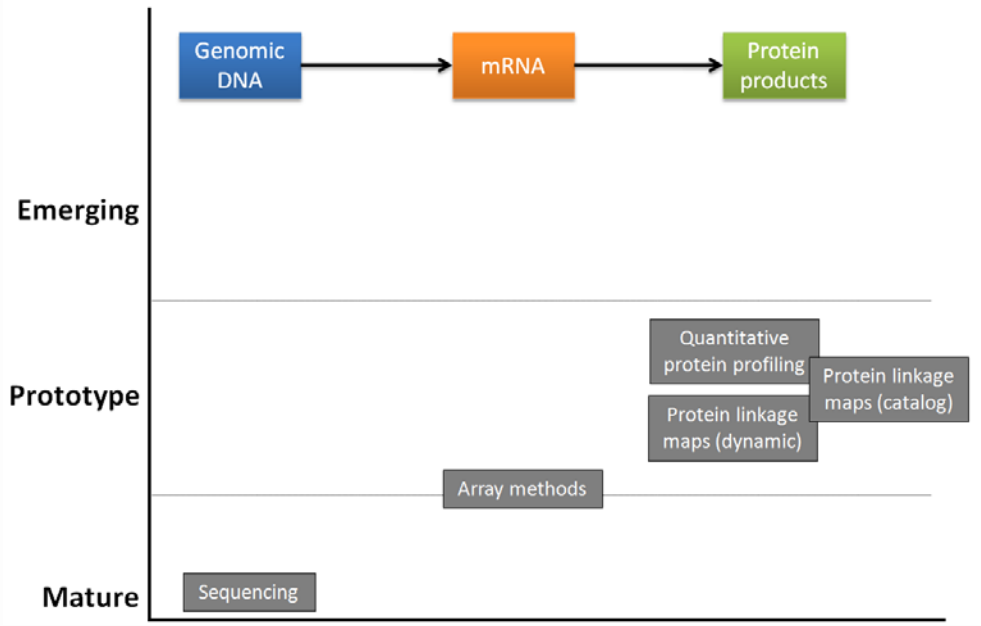
THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

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

National Cancer Institute

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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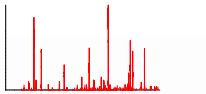
CLINICAL PROTEOMIC TECHNOLOGIES FOR CANCER

nature biotechnology

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



caTranche

FDA

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) presubmission for proteomic platforms**
  - Educate new generation of developers
- **Established Antibody Characterization Laboratory**
  - Provides high quality regents at minimum cost to community
  - All characterization data posted on public database
  - Industry partners and collaborations

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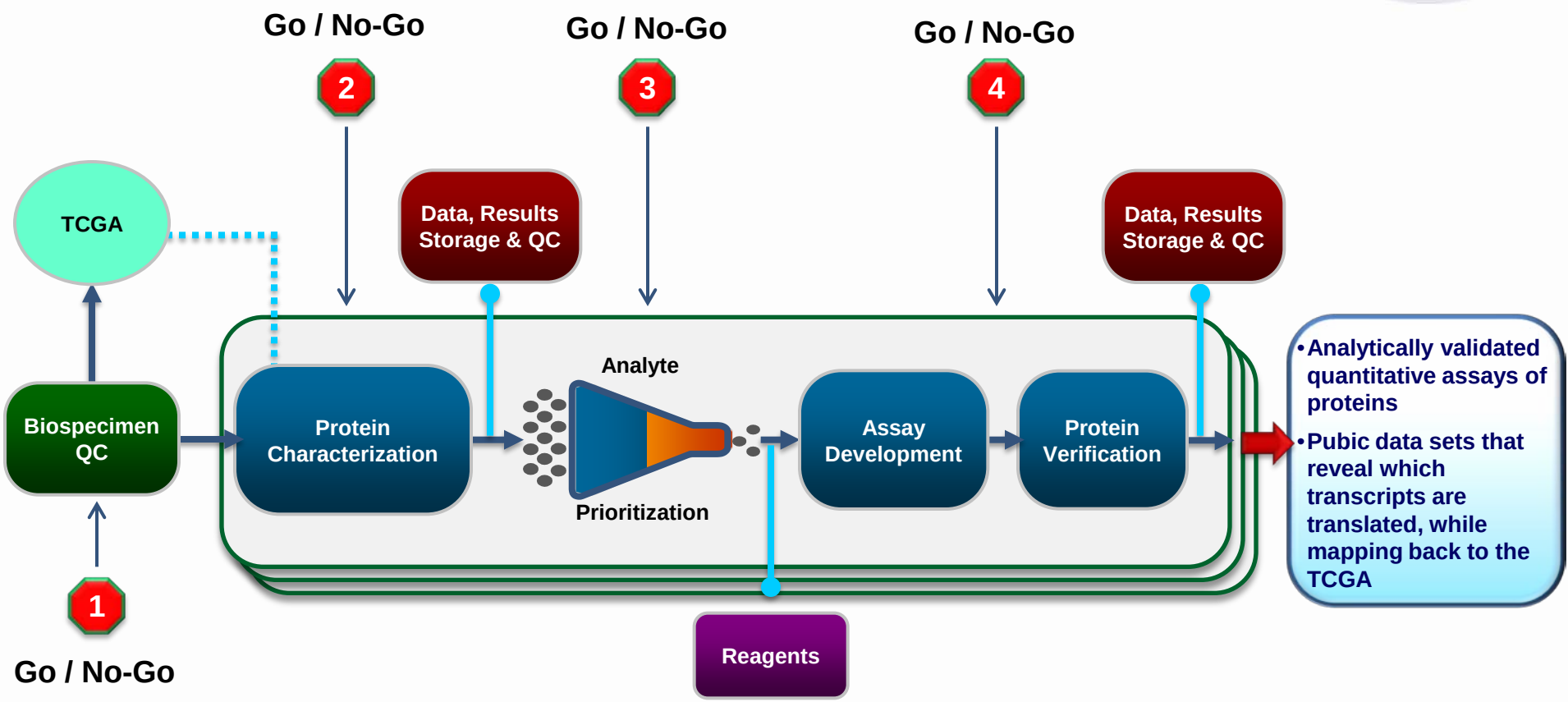
Full Steam Ahead: CPTC Phase 2 Pipeline (Summer ’11)



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

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LOTS of Quantitative and Reproducible Data

	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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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

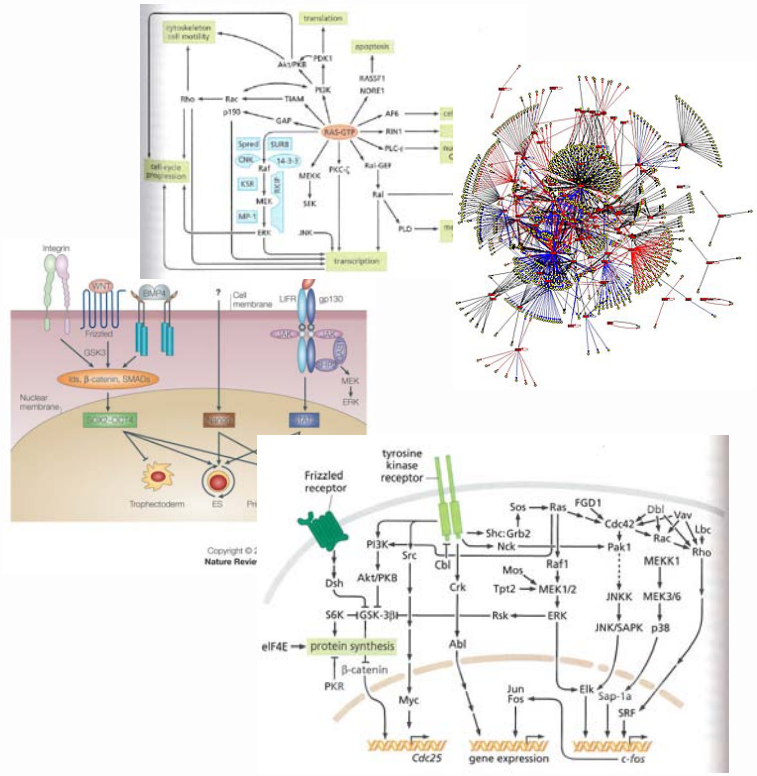
Consensus Scientific Themes

- 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

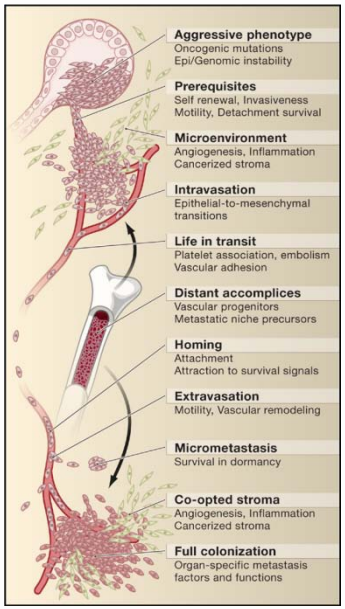
Consensus Needs

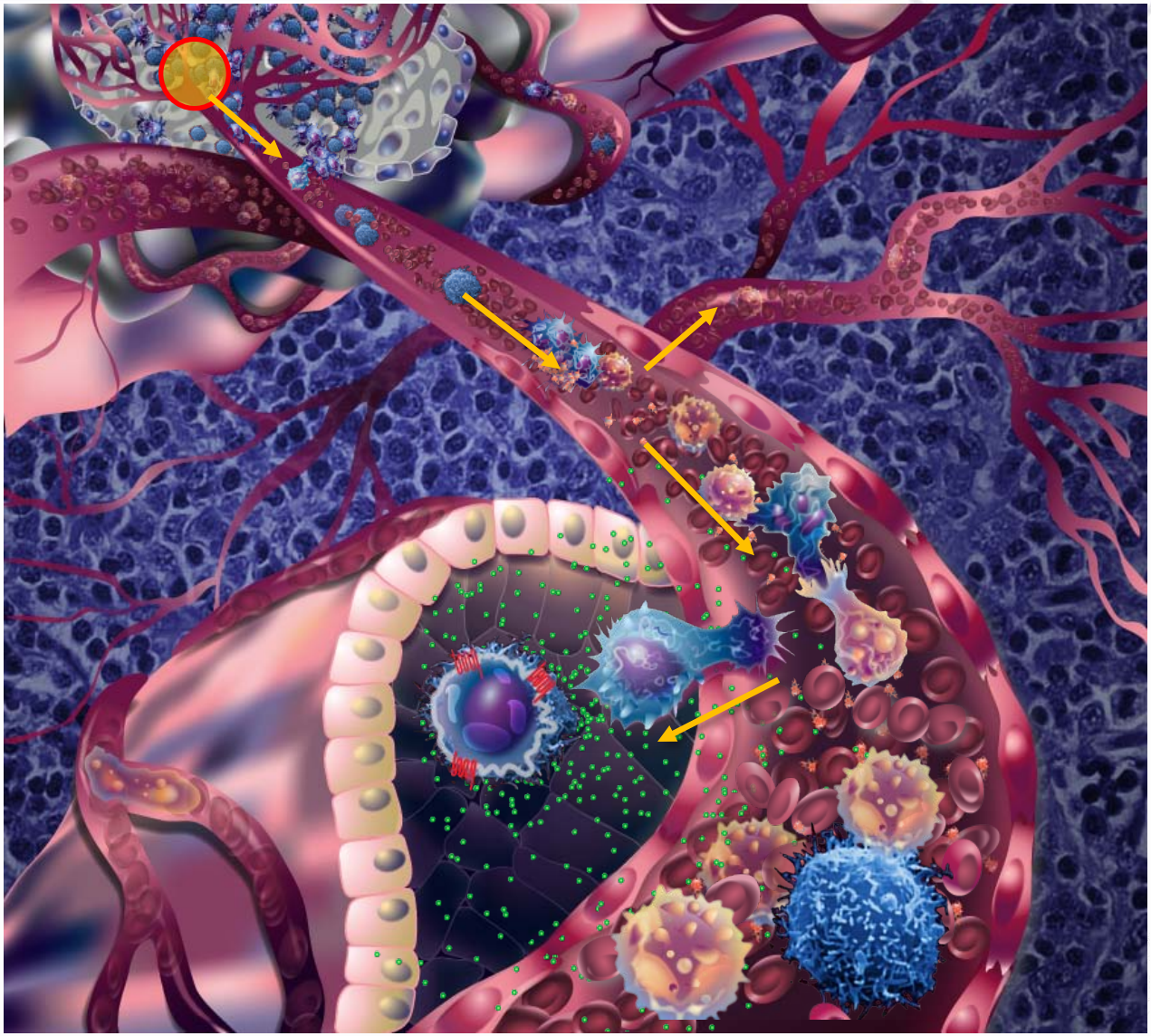
- Establish trans-disciplinary physical sciences-oncology centers
- Centers composed of integrated physical sciences-oncology teams
- Focus on theme(s) for center framework
- Centers led by physical scientists with co-investigator(s) from cancer biology/oncology

Critical to Think in Terms of Space and Time

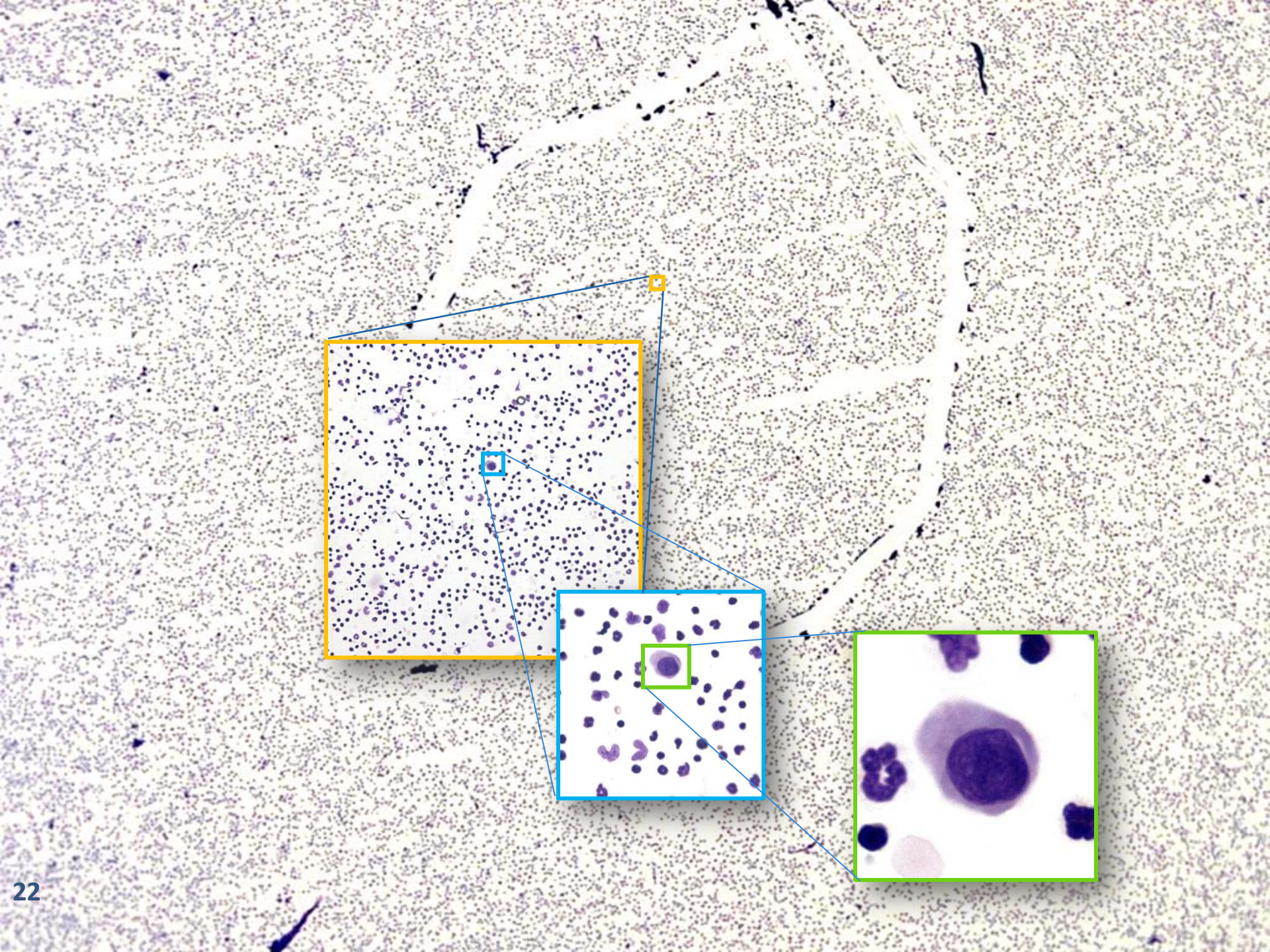


Metastasis: Rare, Random, Deleterious



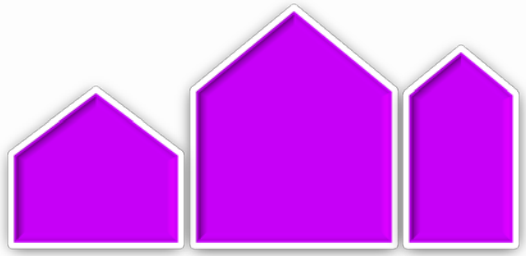


Well-known to be an inefficient process (0.01%)



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"

Physical Sciences-Oncology Centers (PS-OC) Network

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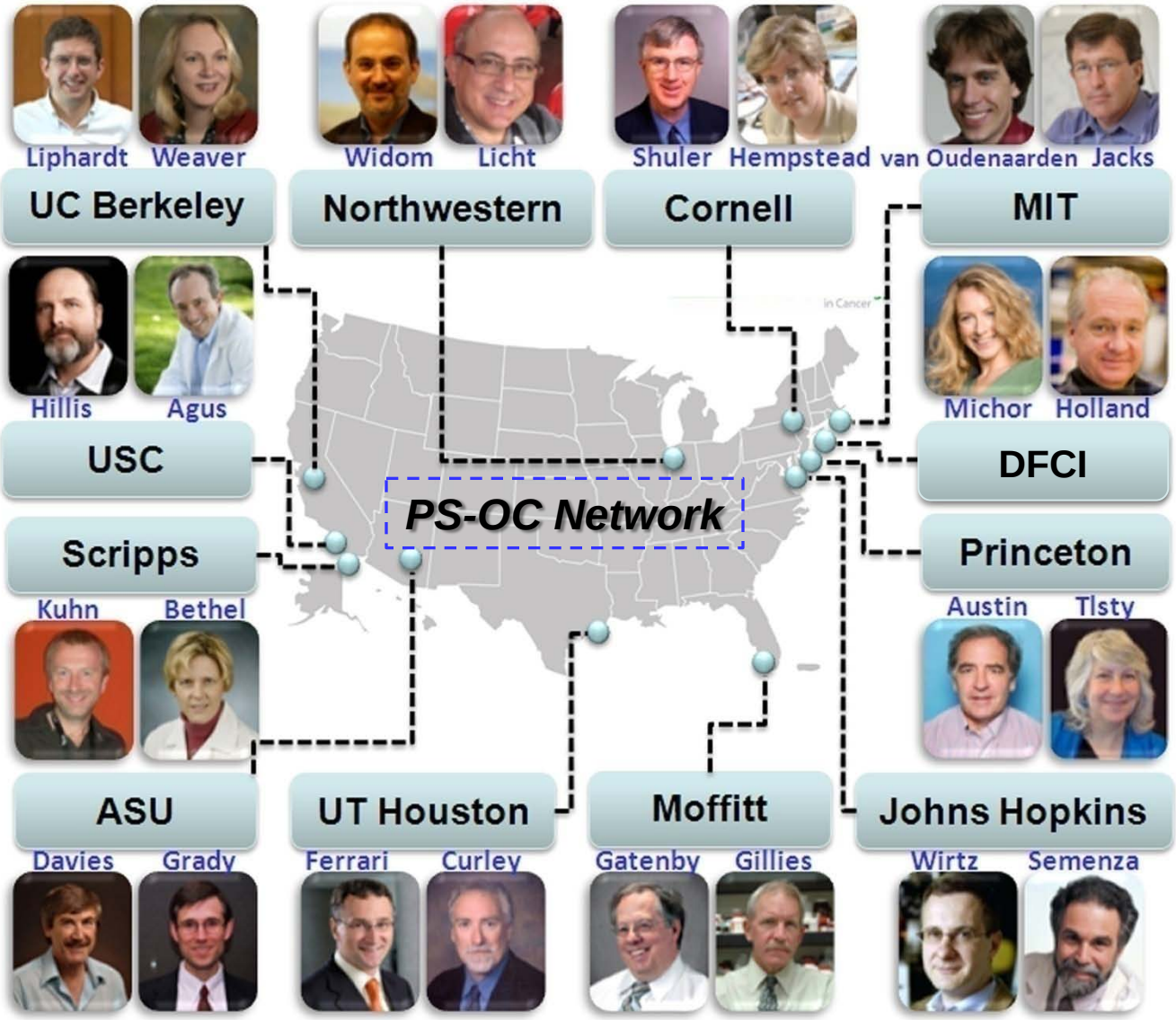
Physics of Cancer

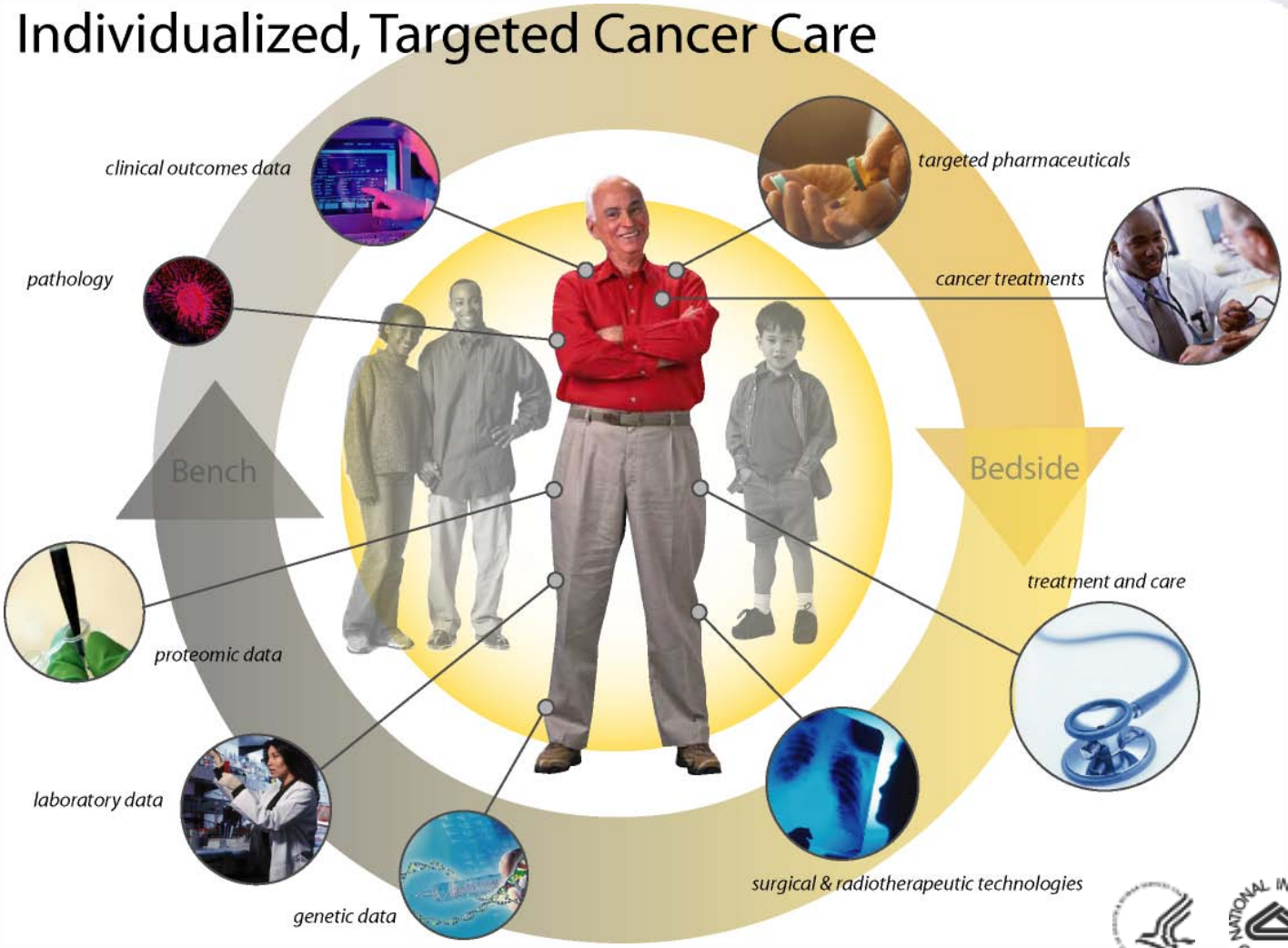
Evolution and Evolutionary Theory of Cancer

Information Coding, Decoding, Transfer, and Translation in Cancer

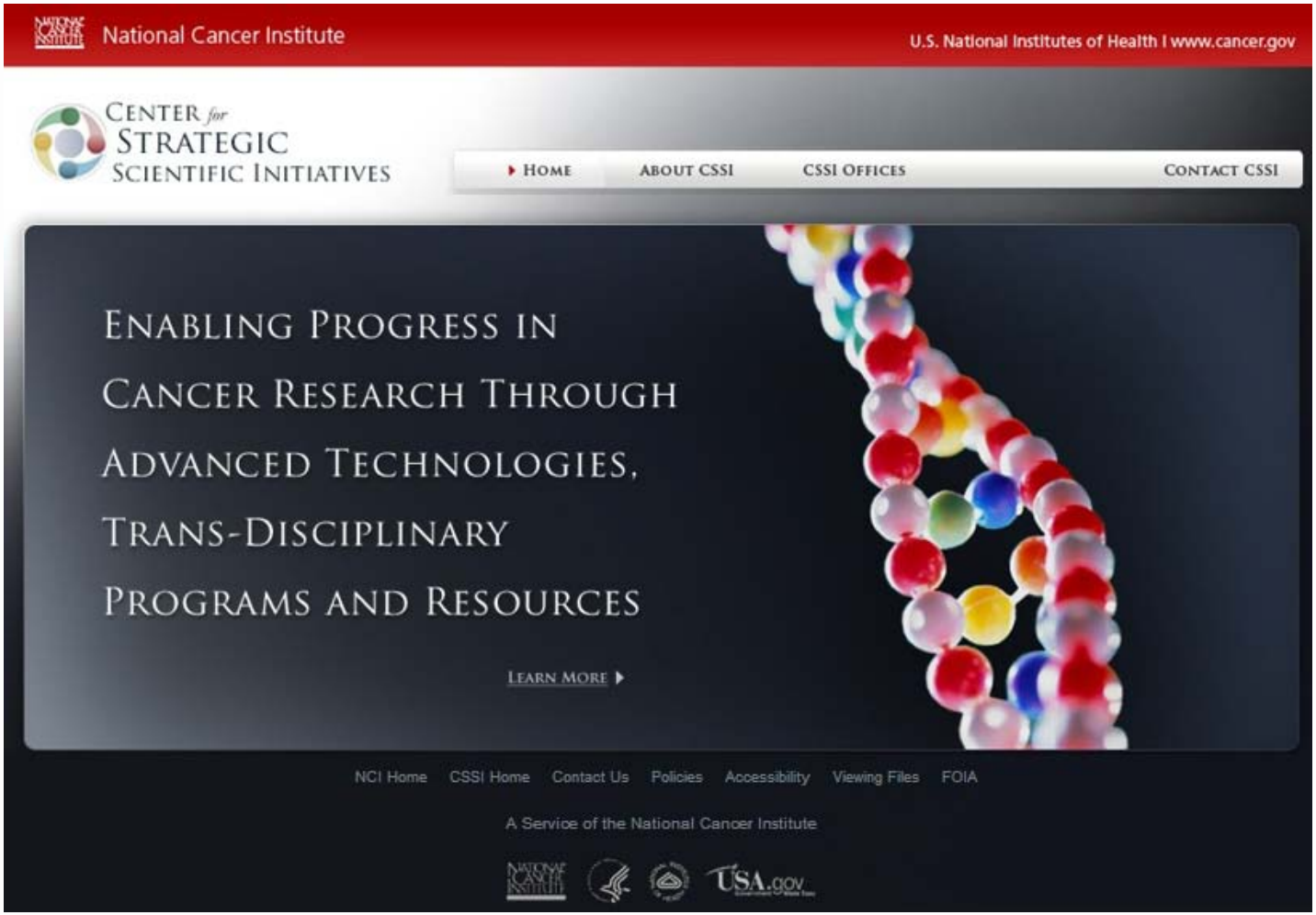
De-convoluting Cancer's Complexity



A Future Where Personalized Medicine Becomes Reality



Learn More About CSSI…



http://cssi.cancer.gov