Building the Ohio Innovation Economy

Biomedical Grown Opportunities – Advances in Cancer Research

April 25-26, 2011

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Today's Thoughts

- What is the cancer reality?
- How do we see and characterize the future of healthcare (read personalized medicine)?
- If disruptive innovation is our best hope – what areas represent opportunities/barriers?
- Are there current examples of high promise?
- And the future?

Reality: Two Messages – Both Important but Increasingly Challenging

President Barack Obama, National Academy of Sciences, April 27, 2009

"…we can harness the historic convergence between life sciences and physical sciences that's underway today, undertaking public projects in the spirit of the human genome project to create data and capabilities that fuel discoveries in tens of thousands of laboratories and identifying and overcoming scientific and bureaucratic barriers to rapidly translating scientific breakthroughs into diagnostics and therapeutics that serve patients…" (THE NOT ONE SIZE FITS ALL INNOVATION IMPERATIVE – WILL WE HARNESS CONVERGENCE?)

…Today, of course, we face more complex challenges than we have ever faced before, a medical system that holds the promise of unlocking new cures and treatments attached to a health care system that holds the potential for bankruptcy to families and businesses…" (THE HOW MUCH TECHNOLOGY CAN WE AFFORD QUESTION)

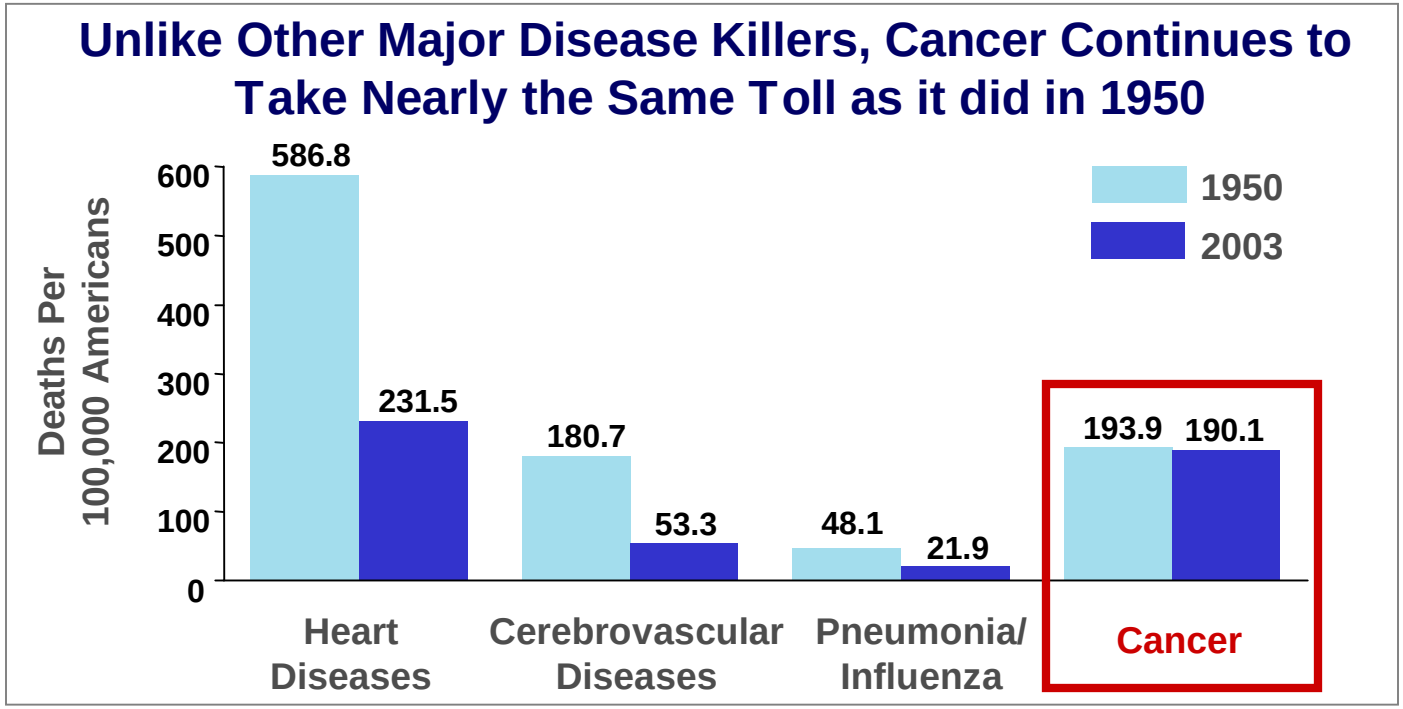
4oth Anniversary: Official Launch of the U.S. "War on Cancer"

December 23, 1971, President Richard Nixon signs National Cancer Act

- **1969 – Full Page New York Times: "Mr Nixon You Can Cure Cancer"...Just lack the will and resources that put a man on the moon"**
- **Senator Yarborough: "…achieve cures for the major forms of cancer by 1976 – . bicentennial of the republic!"**

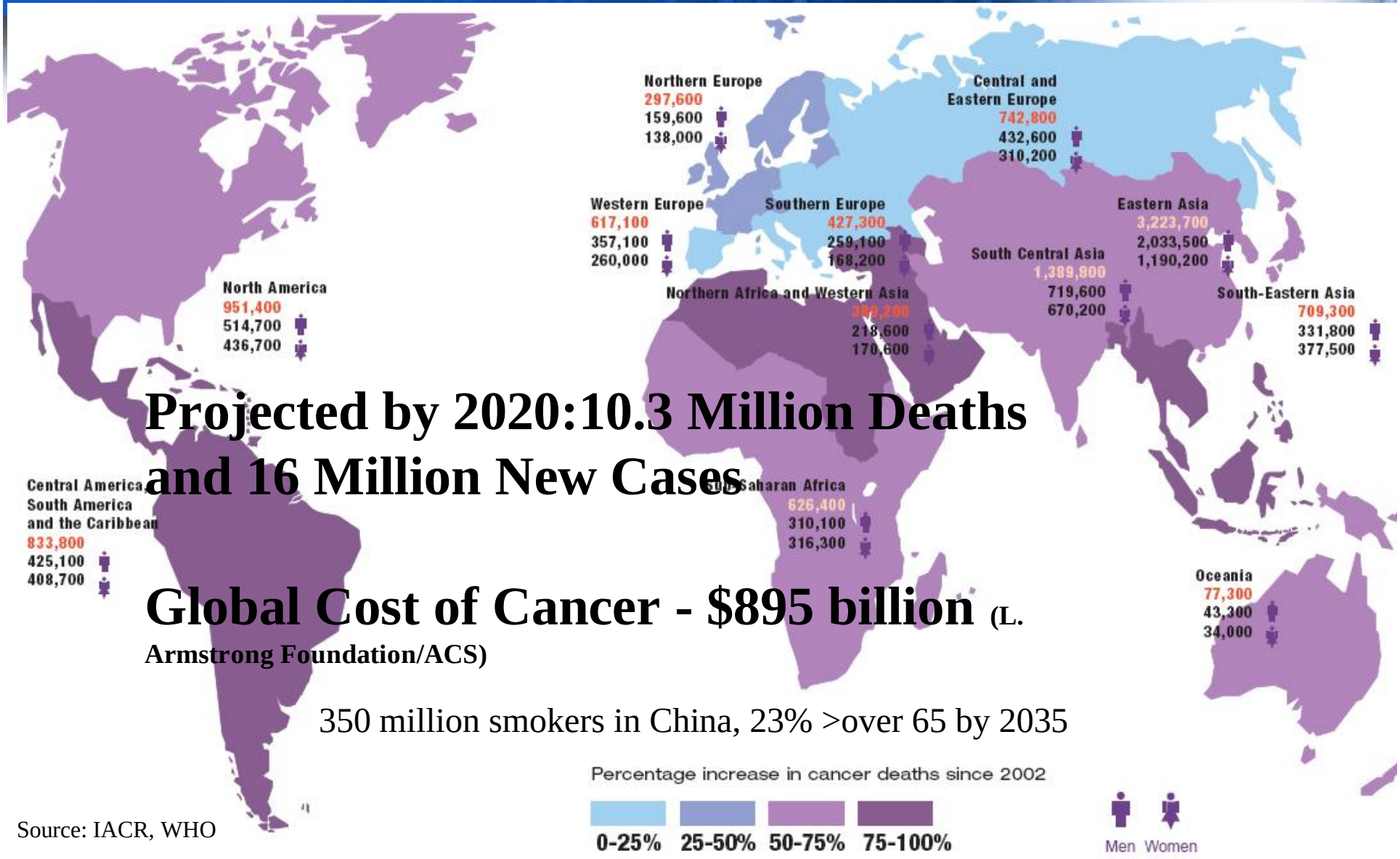
Cancer Reality

- ~ 560,000 Americans will die of cancer this year
- ~ 1.5 million Americans will be diagnosed with cancer this year
- ~ $264 billion (economic burden of cancer in 2010 (ACS)
- New cancer cases will increase by 30-50% as we approach 2020
- ~ 65,000 new cancer cases in Ohio this year



Source for 2006 deaths and diagnoses: American Cancer Society (ACS) 2006 Cancer Facts & Figures; Atlanta, Georgia
Source for 2003 age-adjusted death rate: National Center for Health Statistics, U.S. Department of Health and Human Services, NCHS Public-use file for 2003 deaths.

Reality: Global Burden - 7.6 Million (2008) Cancer Deaths



Projected by 2020:10.3 Million Deaths and 16 Million New Cases

Global Cost of Cancer - $895 billion (L. Armstrong Foundation/ACS)

350 million smokers in China, 23% >over 65 by 2035

Source: IACR, WHO

Reality of Metastatic Cancer

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

Reality of Today vs. the Vision That Is Extant for 21st Century Medicine

Reality of Today	21s Century Medicine
§ Healthcare spending in 2009 projected - $2.5 trillion	§ Focus on predisposition, early detection and biological processes
§ Expected to rise one percentage point this year (17.9% of U.S. economy - largest increase since CMS began tracking)	§ Diagnosis based on molecular characterization of patients vs. morphologic and pathologic analysis
§ Increases expected to continue through 2018 ($4.4 trillion - ~20% of economy – 50% public spend)	§ Evidence-based - continually assesses standard of care –and rapidly integrates improvements
§ Investment in private healthcare declined (3.9% this to 15 year low; – prescription drug spending slowed (1.4%)	§ Connects research clinic in seamless *feedback loop – using IT platforms*

21st Century Medicine – Delivering Evidence Based Intervention at the Right Time for an Individual Patient

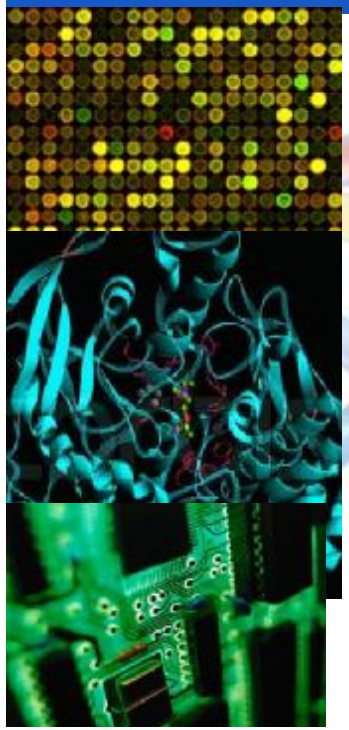
Driver for Innovation-Based Progress in Cancer Research – Ultimately Healthcare

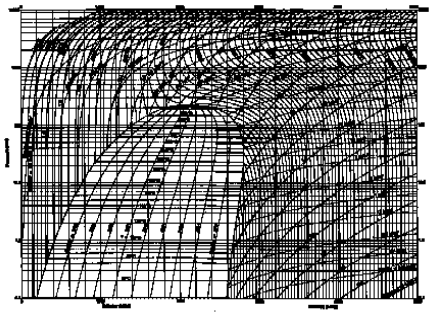
Living in an Era of CONVERGENCE

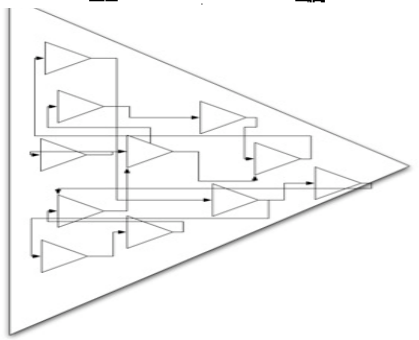
MOLECULAR SCIENCES,
BIOINFORMATICS/COMPUTATIONAL SCIENCES,
PHYSICS, ENGINEERING

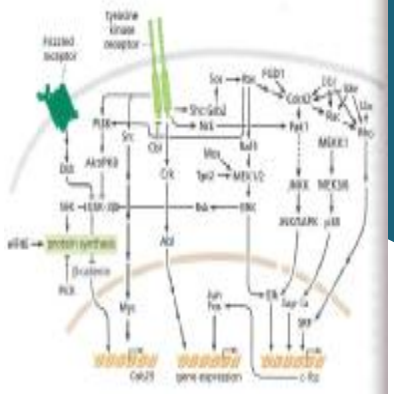
Defining Opportunity for Disruptive Innovation

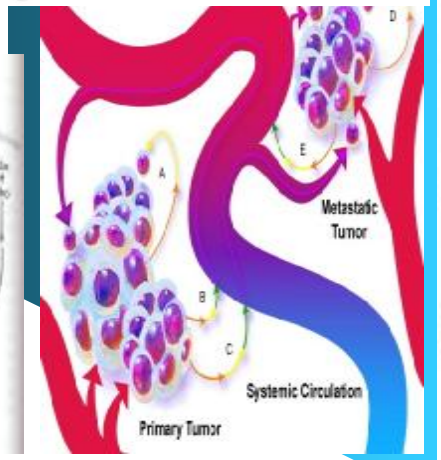
Convergence of Molecular Biology, IT, Computation, Physics, Engineering, and Innovative Delivery Technologies











INFORMATION

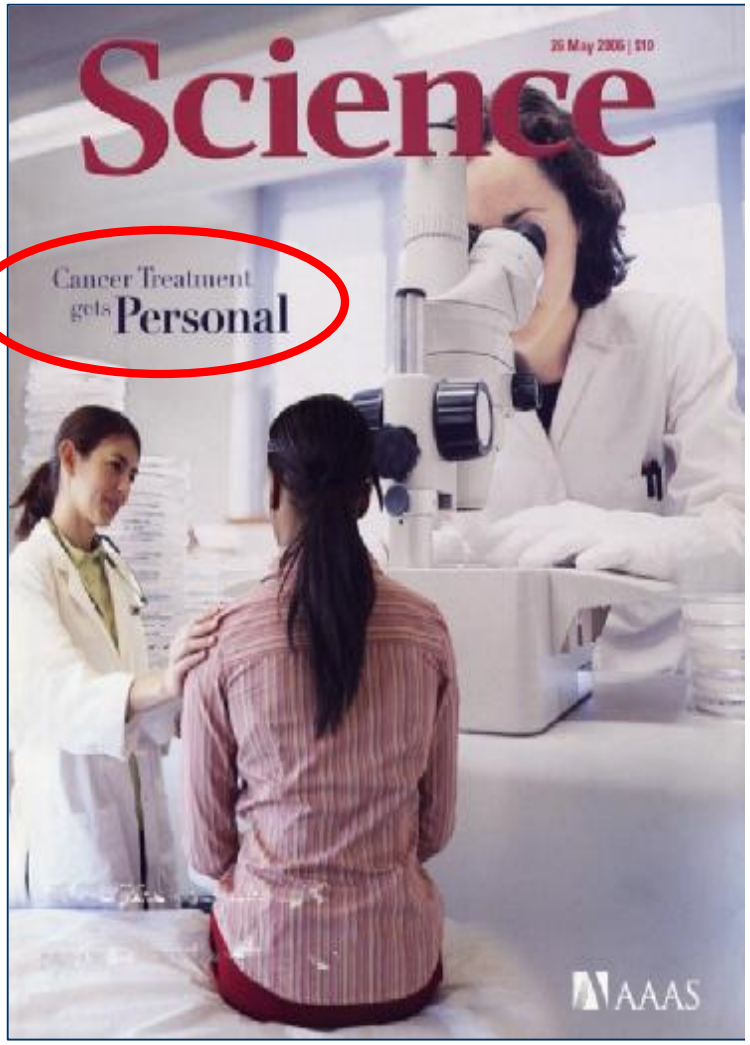


Image courtesy of *Science*, May 26, 2006

CSSI Programs Initiated to Enable Progress Toward Molecularly Based Cancer Medicine

Focus\Need Area	NCI Initiative
Physical Sciences	Physical Sciences Oncology Centers
Nanotechnology	***Nanotechnology Alliance for Cancer***
Cancer Genomics	***Analysis – Functional Genomics Centers***
Proteomics/Biomarkers	**Clinical Proteomics Initiative**
Large Scale Genomics	***The Cancer Genome Atlas***
Biospecimens	***caHUB (Cancer Human Biobank)***

Bioinformatics: The Cancer Bioinformatics Grid – caBIG

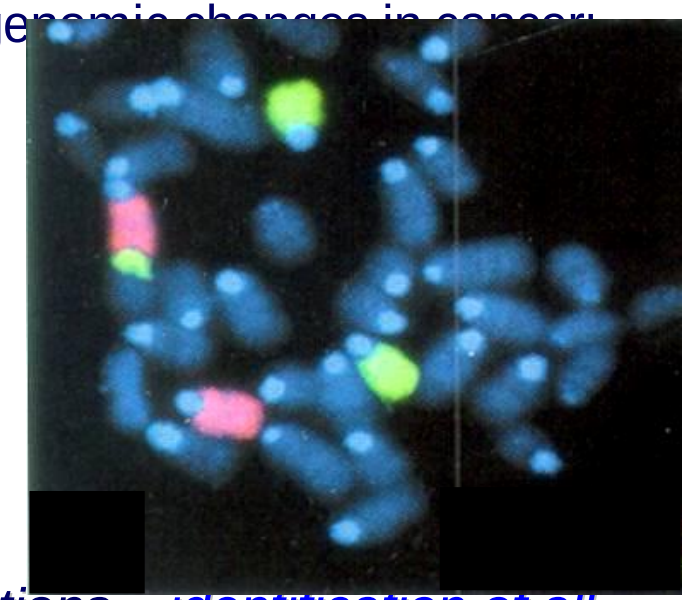
Note: Cost of these programs (without caBIG) ~2.7% of NCI's total budget

Examples of Fields/Programs Driving Innovation -

- **Genomics – The Cancer Genome Atlas**
- ***Physics/Engineering/Computation – Physical Sciences Oncology Centers Nanotechnology***
- ***Nanotechnology Alliance***

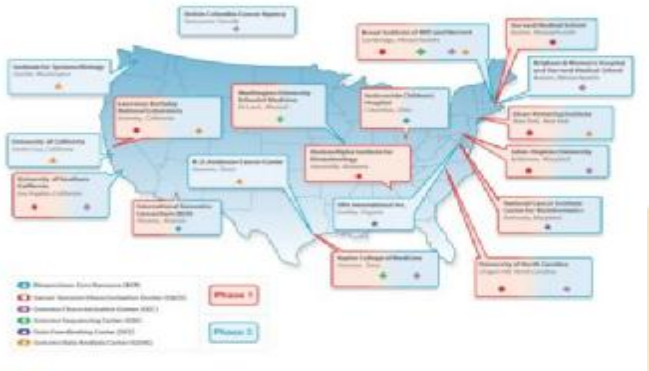
The Genomics Era: Understanding the Digital Information

- Biological significance of understanding genomic changes in cancer:
  - Copy number
  - Expression (regulation of)
  - Regulation of translation
  - Mutations
  - Epigenome



Cancer is a disease of genomic alterations – identification of all genomic changes would enable defining cancer subtypes – potential to transform cancer drug discovery, diagnostics and prevention

TCGA Network is Big Science



Data Management, Bioinformatics, and Computational Analysis

- Data Coordinating Center, DCC
- Analyses of data

Technology Development

- Increased sensitivity of molecular characterization platforms
- Analysis of biomolecules from 1000 cells or less

Genome Sequencing Centers

High throughput sequencing of genes and genomic regions identified through cancer characterization

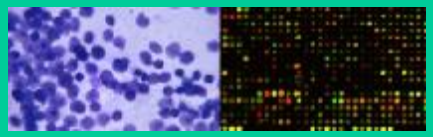
Human Tumor Samples: DNA/RNA

Molecular Characterization Data

Sequencing Data

Analysis Approaches

Cancer Genome Characterization Centers

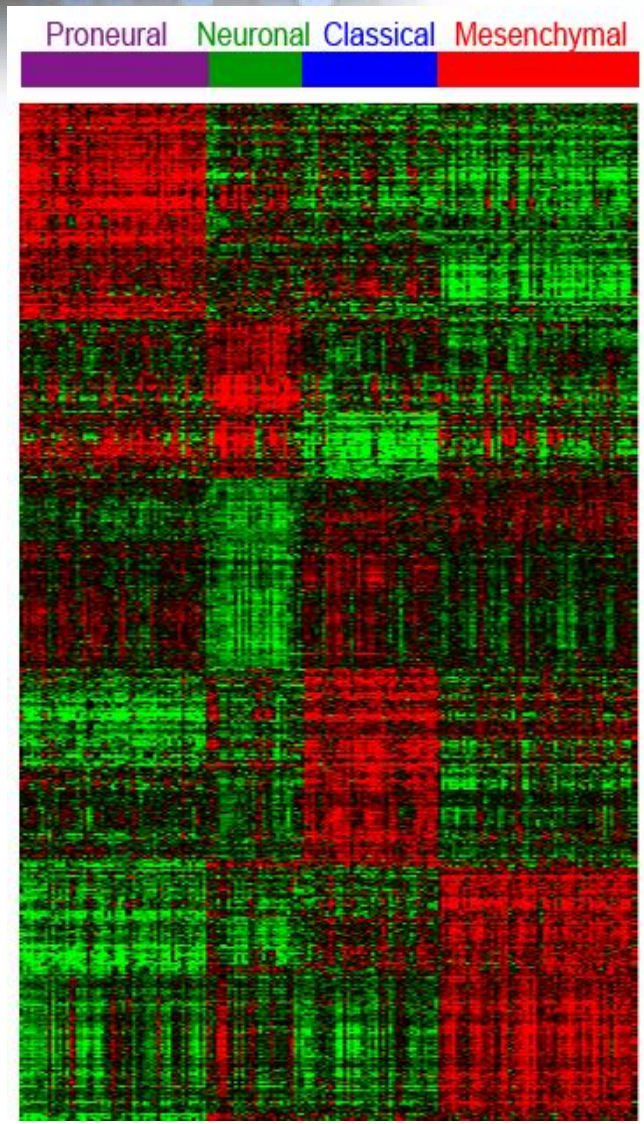


- Identification of expression alternation
- Detection of DNA fragment copy number changes and LOH
- Epigenetics

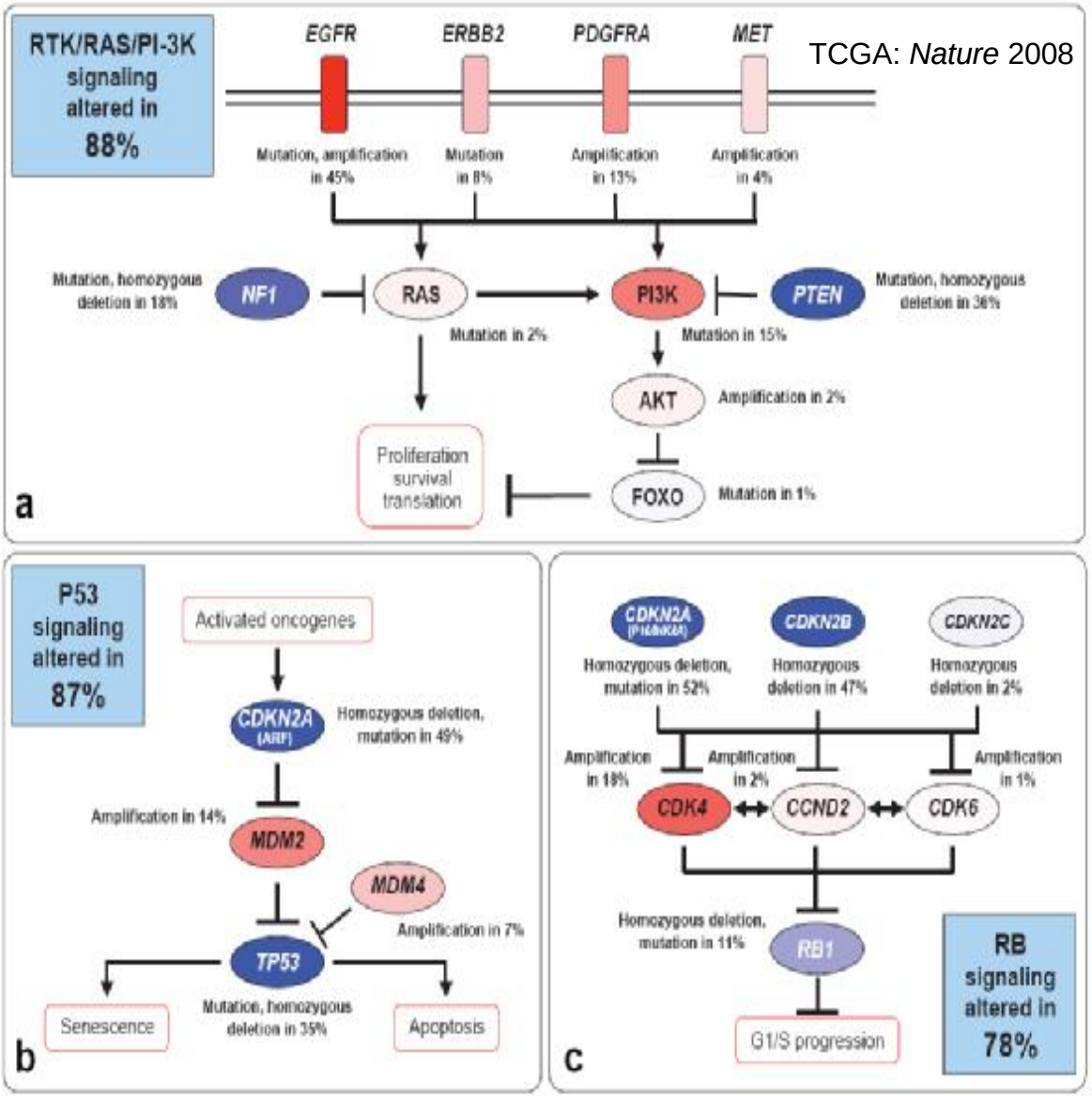
Human Cancer Biospecimen Core Resource

- Biospecimens-related data storage
- Histopathology confirmation performed
- Biomolecules isolated, QC'ed and distributed

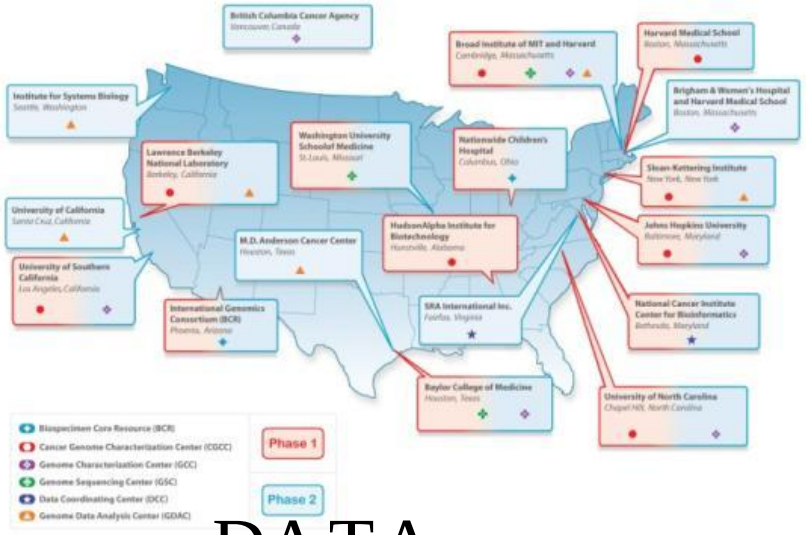
TCGA: Glioblastoma Multiforme (Adult Brain Tumors) Subtypes Molecular Pathways



TCGA: *Nature* 2008



TCGA – Data Paralysis or Progress



DATA

DATA

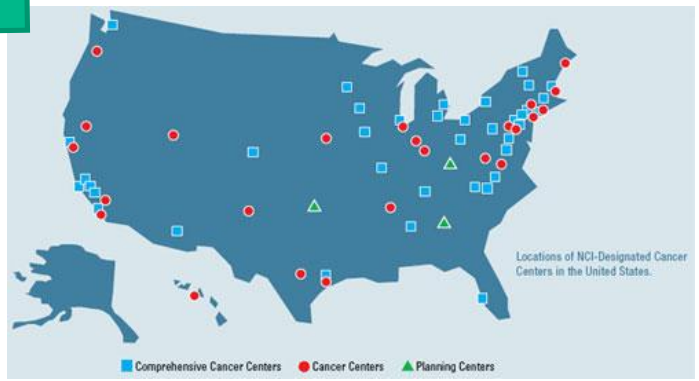
DATA Drug Development

Investigator Initiated Research

DATA

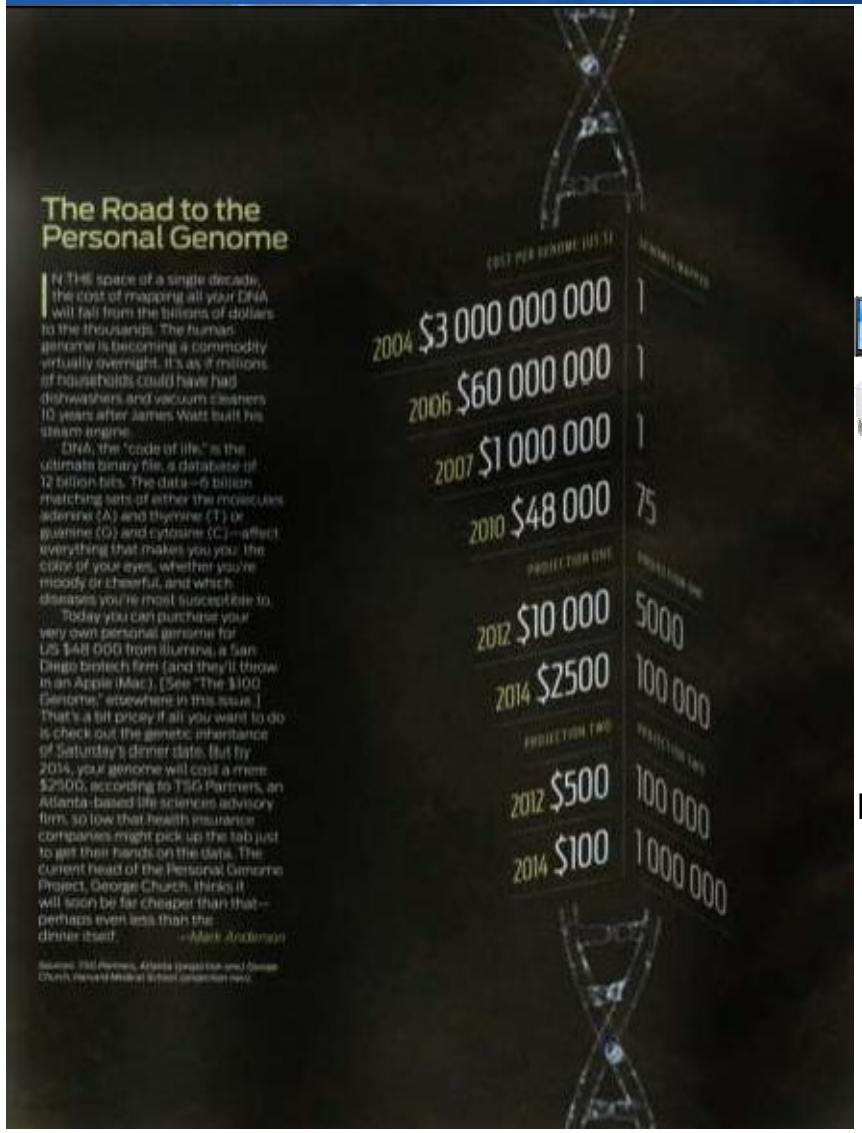
Patients

Molecular Diagnostics



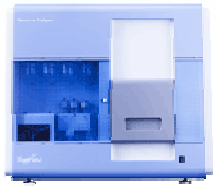
Cancer Centers

Genomics Technologies – Closing in on the $1000 Genome



Source: Sequencing; IEEE Spectrum 2/10

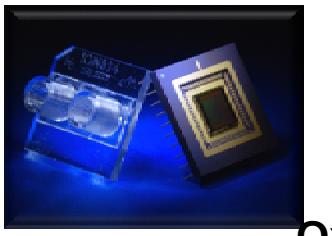
Richard Gibbs

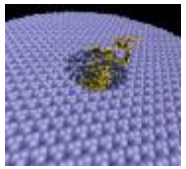


Complete Genomics

Complete Genomics

Illumina



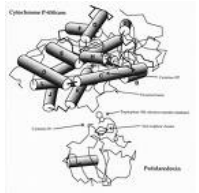


Oxford Molecular

454

Helicos

Ion-Torrent



NABsys

LaserGen, Inc.

Agilent

Nimblegen

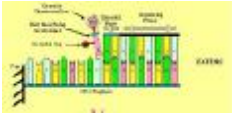
Raindance

PacBio

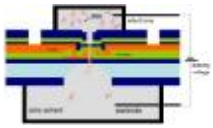
SOLiD

ZSGenetics

LaserGen



IBM

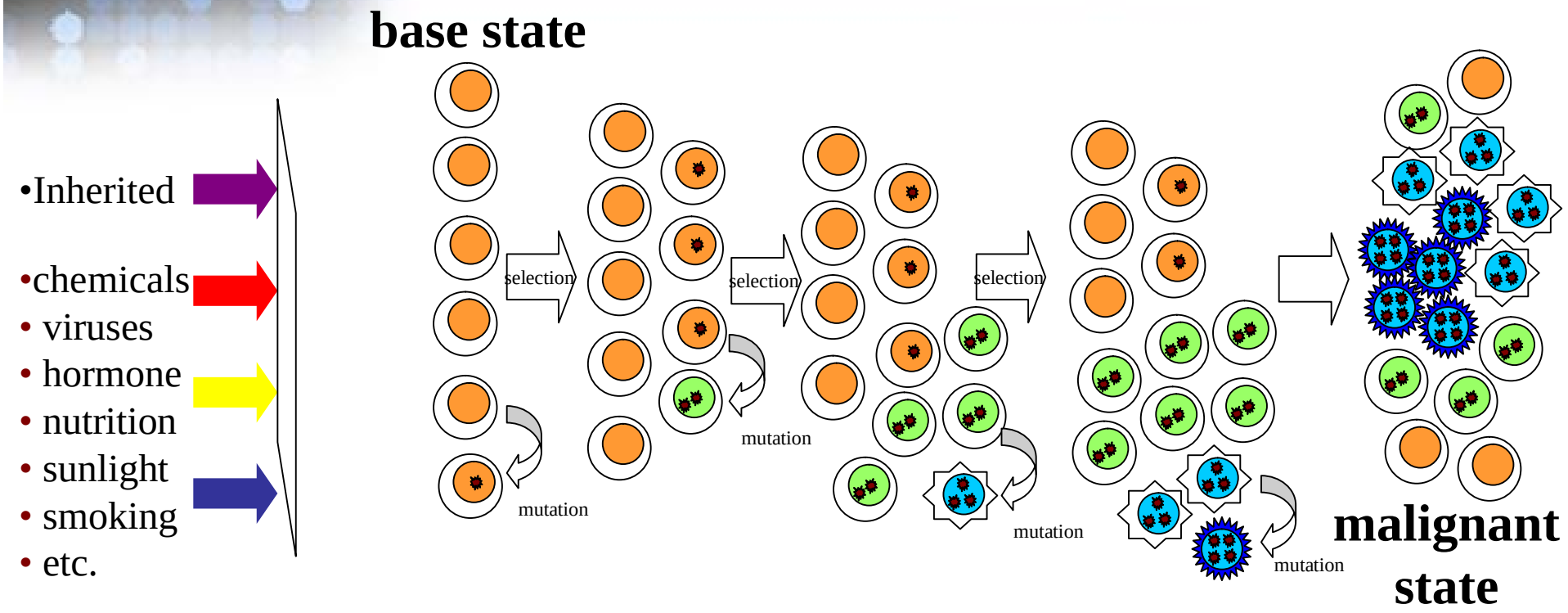


Intelligent Biosystems

Halycon

Febit

Cancer: A Complex Information Driven Evolving System



Fundamental Understanding of Cancer: Beyond Changes in the Genome, Need Knowledge of Changes in the "Biological Space"

Thinking Differently About Key Questions in Cancer

Including Innovation in the Equation

Innovation as Viewed by the NYT - Highlight from 2009

FORTY YEARS' WAR

Grant System Leads Cancer Researchers to Play It Safe

Bryce Vickmark for The New York Times

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

By GINA KOLATA
Published: June 27, 2009

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

RECOMMEND

COMMENTS

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

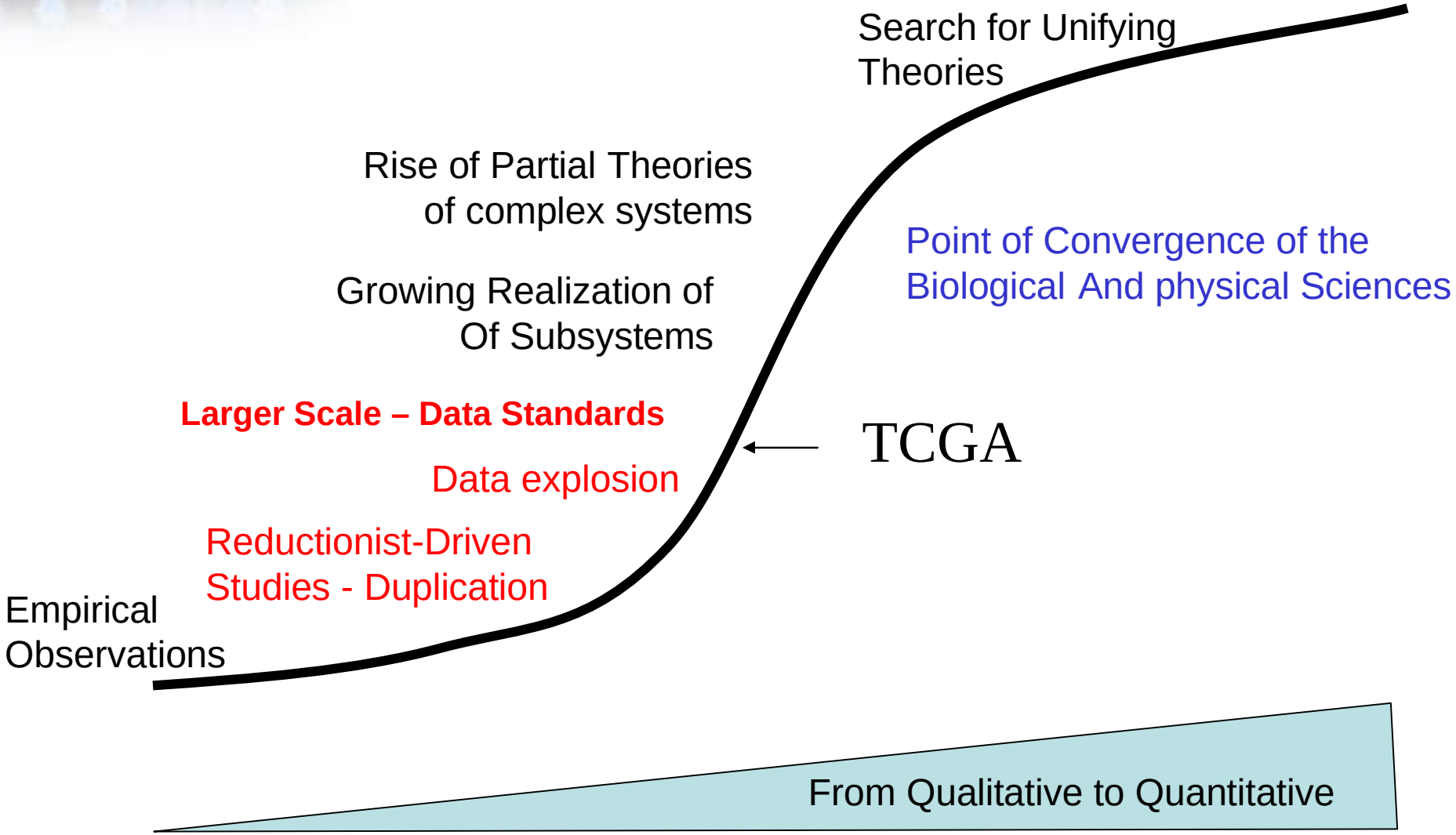
- …One major impediment, scientists agree, is the grant system itself. It has become a sort of jobs program, a way to keep research laboratories going year after year with the understanding that the focus will be on **small projects unlikely to take significant steps toward curing cancer…**
- …In fact,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

Are We Doing Enough to Drive Disruptive Innovation?

- Rejects the most obvious solution to a problem – not just new answers – new questions
- Find ways to generate multiple “non-obvious” solutions
- Driven by individual insights At the “intersection” of fields/technologies
- Combines solutions and methods from unrelated fields
- Disruptive to current dogma – challenges assumptions

State of Biomedical/Cancer Research – the S Curve

Adapted from E. Zerhouni

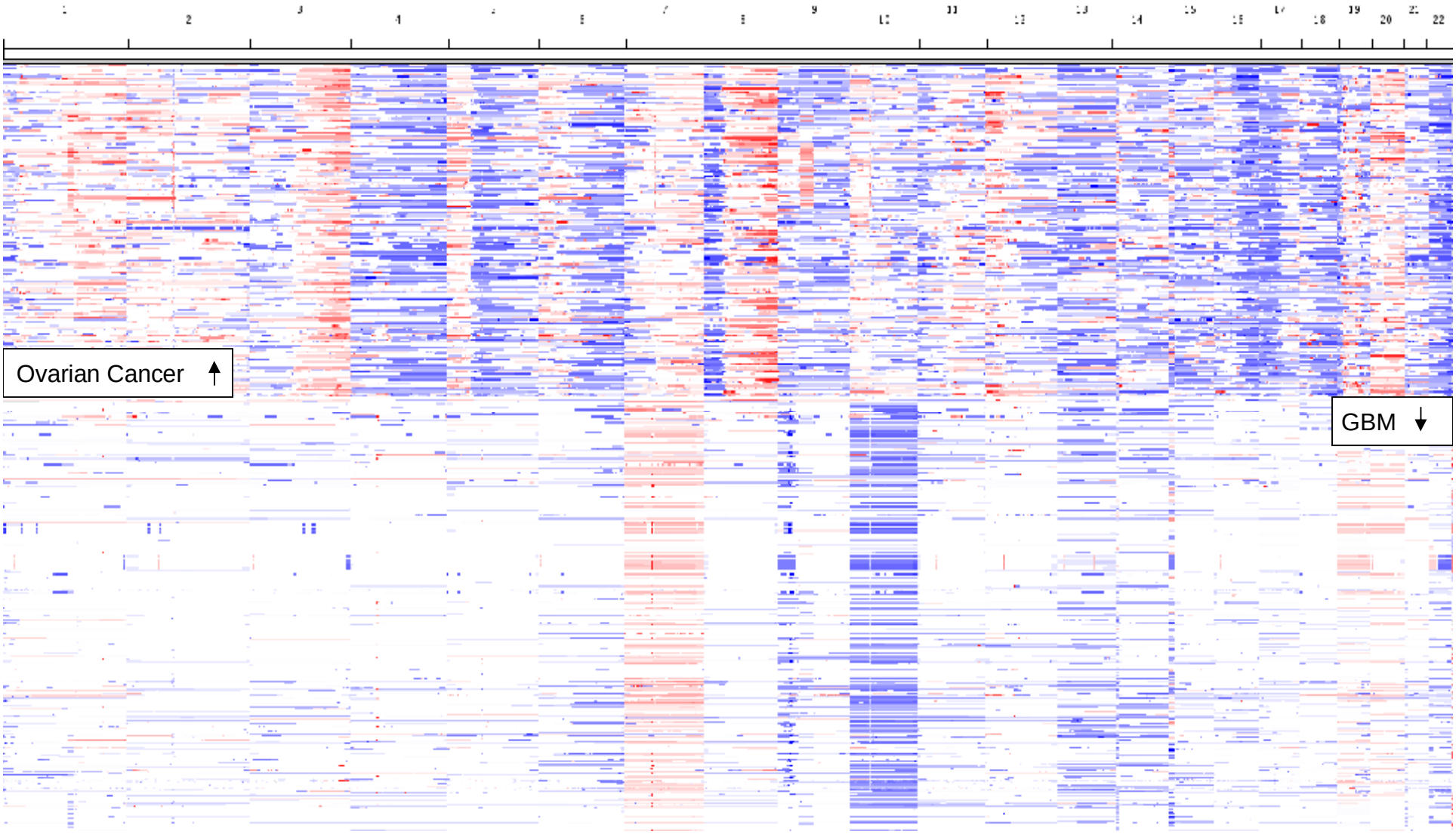


Complexity: No two snowflakes are alike

Micro (heterogeneity)
vs.
Macro (problem)

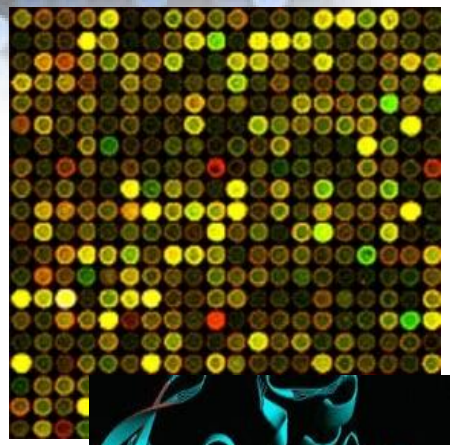
Snowcrystals.com

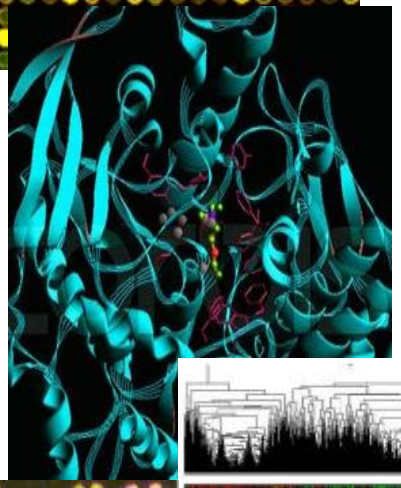
Complexity: Copy Number Alterations in GBM and Ovarian Cancers

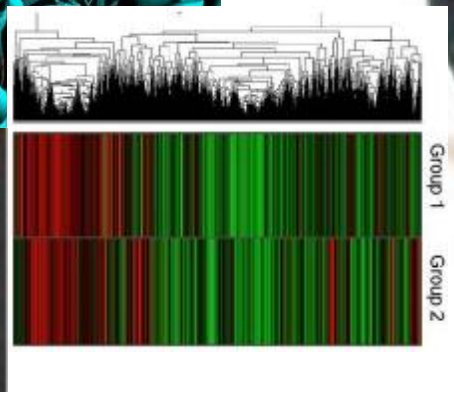


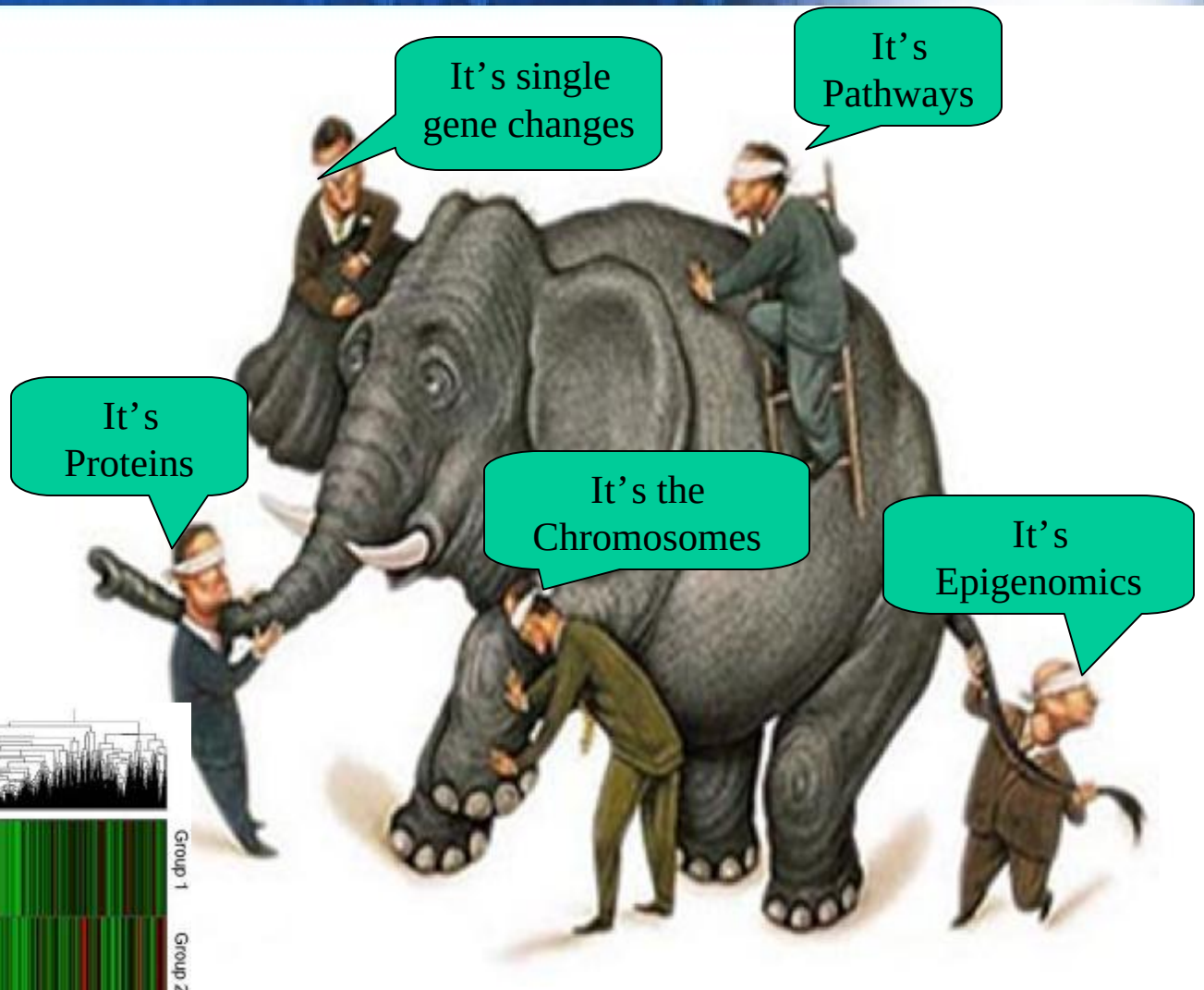
Courtesy of The Broad Institute and Memorial Sloan Kettering Cancer Center

Convergence Across the Genome = Data "Tsunami" = May be Paralyzing Complexity









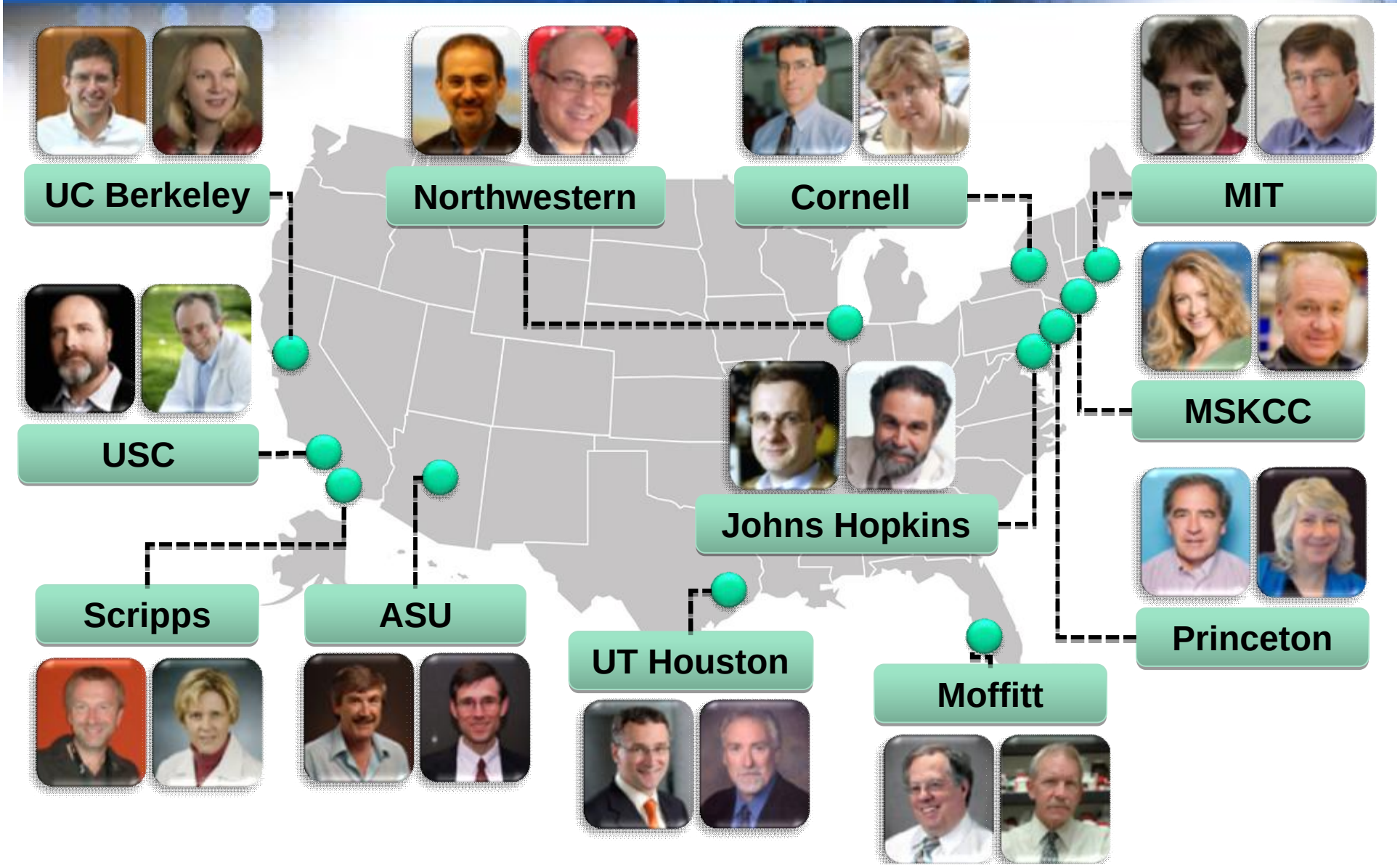
Cancer is a Result of Translation of Digital Information Across Length and Time Scales

Length Scale	Players		Group Behavior	Time Scale
10^{-0} m	Organisms	→	Population	Years
10^{-2} m	Organs	→	Organism	Months
10^{-4} m	Cells	→	Organ	Days
10^{-6} m	Organelles	→	Cell	Minutes
10^{-8} m	Molecules	→	Organelle	Seconds

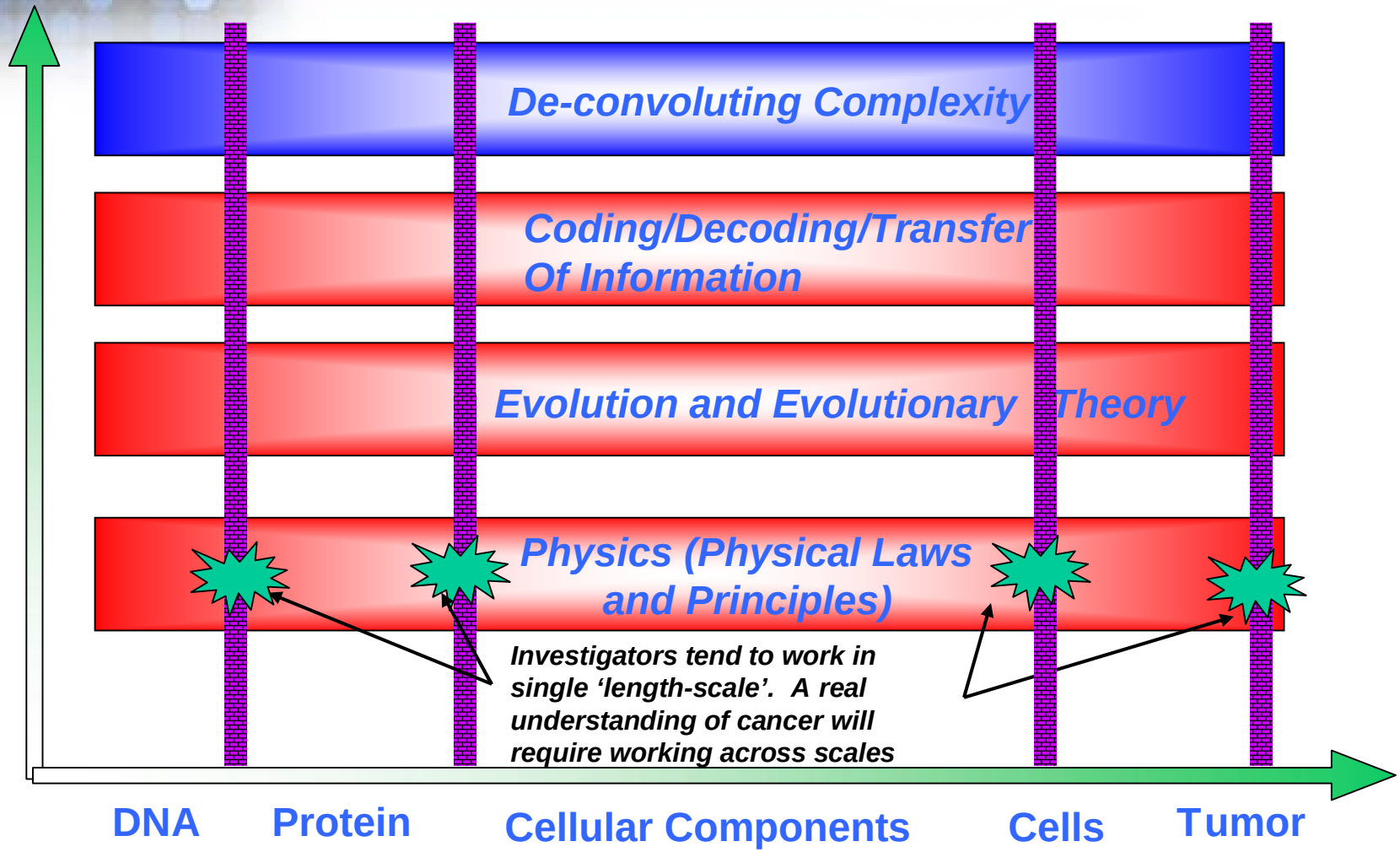
Interactions

For decades, we have endeavored to de-convolute the complexity of cancer by understanding each part at its most basic level. However, itis the interactions (across scales) that lead to emergent properties of cancer

Physical Sciences-Oncology Centers (PS-OC) Network



PS-OC Emerging Focus Areas



Length Scale – In Reference to Size (Ranging from 1 nm – 1 mm)

Building an Innovation Driven System of 21st Century Cancer Medicine – All Medicine

Innovation: Create a Personalized Cancer Medicine System

- Connected and interoperable IT infrastructure to translate research advances
- National system of biospecimen collection – storage – characterization, stewardship and access
- Technology standards
- Compendium of all genomic changes in all tumors/ subtypes
- Defined/validated biomarkers – signatures – as appropriate for all tumors/subtypes
- Appropriate and Responsive translational research infrastructure
- New clinical trials models – and networks
- Payer inclusion in process – enable reimbursement through involvement and knowledge