Computational Challenges and Opportunities in Personalized Medicine

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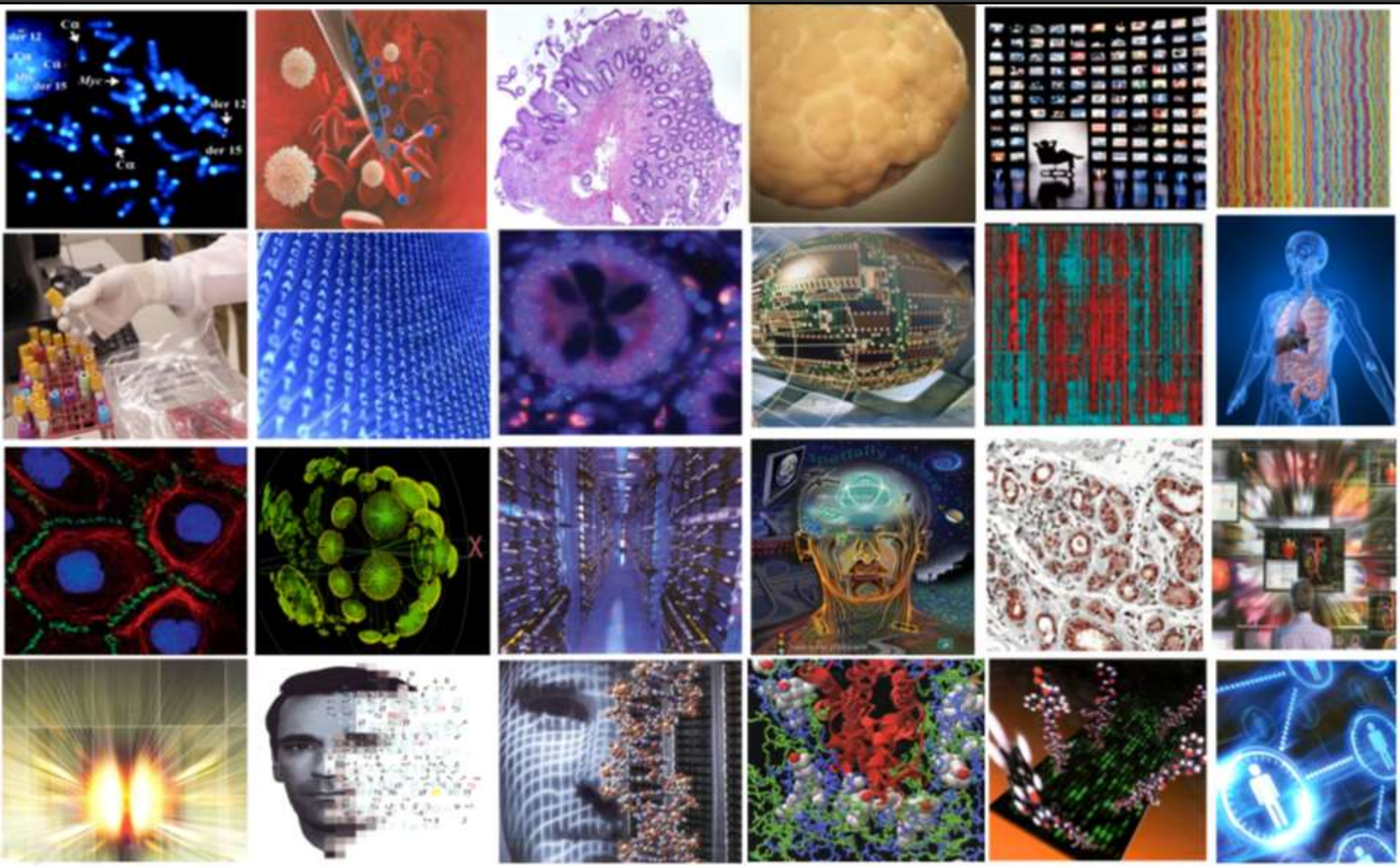
Slides available @ http://casi.asu.edu/



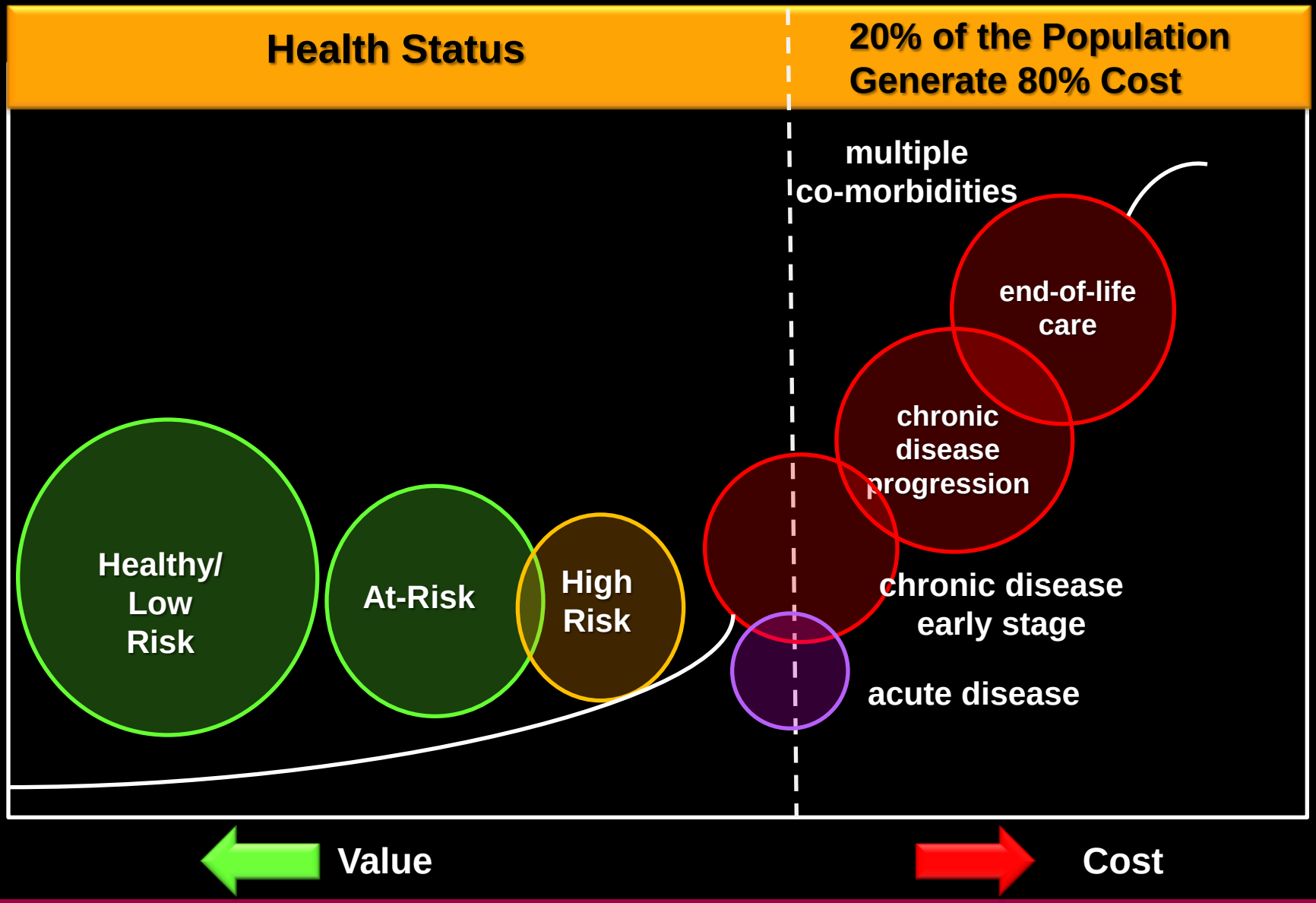
Healthcare: An Expensive Menu Without Prices

Sustainable Health: Societal (Economic) and Individual (Wellness)

Managing the Demands of an Aging Society and Escalating Chronic Disease Burden in an Era of Economic Constraint

From a "Do More, Bill More" Healthcare System to Managing System and Individual Risks for Improved Health Outcomes and Cost Control

The Economic, Social and Clinical Benefits of Proactive Mitigation of Disease Risk and Chronic Disease Co-Morbidities



New Value Propositions:
Risk Reduction and The Wellness Premium

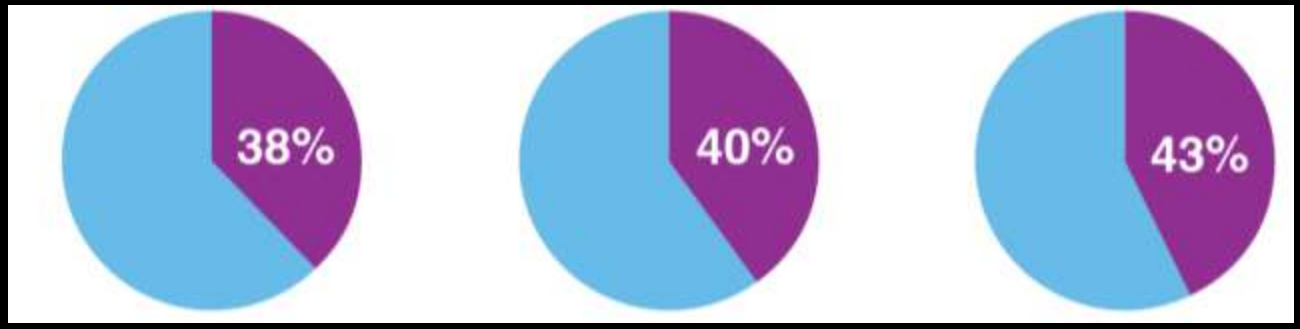
Emergence of a New Health Information Ecosystem
via
Convergence of Molecular Medicine, Digital Networks and Social Media

Shift from Reactive, Incident-Centric Care
to
Proactive Engagement to Mitigate Individual Risk

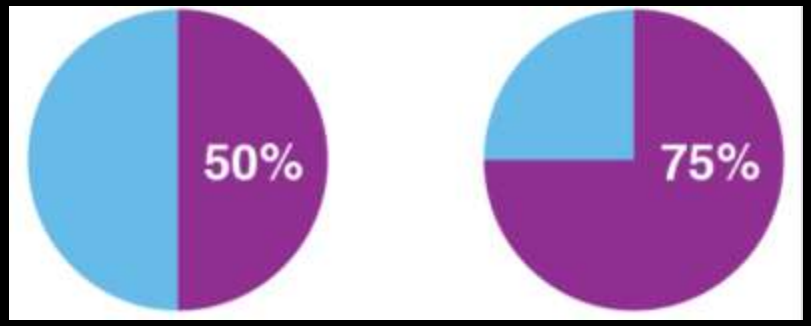
From "One Size Fits All" Treatment Approaches
to Individual Molecular Profiling and Personalized Medicine

One Size Does Not Fit All: The Huge Economic Waste in Therapeutics

Percent of population for whom class of drugs do not work



Antidepressants Asthma Diabetes

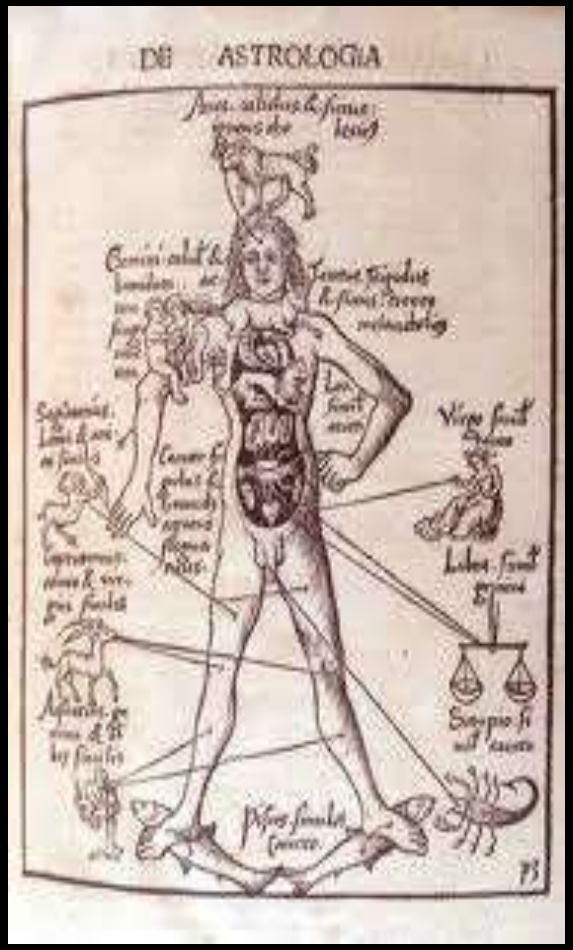


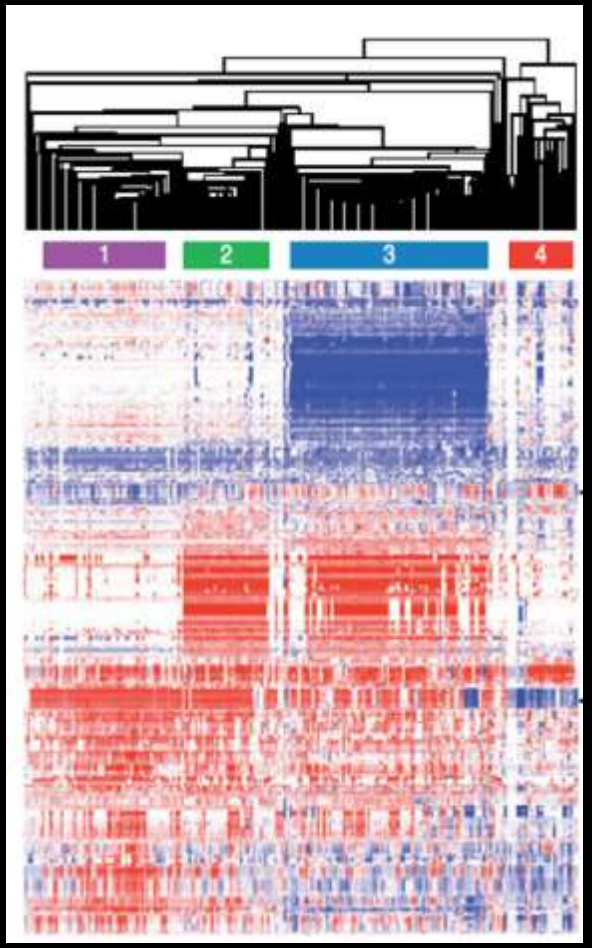
Arthritis Cancer

Cost of Ineffective Rx

- 90% of drugs work in only 30-50% individuals
- 2011 global sales of $880 billion ≡ $350 million wasted

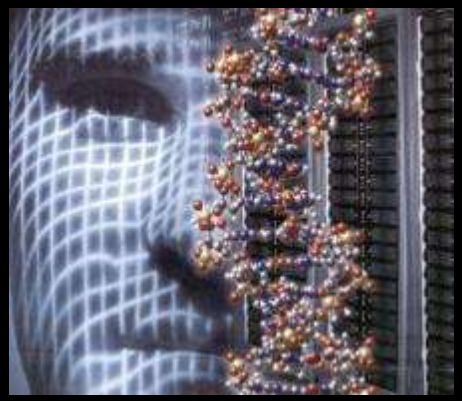
Medical Progress:
From Superstitions to Symptoms to Signatures



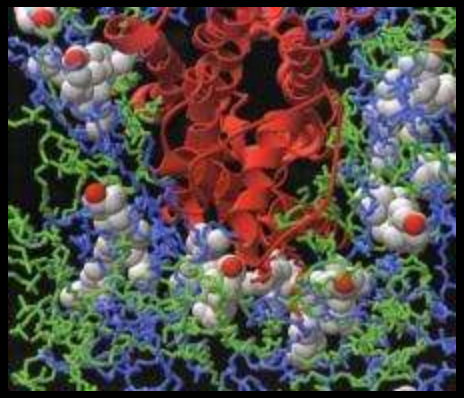


Mapping The Molecular Signatures of Disease: The Intellectual Foundation of Rational Diagnosis and Treatment Selection

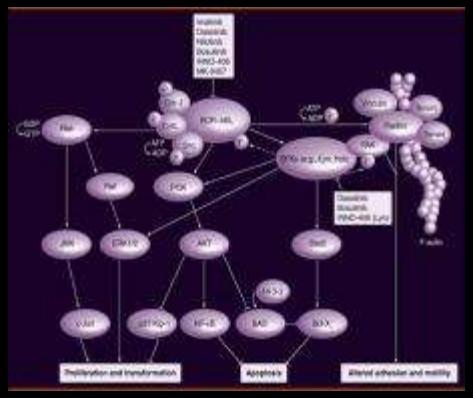
Genomics



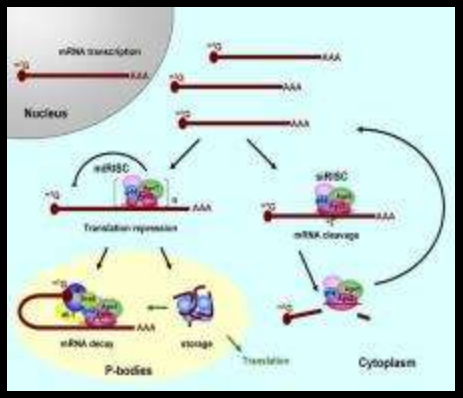
Proteomics

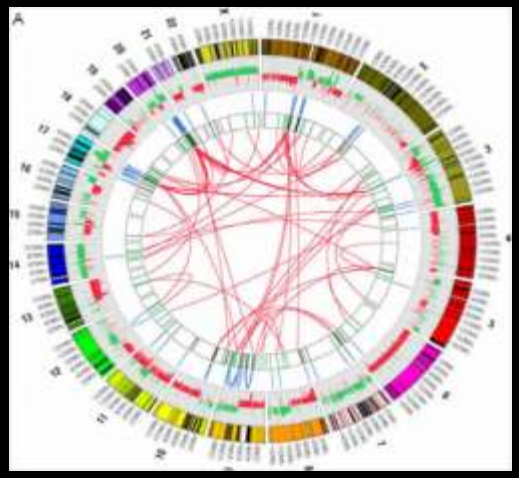


Molecular Pathways and Networks



Network Regulatory Mechanisms





ID of Causal Relationships Between Network Perturbations and Disease

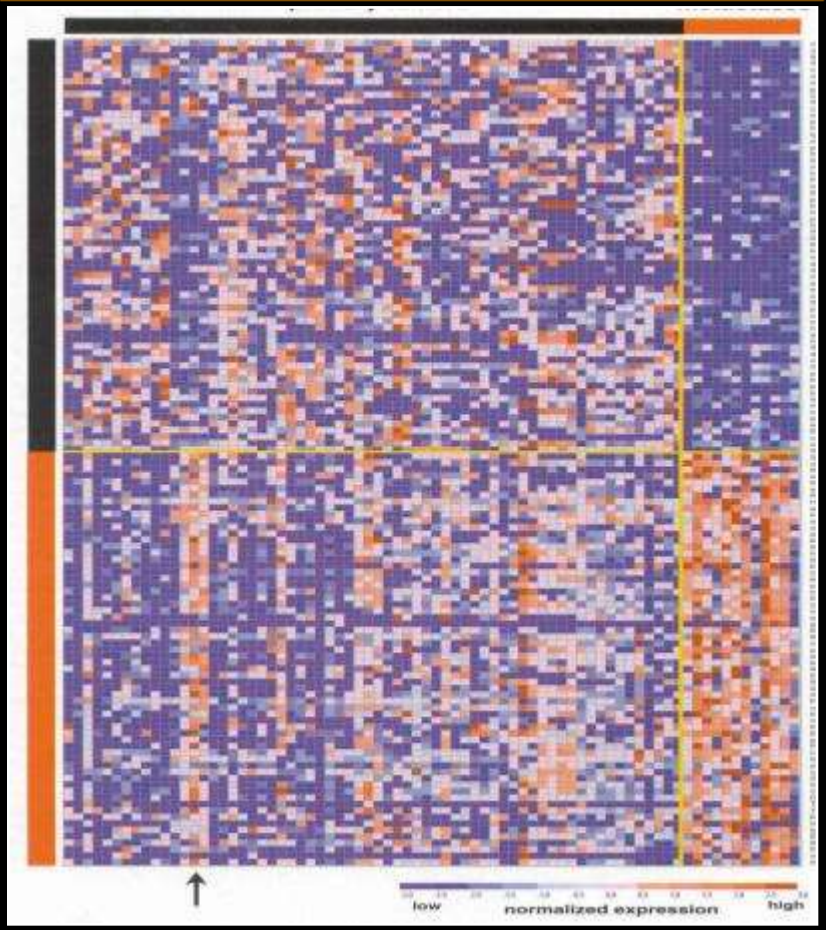
Patient-Specific Signals and Signatures of Disease or Predisposition to Disease

Personalized (Precision) Medicine

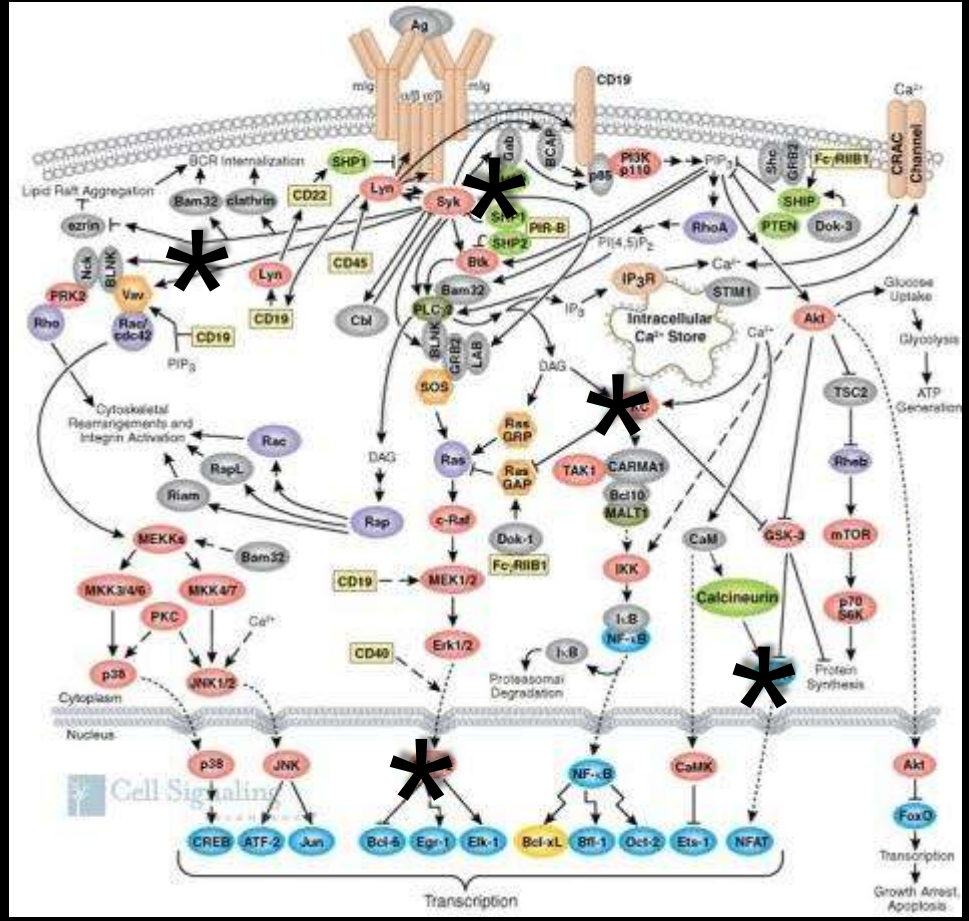
- right diagnosis
- right treatment
- right patient
- right time

Mapping Causal Perturbations in Molecular Pathways and Networks in Disease: Defining a New Taxonomy for Disease

Disease Profiling to Identify Subtypes (+ or - Rx Target)

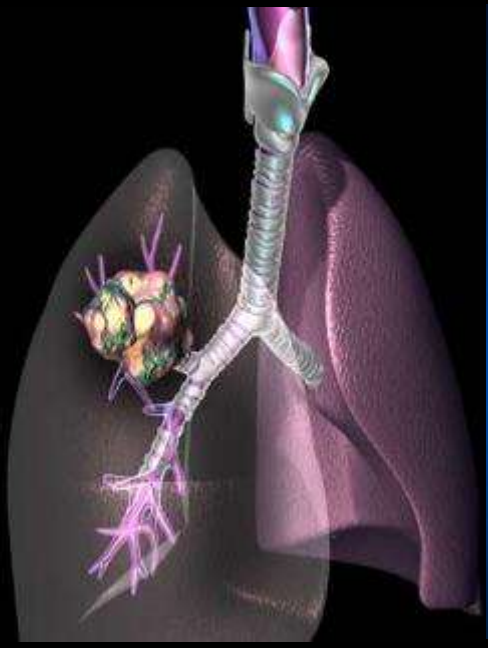


ID Molecular Targets for MDx and/or Rx Action



Mapping the Molecular Signatures of Disease, Disease Subtyping and Targeted Therapy: Companion Diagnostics and the Right Rx for the Right Disease (Subtype)

Her-2+
(Herceptin)



EML4-ALK
(Xalkori)

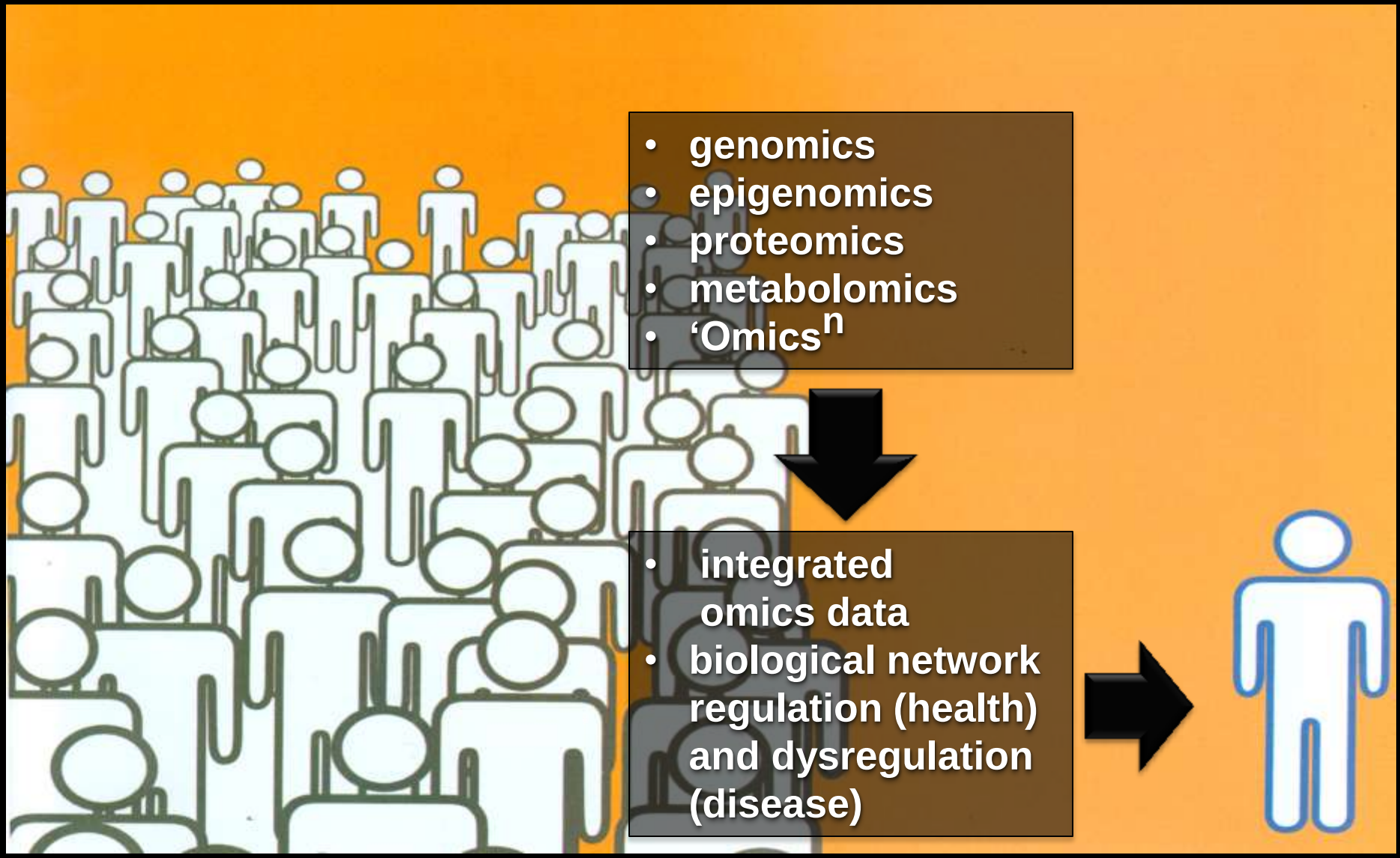
KRAS
(Erbitux)
(Vectibix)

BRAF-V600
(Yervoy)
(Zelboraf)

The Journey to Integrative Personal Omics Profiling (iPOP) and Personalized Medicine

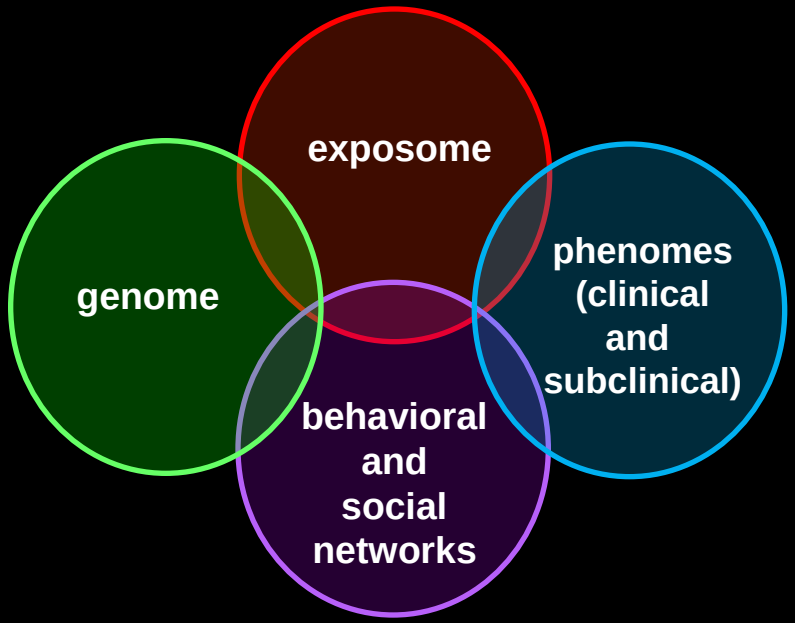
Integrated Omics (iOmics): Building the Core Technical Foundations of Molecular Medicine and Improved Healthcare Delivery

The Integrative Personal Omics Profile (iPOP)



Information-Based Services for Healthcare and Wellness

Precision Profiling of Health Status



Population- and Individual-Datasets

facile integration and analysis of diverse datasets

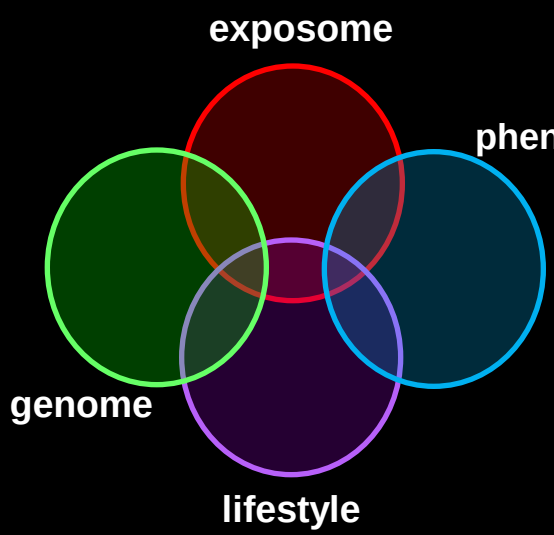
Actionable Information

risk identification and mitigation

Integrated Care and Wellness

VALUE

Information-Based Services for Healthcare and Wellness



data curation and analysis

risk identification and mitigation + decision-support

- earlier detection of disease
- rational Rx
- monitoring of health status
- predisposition risk

profile

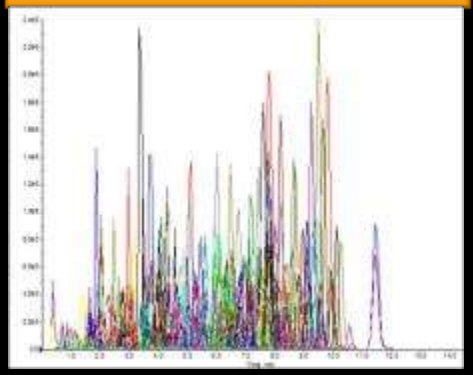
analyze

act

The Evolution of Clinical Diagnostic Testing in 'Omics Era and Device Technologies

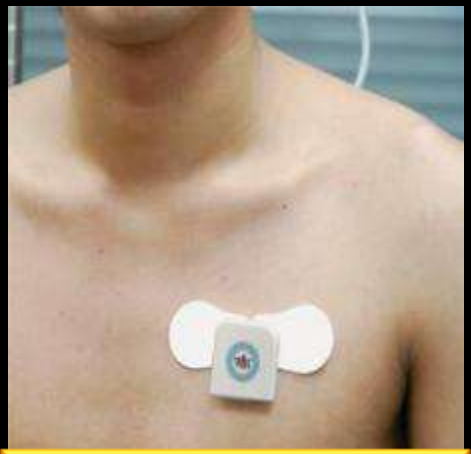
Unianalyte Tests

Multianalyte Tests



Whole Genome Sequencing

Centralized Testing and Large Capital Instrumentation Investment



On-Body: In-Body Sensors

Portable and Point of Need

Increasingly Decentralized Testing

The Transformation of Biomedical Research and Clinical Care Into Information-Intensive Domains

The Big Data Challenge and Disruption of Academic Research, Clinical Care, Supply Chains and Current Business Models

New Operational Competencies
and
New Value Propositions

Will Low Cost Whole Genome Sequencing Change Everything?

Source: Davies, Kevin (2011). The Road to the 1000 Genome. PHT/SLA Spring Meeting

- 1 million genomes x $1,000 = $1 billion
  "It's not even a scary number anymore!"

Lander E. S. (2011) Nature 470, 187-197

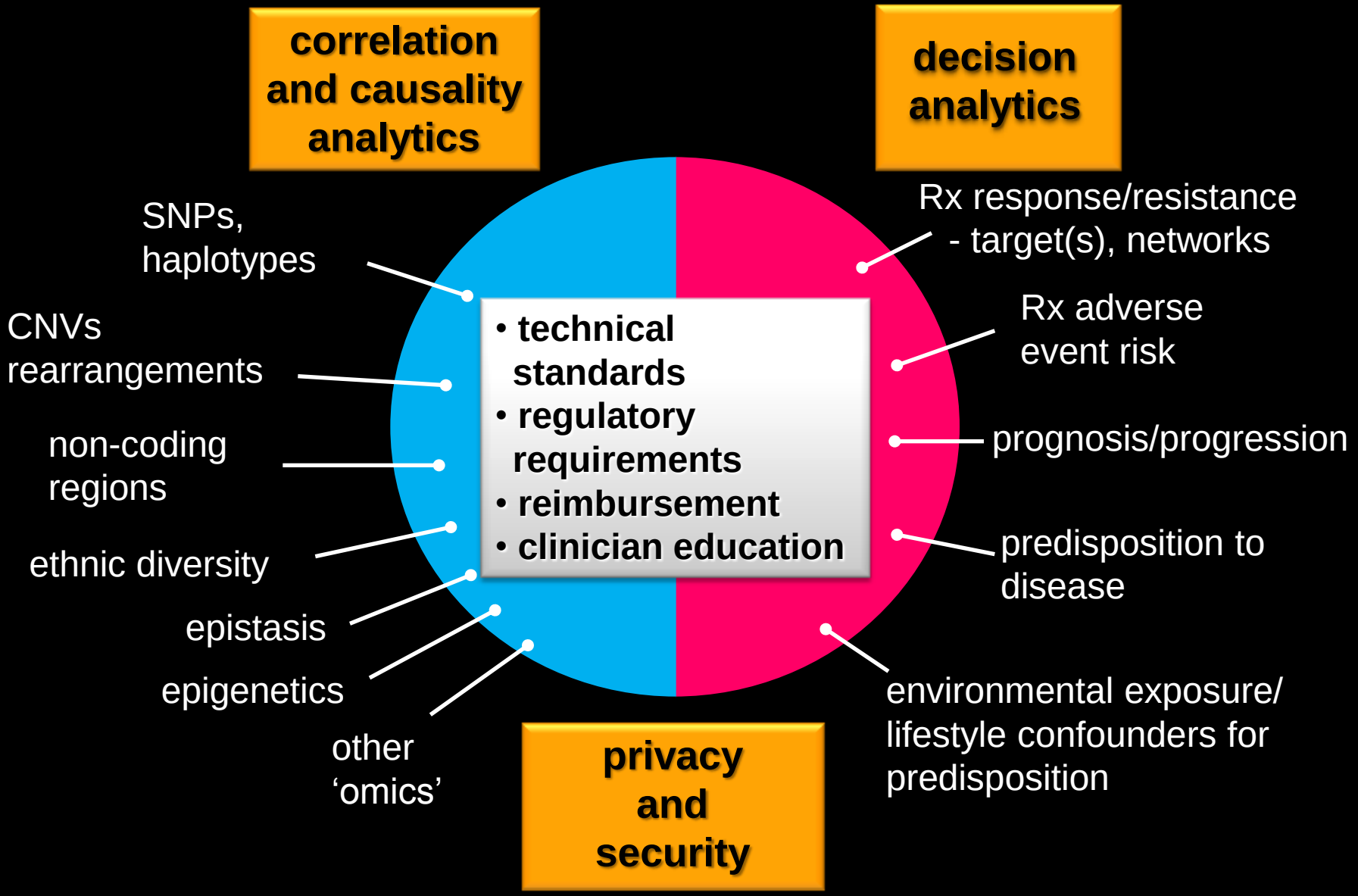
The Cost of Whole Genome Sequencing (WGS) Vs. The Cost of Computational Analysis and Storage

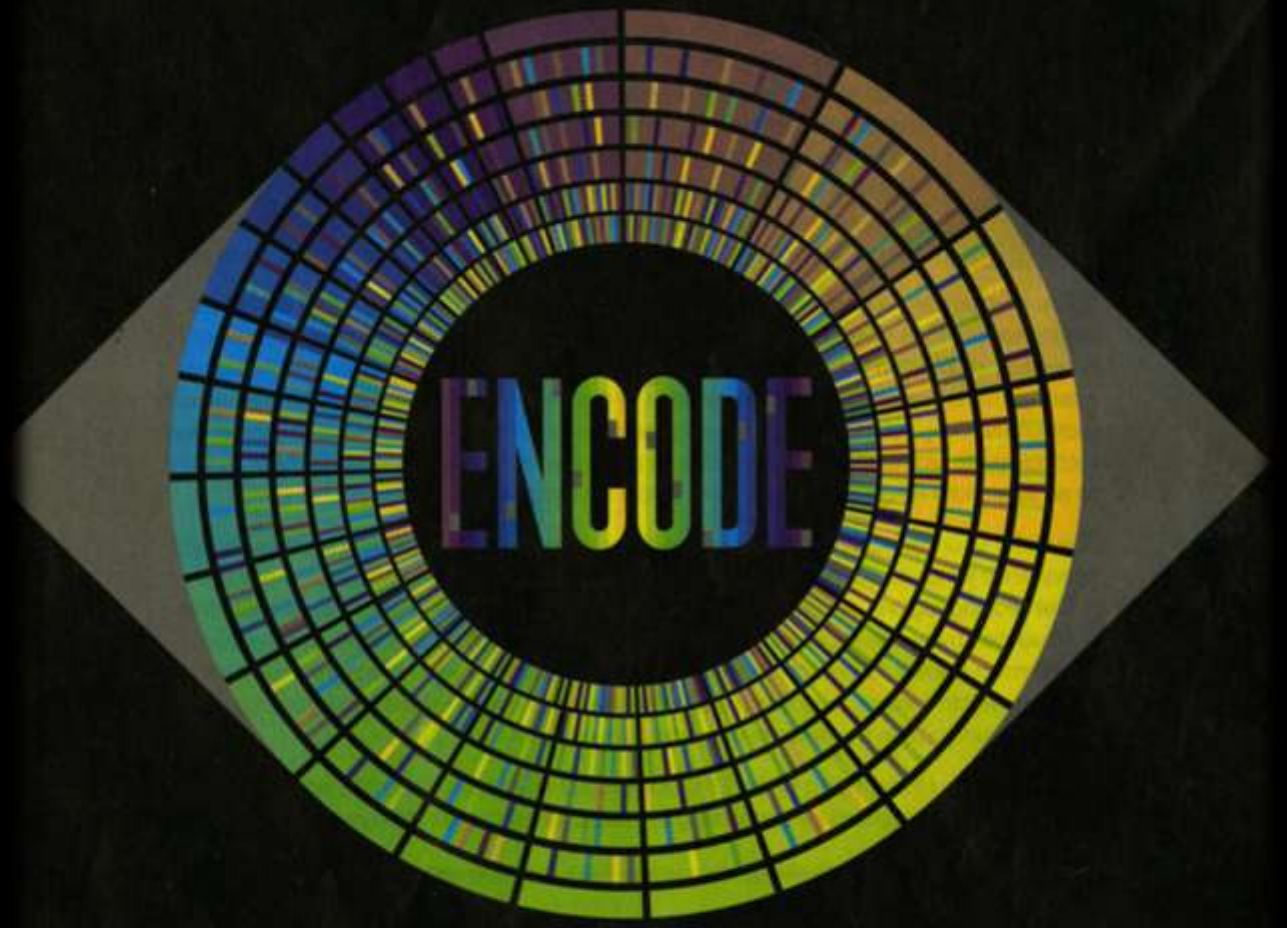
- the $1000 genome
  - the $? analysis and interpretation cost
  - the $? storage, retrieval and security costs
- turn around time (TAT) and cost for clinical use
- regulatory and reimbursement policies

What Is A Complete and Accurate Analysis of Genome Sequence, Architecture, Topology and Regulatory Networks?

What Standards of Accuracy Will Regulatory Agencies Require For Use of Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS) in Clinical-Decisions?

Low Cost Whole Genome Sequencing and Molecular Medicine: Dependency on Large Scale (Massive) Data Annotation and Analytics





GUIDEBOOK TO THE HUMAN GENOME

The Human Genome (ENCODE 2012)

- protein-coding DNA = c.1.5% genome= 20,687 protein-coding genes
- pervasive genome transcription
  - 93% bases transcribed into RNA
  - 18,400 non-coding RNA genes
  - 70,000 promoter regions, 400,000 enhancer regions
  - diverse transcription and (co)splicing processing patterns
- 11,244 DNA pseudogene regions with variable transcription
- 42% DNA accessible at 3.0 million sites for interaction with regulatory elements
- complex 3-D topology
  - average 3.9 distal (long range) DNA regions link with beginning of each gene

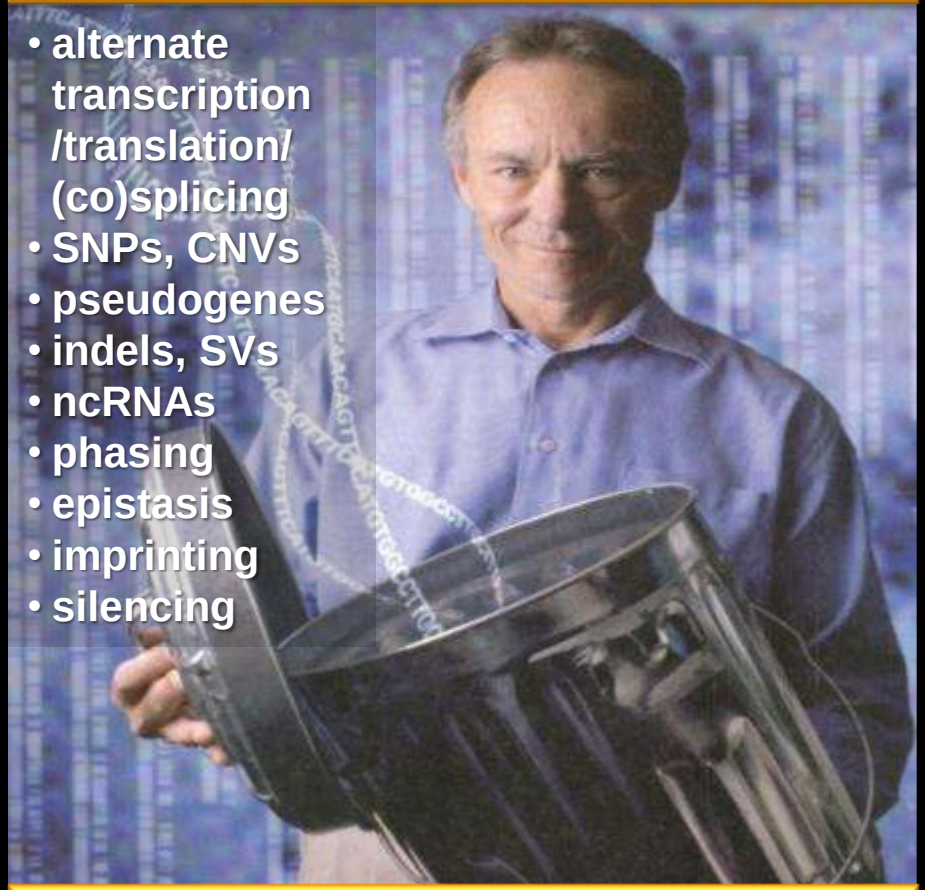
Genes For ….
The Overly Simplistic and Deterministic Dangers of a Genome-Sequence Centric Perspective

The Over-Simplified Perspective That While Exome-and Whole Genome-Sequencing Will Reveal the Full Etiology of Disease Pathogenesis

Its the Network, Stupid!

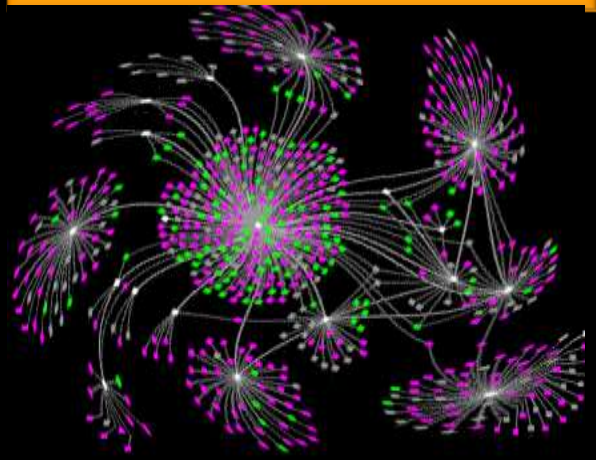
Individual Variation, Genome Complexity and the Challenge of Genotype-Phenotype Predictions

Junk No More: Pervasive Transcription

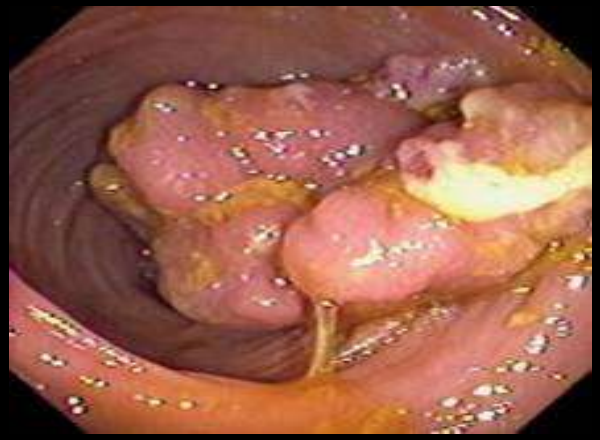


recognition of genome organizational and regulatory complexity

Cell-specific Molecular Interaction Networks

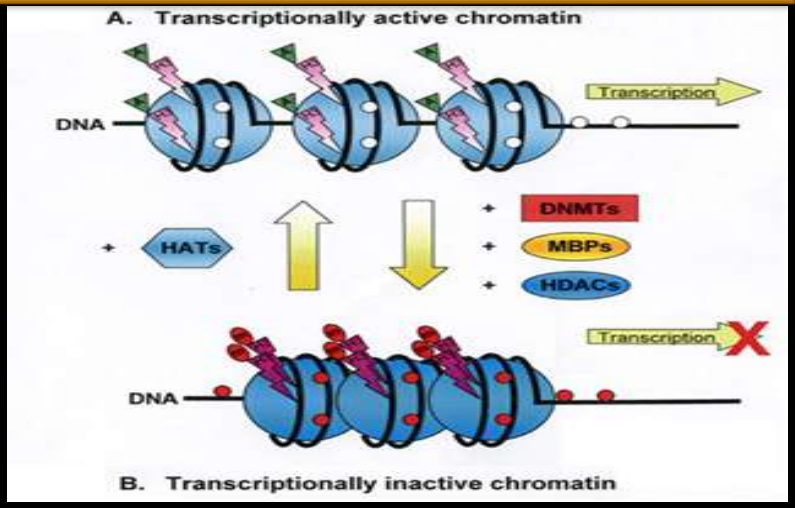


Perturbed Networks and Disease



The Epigenome

Modulation of Gene Expression/Regulation by Environmental Factors, Xenobiotics and Rx (The Exposome)



Effect of Maternal Diet/Stress/Rx exposure on Germ Line Genome Imprinting (+ trans-three-generational?)

IHEC
International Human Epigenome Consortium

International Human Epigenome Consortium

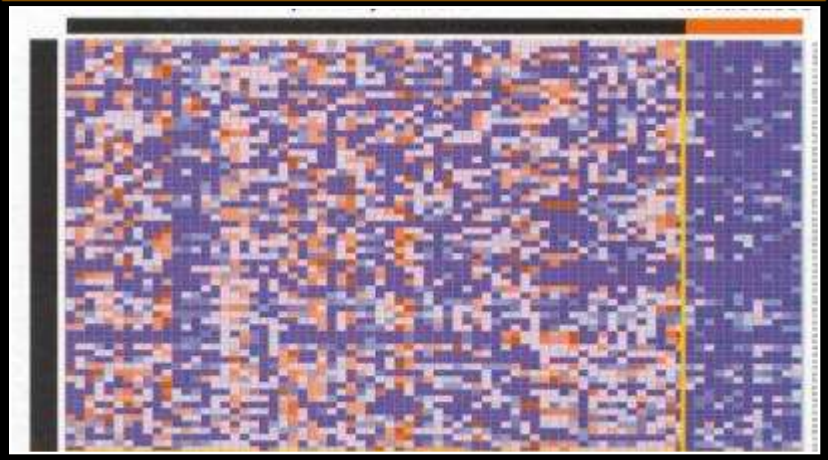
- 1000 reference genomes by 2020

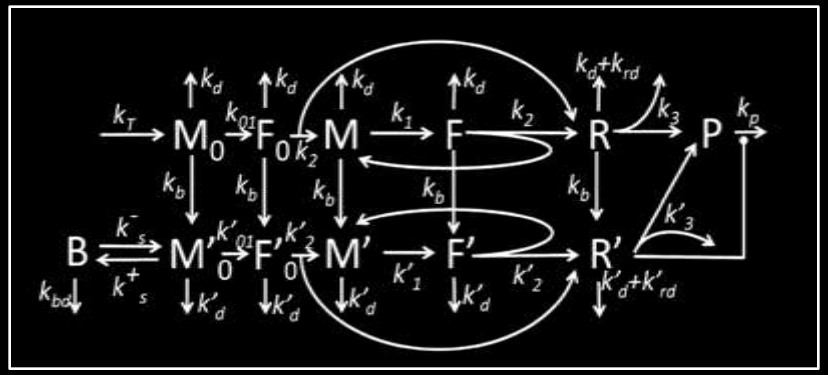
project blueprint

- launch September 2011 with €30-million
- map epigenome in 60 human blood cell classes and neoplastic counterparts

Mapping Causal Perturbations in Molecular Pathways and Networks in Disease: Defining a New Taxonomy for Disease

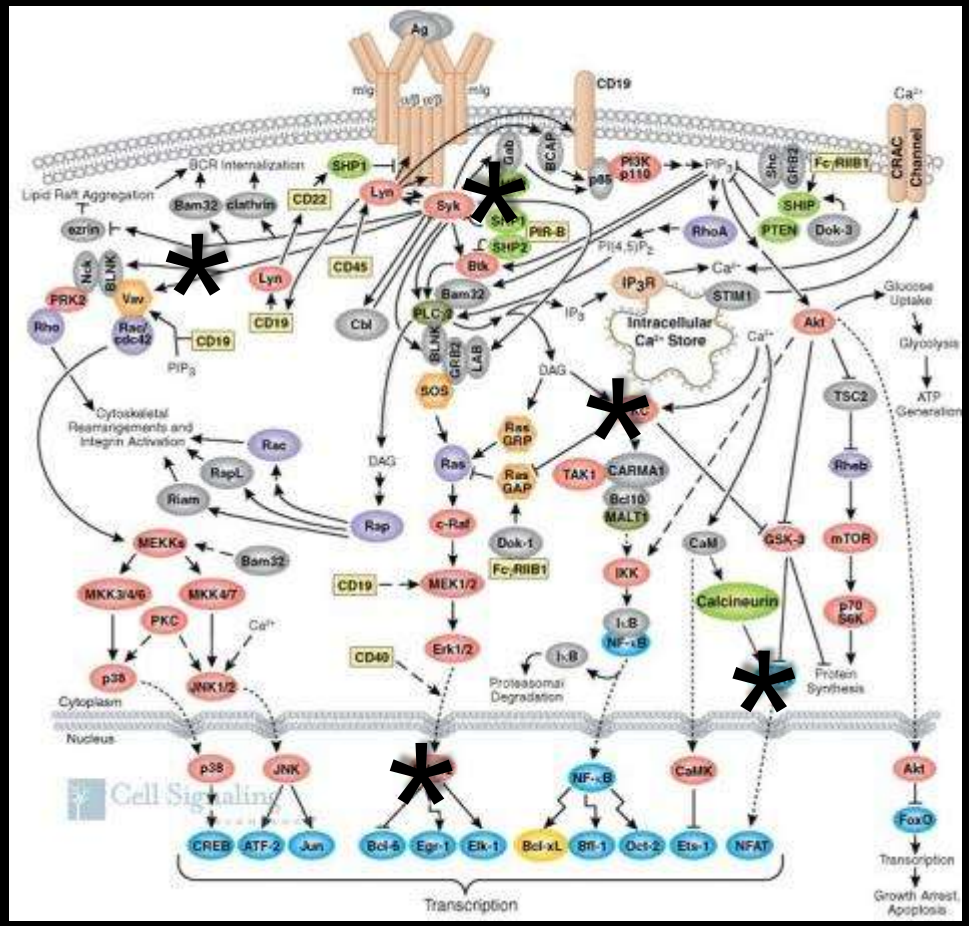
iOmics Profiling to Identify Disease Subtypes (+ or - Rx Target)





Modeling of Information Flow in Biological Networks

Altered Network Structure and ID of Molecular Targets for MDx and/or Rx Action



Initial Response (A/B) of BRAF-V600 Positive Metastatic Miliary Melanoma After 15 Weeks Therapy with Vemurafenib (Zelboraf® - Roche) Followed by Rapid Recurrence of Rx-Resistant Lesions with MEKI C1215 Mutant Allele After 23 Weeks Therapy

From: N. Wagle et al. (2011) J. Clin. Oncol. 29, 3085

http://jco.ascopubs.org/content/29/22/3085.full.pdf+html

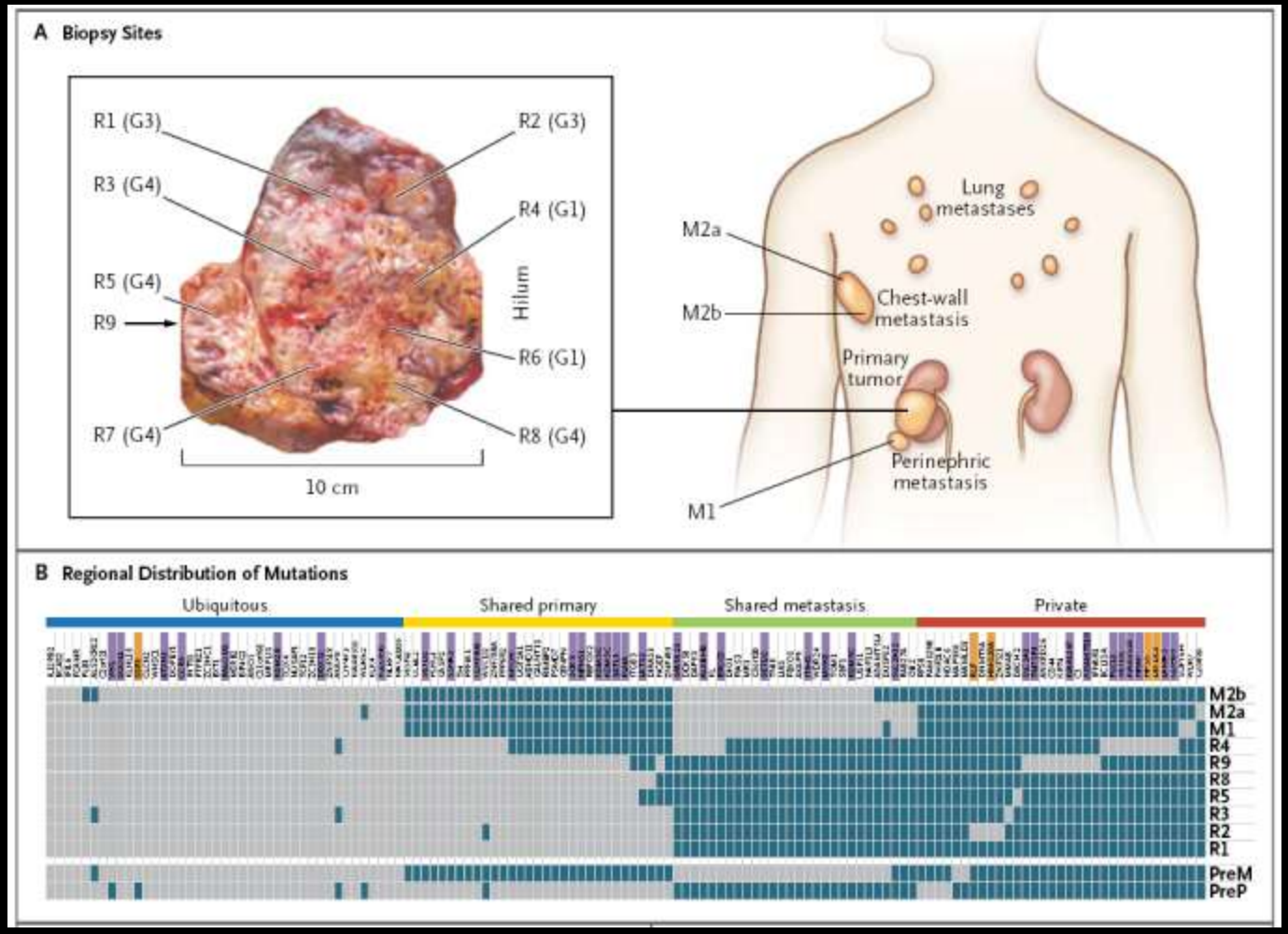
Reducing The Failure Rate of Investigational Drugs in Clinical Trials

- targeted therapies, YES!

but

- improved success requires targeting network modules, pathways and subnetworks not single molecular targets
- network pharmacology

Intratumor Genetic Heterogeneity in Multiple Regions of Primary Clear Cell Tumor and Three Metastases (Perinephric and Chest Wall) in RCC

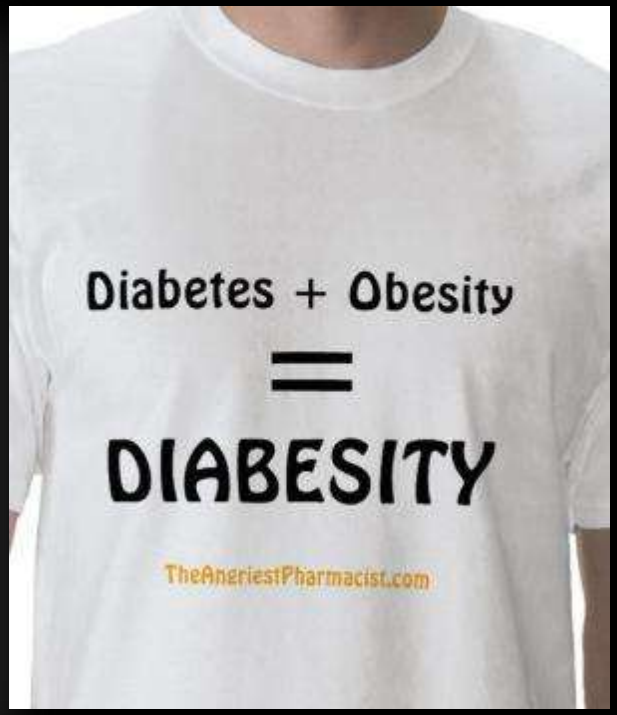
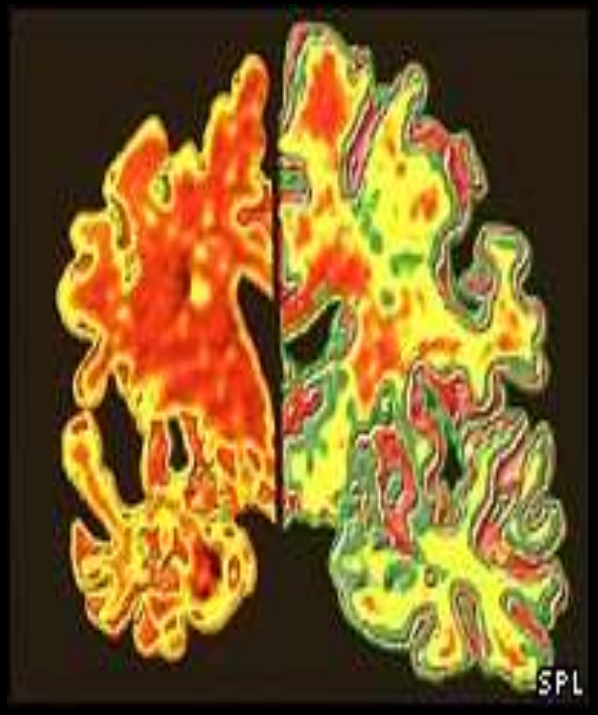


From: M. Gerlinger et al. (2012) NEJM 366, 883

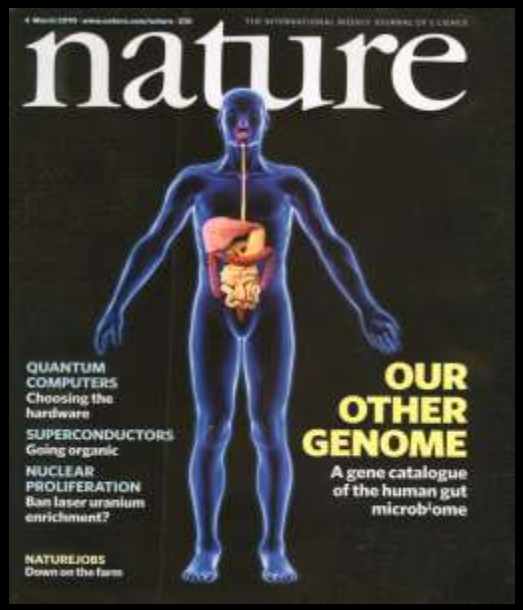
Molecular Network Perturbations in Complex Chronic Diseases
A Perplexing Emerging Question

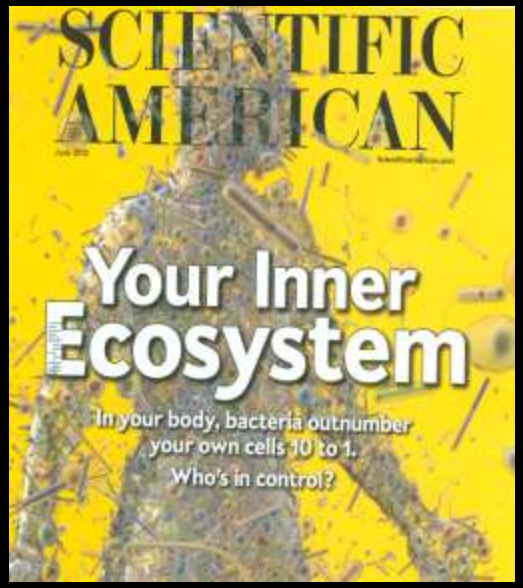
- is the multiplicity of pathways dysregulated in advanced metastatic cancer and the degenerative neuropathies (Alzheimers disease) an insurmountable technical barrier to design of poly-target (promiscuous) agent/combinations?
  - highest failure rates of new Rx in any therapeutic category

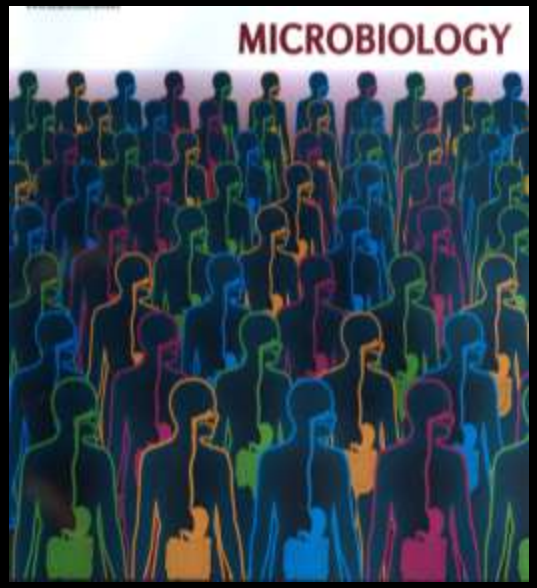
The Ever Earlier Detection of Major Diseases: Different Clinical Scenarios

Cancer: Detection Before Metastasis	Cardiovascular/ Metabolic Diseases	Neurodegenerative Diseases
		
Early Diagnosis and Curative Surgery	Lifestyle Changes and/or Rx to Limit Risk	The Dilemma of Early Diagnosis Without Rx

We Are Not Alone:
The Scale and Diversity of Our Companion Microbiomes







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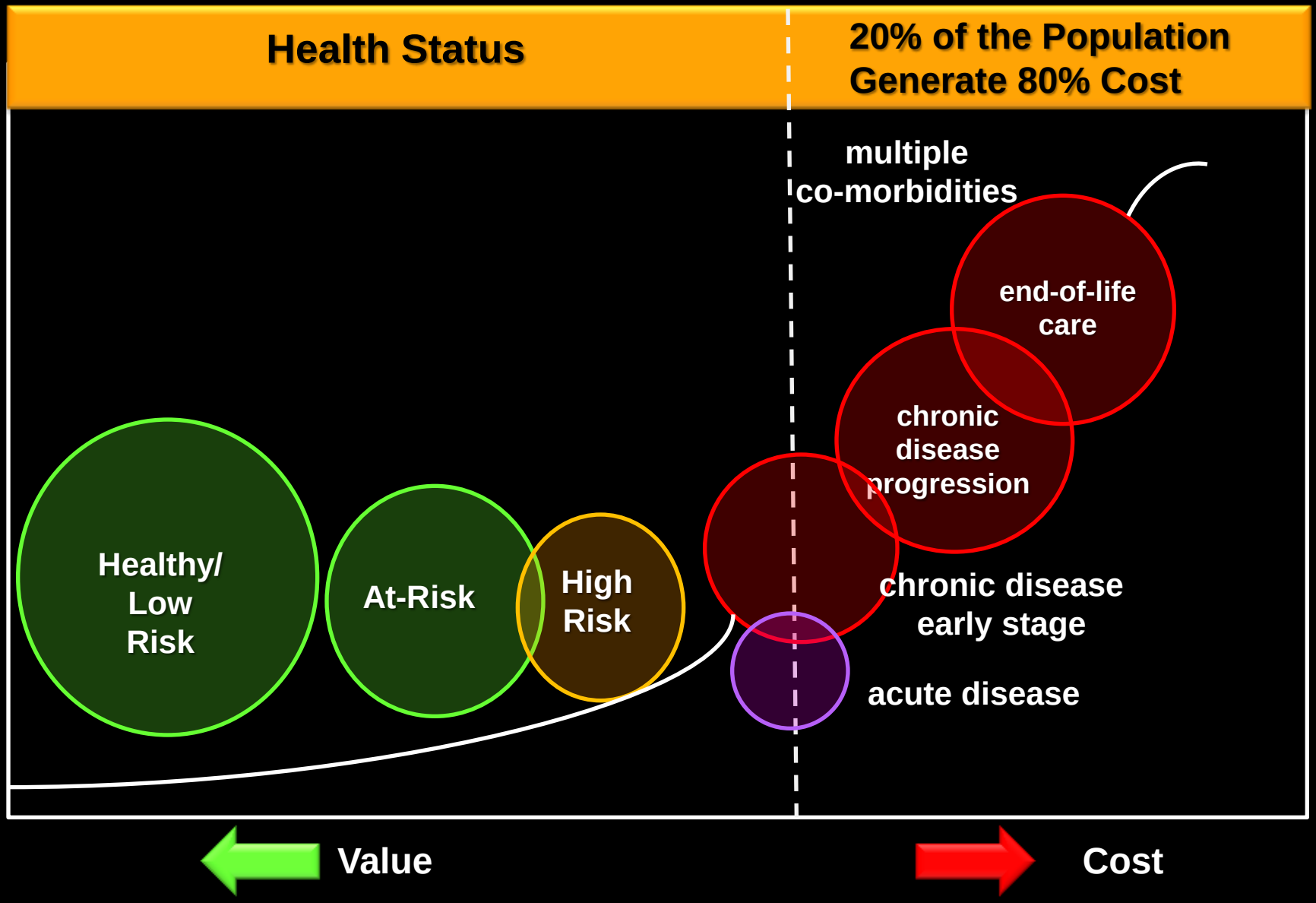


The Wellness Premium

Greater Engagement and Incentivization of Consumers/Patients in Care Decisions and Sustaining Wellness

“Patient-Centric Healthcare Without Patient Engagement Is An Illusion”

Invasion of the Body Trackers

Individual Biosignature Profiling Via On Body: In Body (OBIB) Sensors and Devices

Remote Health Status Monitoring

M4: Making Medicine More Mobile

m.Health

Remote Health Monitoring and Chronic Disease Management

Lifestyle and Fitness

Information for Proactive Health Awareness (Wellness)

Healthcare Products are Merging into Consumer Retail

Example:

Alivecor's iPhone ECG

Technology-Enabled Independent Living

**“If I’d known I was going to live this long
I’d have taken better care of myself”**

Eubie Blake, Musician on 100th Birthday, 1983

Consumer Health Informatics

- on-line help/support services (practice-and patient-specific unrelated to general web information)
- automation of out-of-office care
- decreased office visits
- e-pharmacy
- new tools for improved compliance and coaching
- reduced hospital readmissions
- m.health and remote health status monitoring

Social Spaces Become Quantifiable

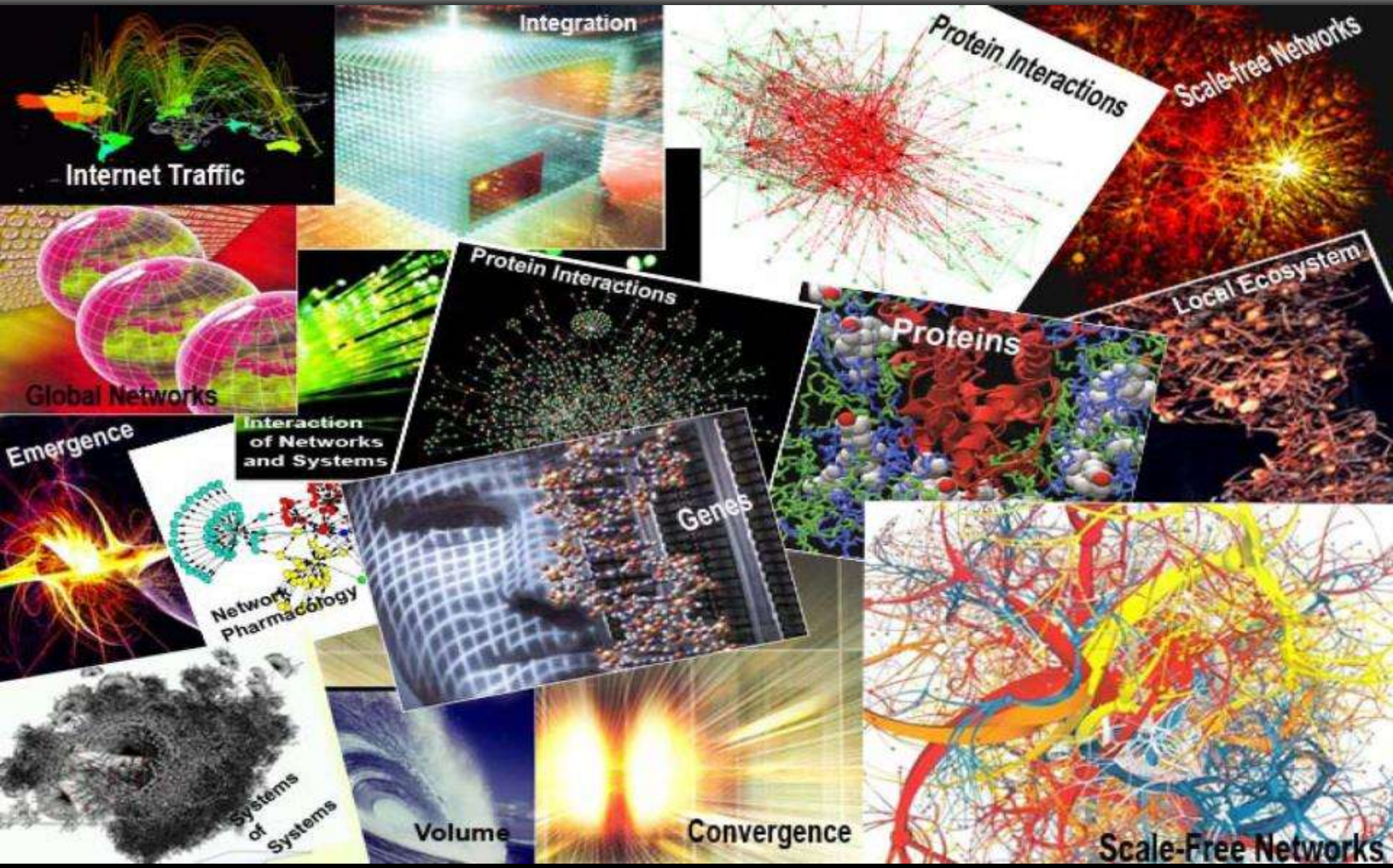
- who knows why people do what they do?
  - the fact is that they do!
- these actions can now be traced and measured with unprecedented precision
- with sufficient data, the numbers reveal increasingly predictable behavior individual risk patterns
- new business opportunities in multiple sectors including healthcare
- new ethical and legal issues

Proactive Engagement of Patient Communities in Investigational Clinical Trials and Observational Outcomes Studies

Interactive Participant-Centered Initiatives (PCI)

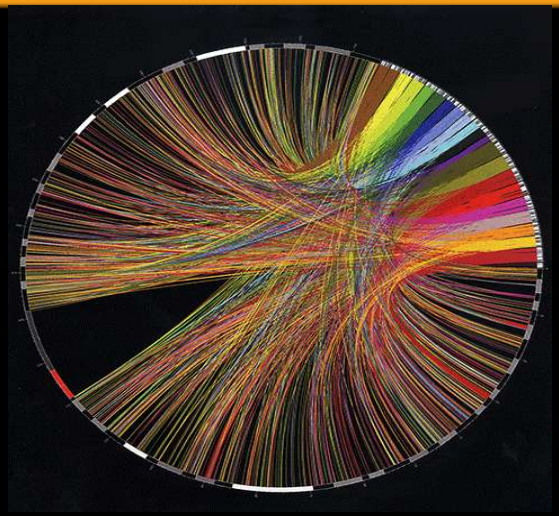
- social media, patient advocacy and consumer/care-giver engagement
- new opportunities to capture, share, mine and integrate data
  - research (deidentified) and clinical care (identified)
- faster recruitment for clinical trials accumulation of large sample sizes for suitable statistical power
- build new repository biobank networks of well curated and standardized samples to support research

Data: The Fastest Growing Resource on Earth

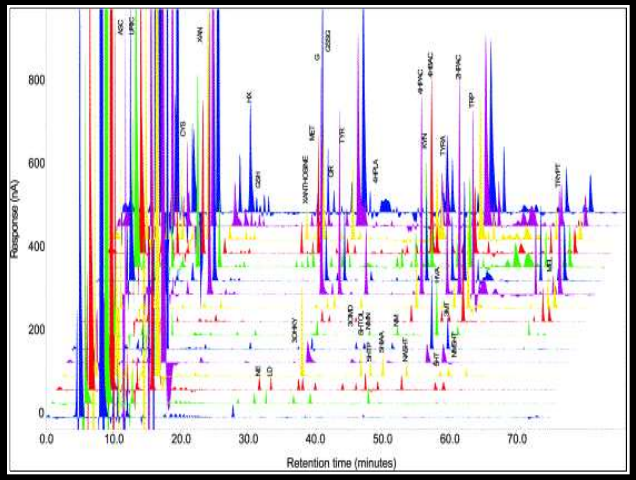


Burgeoning Research Datasets in Biomedical Informatics

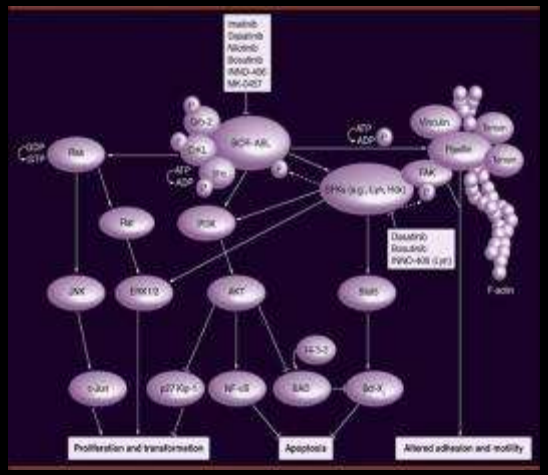
Genomics

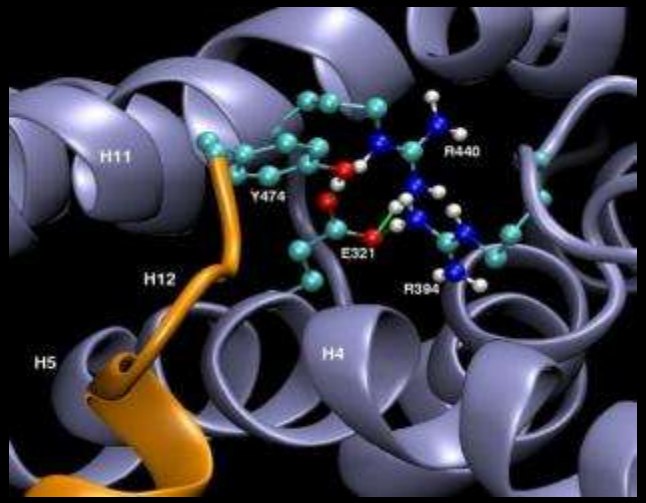


Proteomics

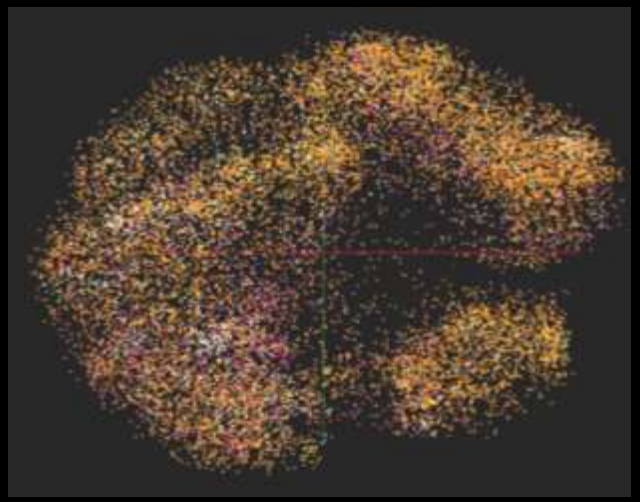


Molecular Pathways





Molecular Interactions



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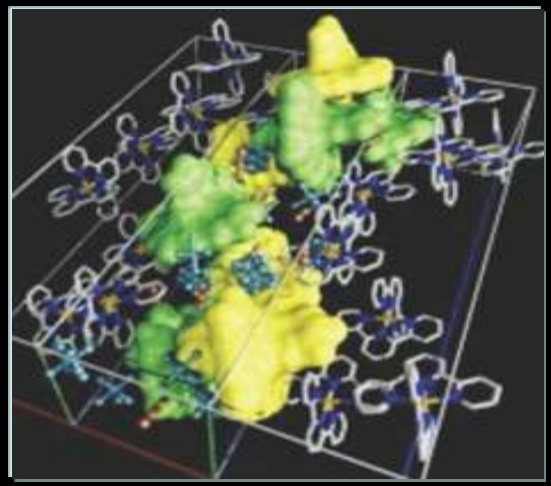
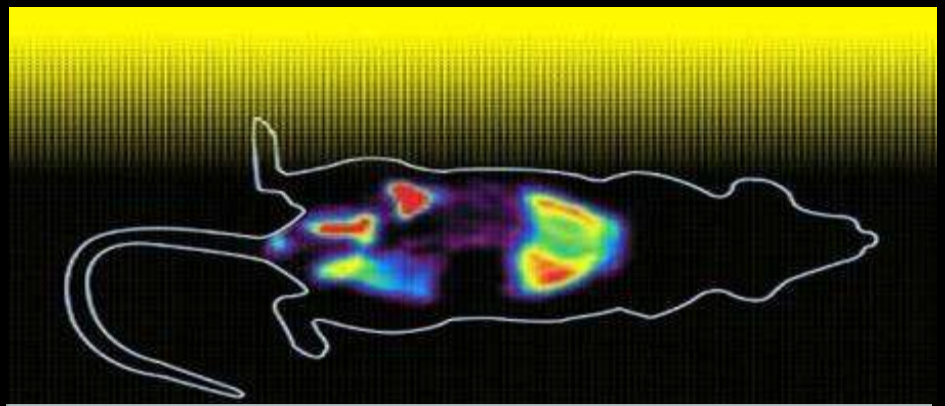


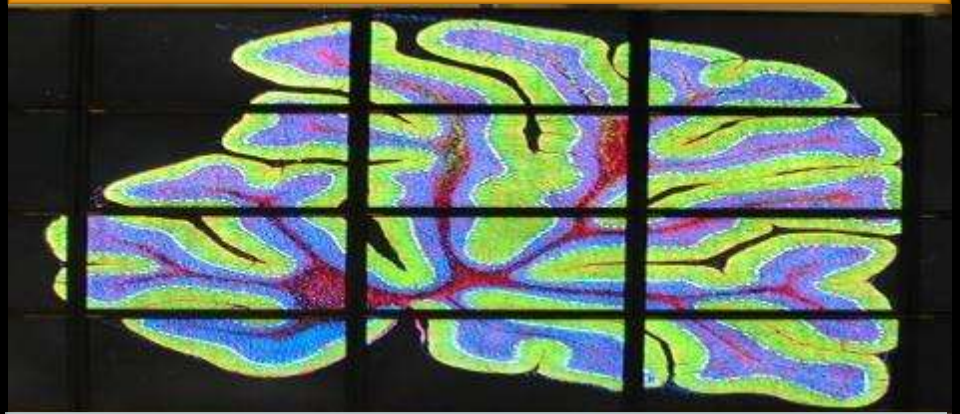
Cell Content Imaging

Large Scale Imaging Datasets

Preclinical



Digital Pathology

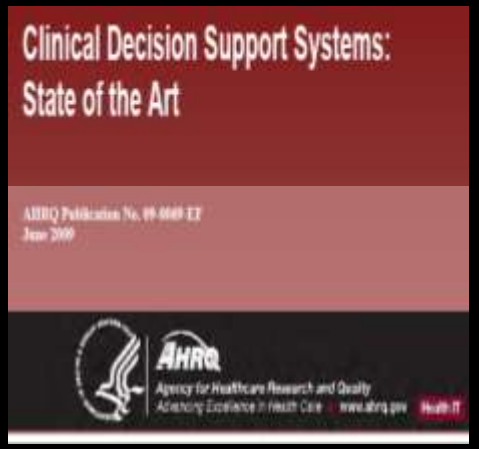


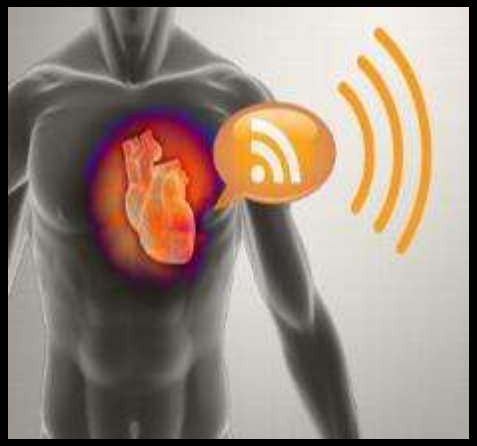
Clinical Imaging

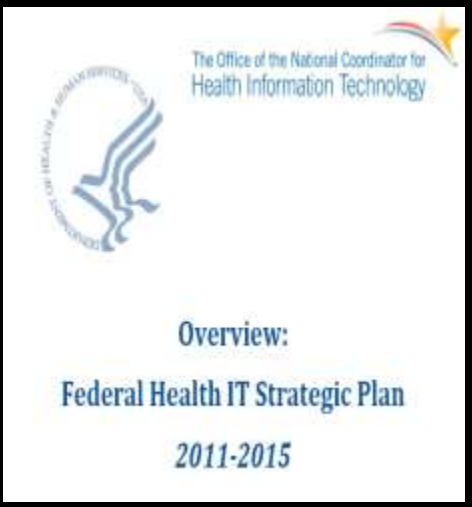
Tele-surgery

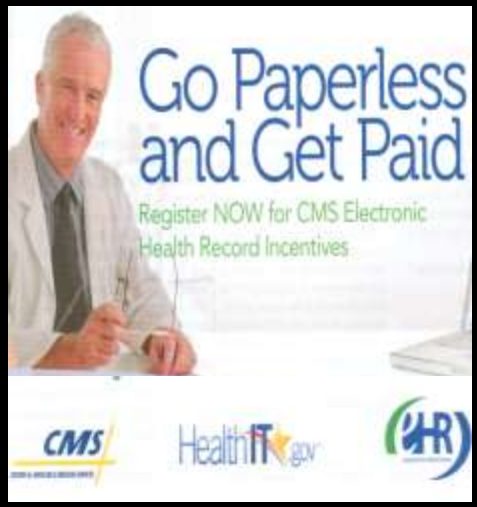
A Learning Healthcare System

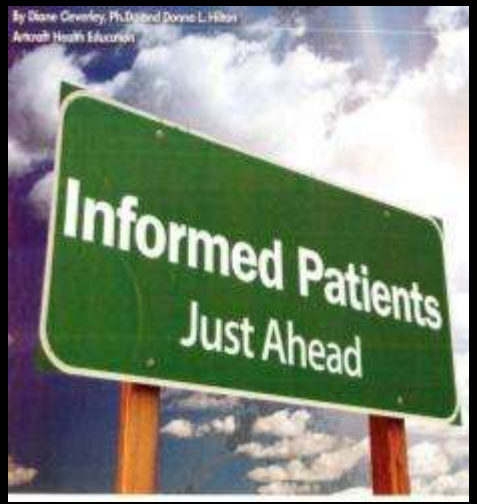
Proliferation of Clinical Computational Systems











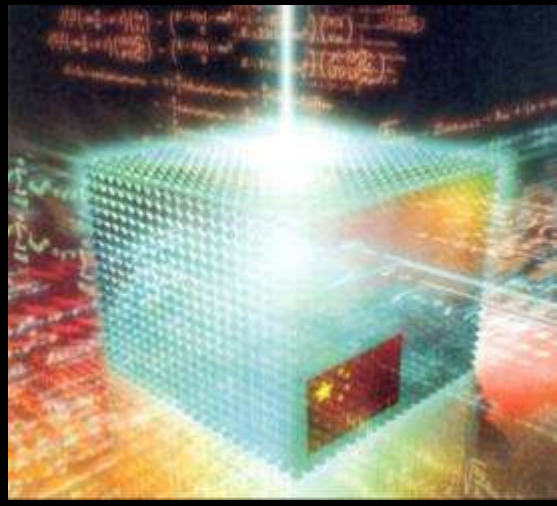
HITECH Mandates	Incentives	EHR and Smart Cards	Informed Consumers/Patients

“Mega-Data” in Biomedicine

volume, variety, velocity

computational scale

global networks



bench to bedside: multiscale heterogeneity

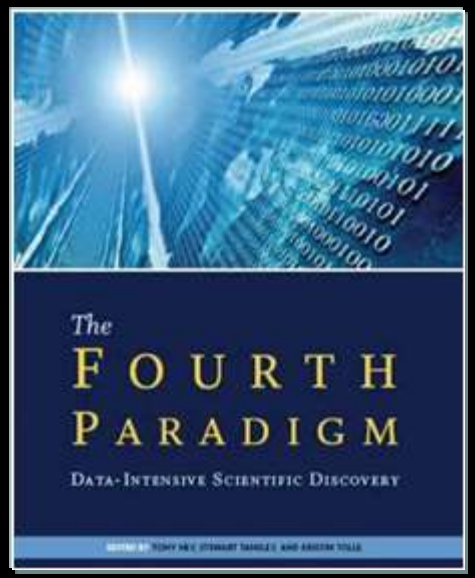
integration

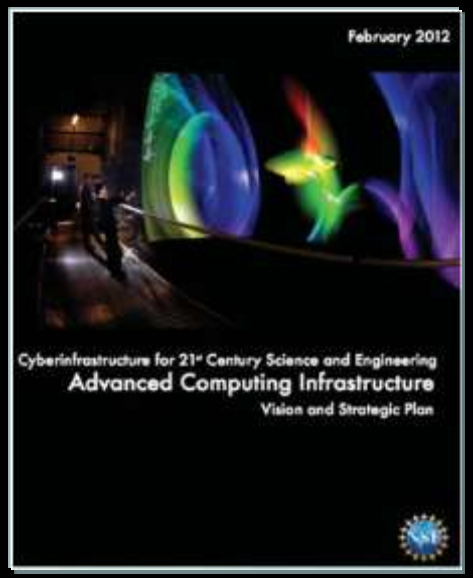
Biomedical R&D and Clinical Medicine: An Unavoidable Transition to Data-and Computation-Intensive Methods

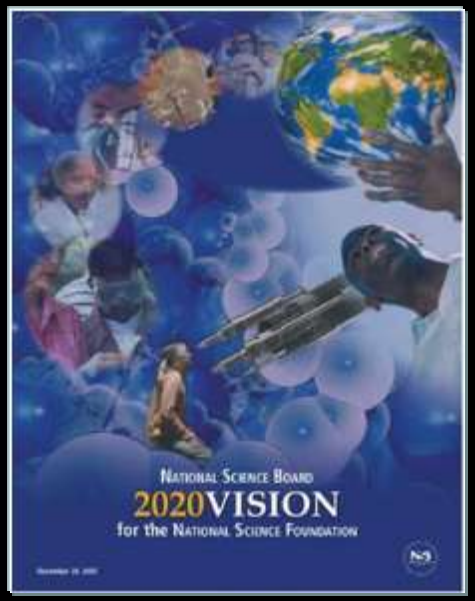
Current Era

- "silos" of research/clinical activities
- opinion-rich, information content-poor
- proliferation of poorly standardized and fragmented data, semantic anarchy and incompatible databases
- unacceptable levels of inaccurate diagnoses, fragmented care provision and flawed clinical decisions
  - highly variable treatment practices and erratic clinical outcomes
- extravagant waste and risk

Data-Intensive Computing, Big Data and New Knowledge Networks in Biomedical R&D and Healthcare Delivery





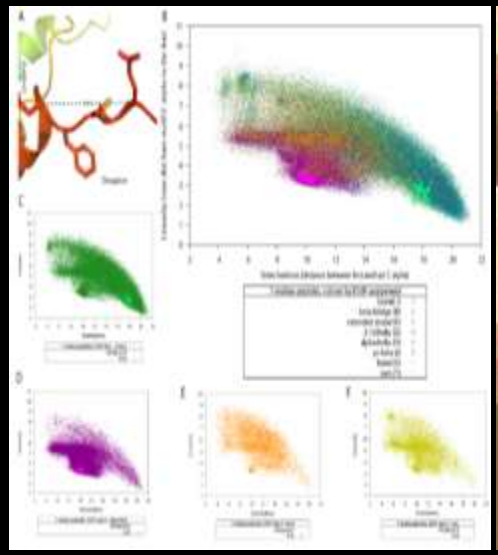
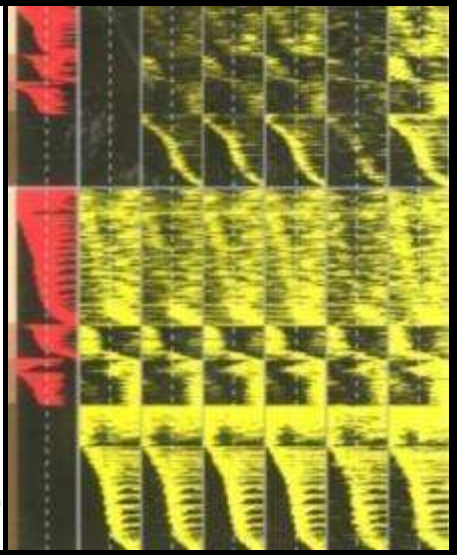
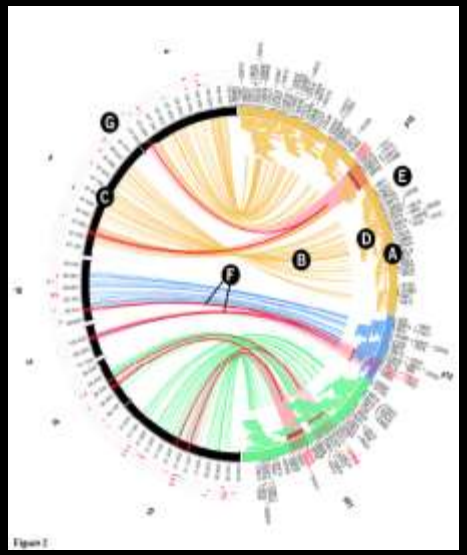


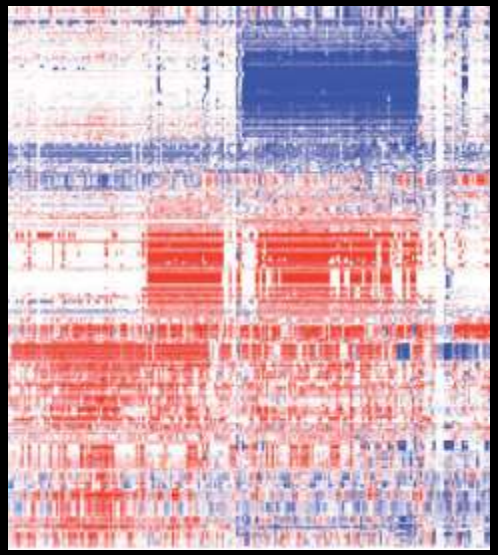
Biomedical R&D and Clinical Medicine: An Unavoidable Yet Essential Transition to Date- and Computation-Intensive Processes

Pending Era

- massive data (big data)
  - V3: volume, velocity, variety
  - automated, massively parallel ‘omics’ profiling (research and clinical)
- cross-sector convergence and integration
  - biomedicine, engineering, computing, telecommunications, social media
- new machine-based analytics for management of mega-data, customized distribution and decision-support

The Imminent Collapse of the Genome Informatics Ecosystem?



- Moore's Law
  - # transistors/circuit board doubles c.18 months
- Kryder's Law
  - hard disk capacity doubles c.12 months
- Butter's Law
  - cost of sending a bit of information over optical network halves every 9 months
- Next Generation Genome Sequencing
  - sequence data doubles every 6 months (other 'omics to follow)

The Tianhe-BGI Bioinformatics & Computing Laboratory

- 14,336 Xeon X5670 Processors
- 7,168 Nvidia Tesla M2050 general purpose GPUs
- 2,048 FeiTeng 1000 SPARC-based processors
- 2.57 petaflops per second performance

http://www.genomeweb.com/newsletter/informatics-iron

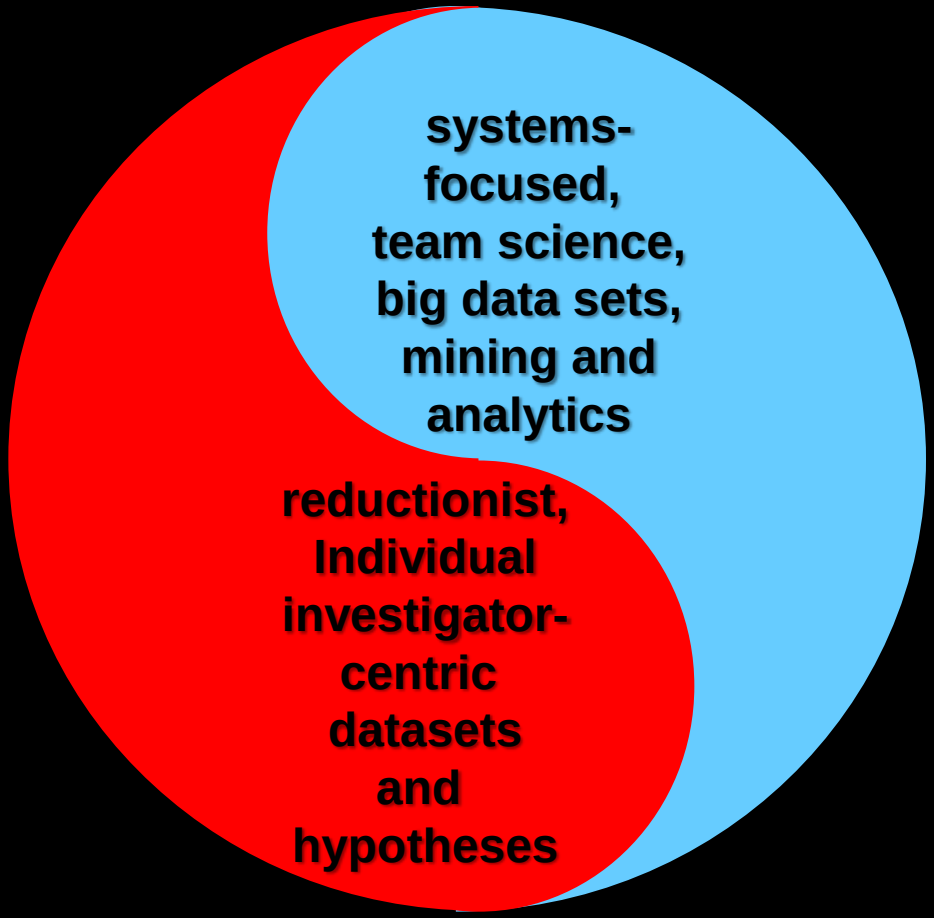
Big Data Rich and Big Data Poor

- difficulty and expense of gaining access to “Big Data” will produce a restricted academic research culture
- automating research and decision-making will dramatically alter knowledge concepts and the nature of learning
- data-intensive research and clinical services will change the dominant intellectual skills and competencies in biomedicine
  - new organizational frameworks
  - looming talent gap
  - new educational curricula and training needs

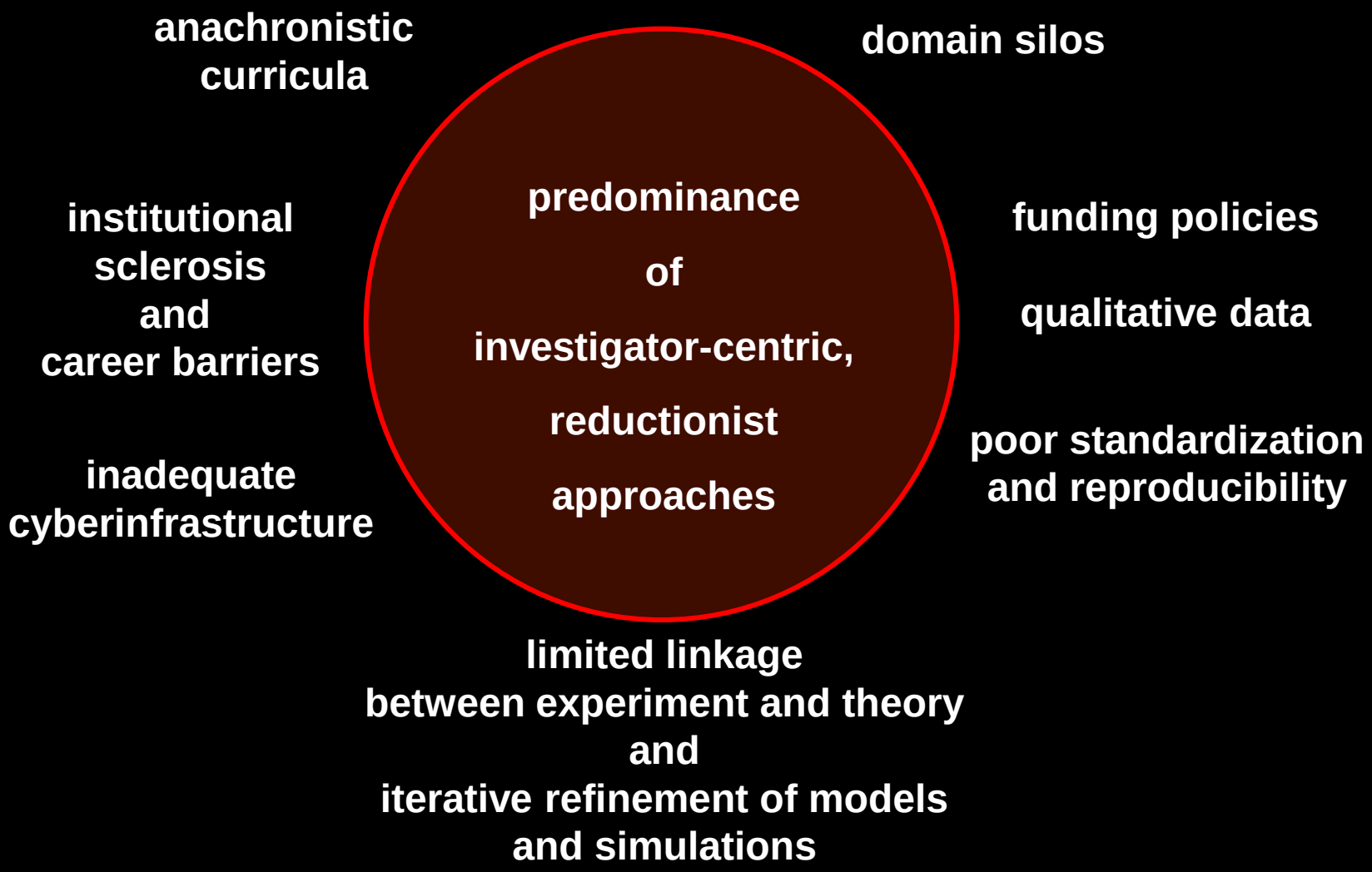
The Challenge of Data-Intensive Scientific Computing

- majority of traditional systems neither scalable nor sustainable for emerging data-intensive scientific computing requirements
  - computation infrastructure/architectures
  - storage shortage and analytics deficits
  - organizational and intellectual silos
- urgent imperative for strategic vision and national leadership (USG, academia, industry)

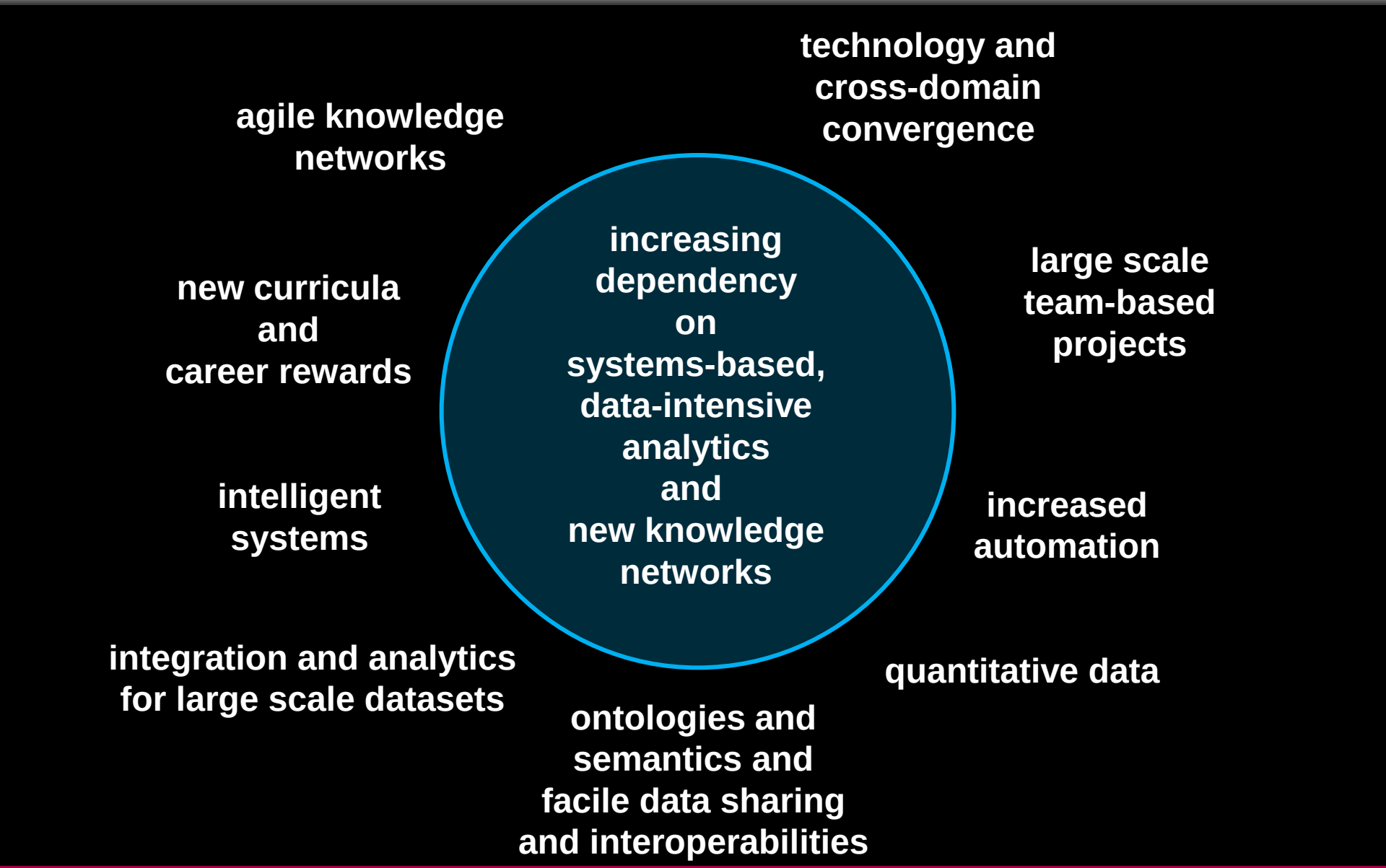
Cross-Domain Convergence, Complexity and Increasing Dependency on Data-Intensive Methods and New Knowledge Networks

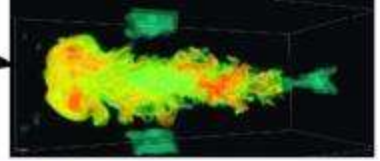


Silos Subvert Solutions: The Slow Response of Biomedicine to Technology Convergence and Cross-Disciplinary Requirements



New Conceptual, Methodological and Organizational Frameworks for Data-Intensive Biomedical R&D





Science Portals: collaboration and problem

Web Services and Application building services

Grid Services: secure and uniform access and management for distributed resources

Supercomputing and Large-Scale Storage

experiment

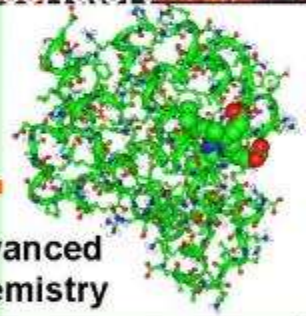
theory

simulation

ESnet: High Speed Networking

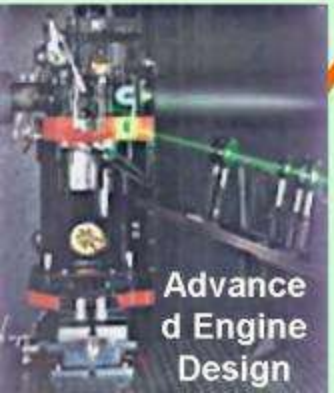
Computing and Storage of Scientific Groups

Supernova Observatory



Advanced Chemistry

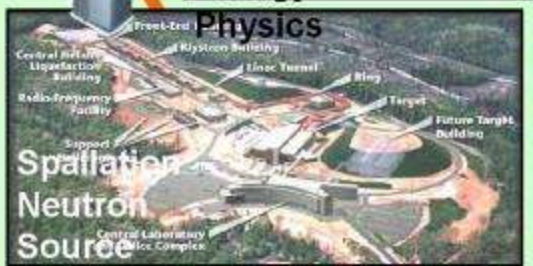
High Energy Physics



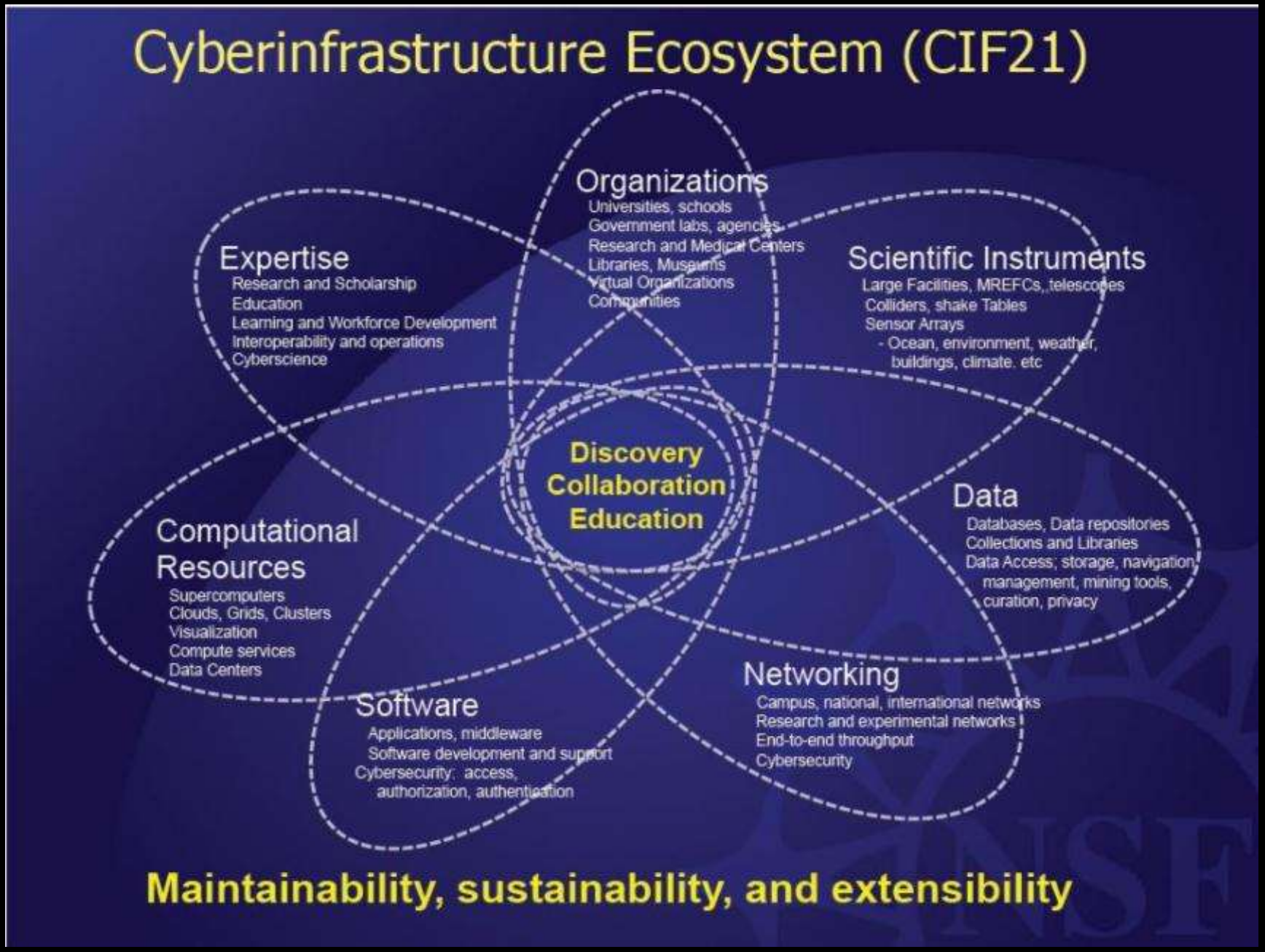
Advance d Engine Design

Macromolecular Crystallography

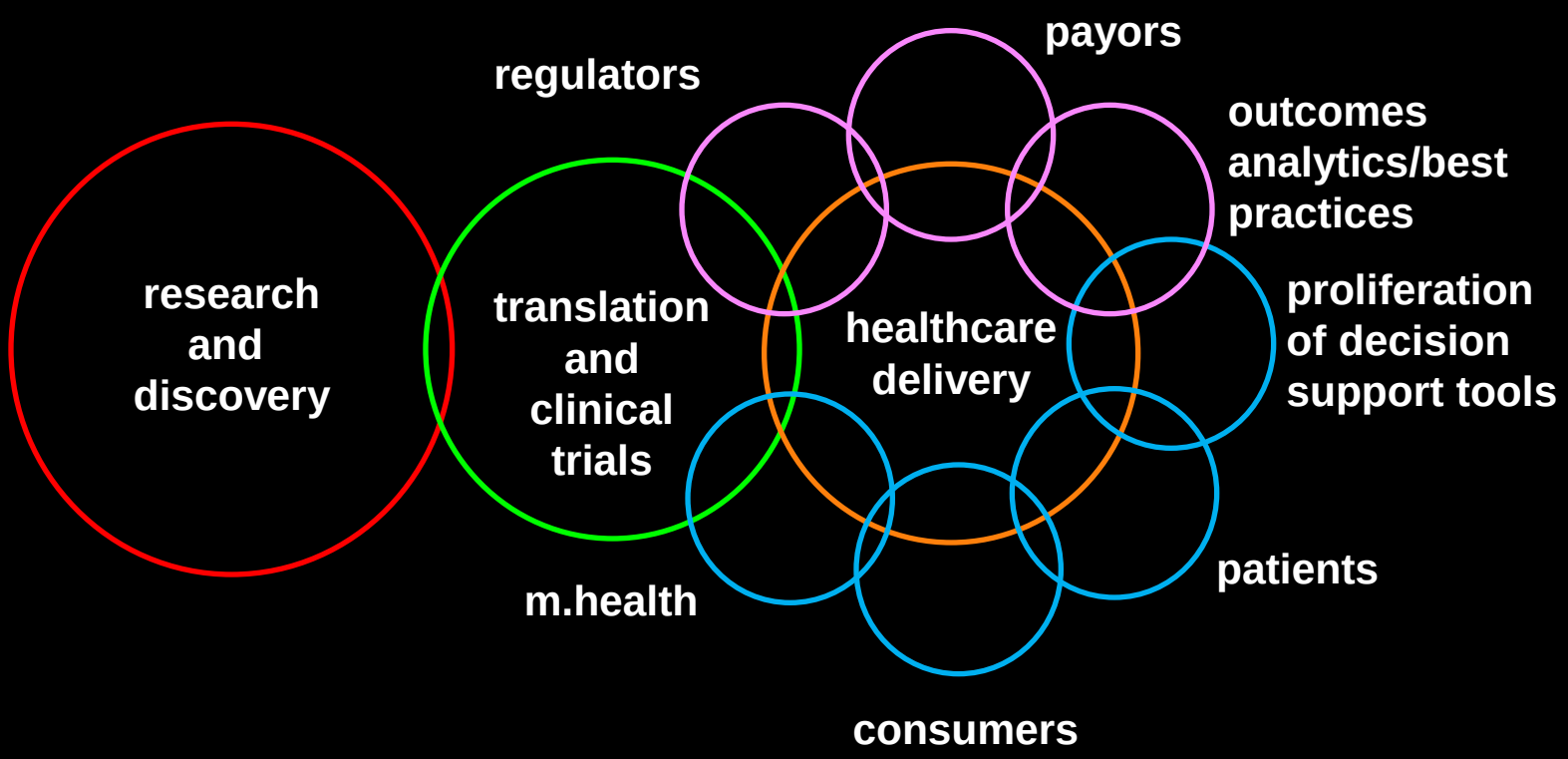
Advanced Photon Source



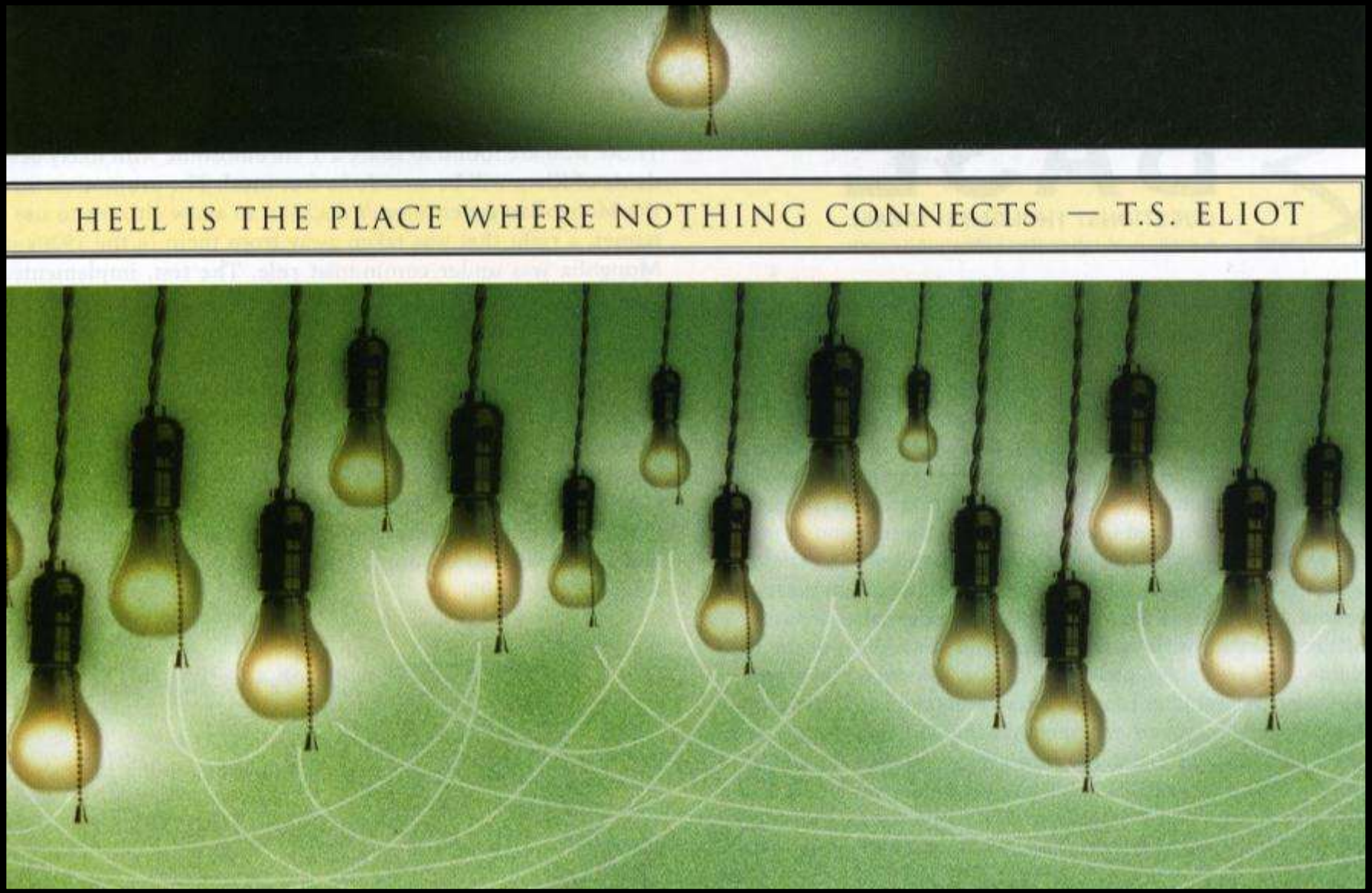
Spallation Neutron Source


Cyberinfrastructure Ecosystem (CIF21)
Organizations
Universities, schools
Government labs, agencies
Research and Medical Centers
Libraries, Museums
Virtual Organizations
Communities
Expertise
Research and Scholarship
Education
Learning and Workforce Development
Interoperability and operations
Cyberscience
Scientific Instruments
Large Facilities, MREFCs, telescopes
Colliders, shake Tables
Sensor Arrays
- Ocean, environment, weather, buildings, climate. etc
Discovery
Collaboration
Education
Data
Databases, Data repositories
Collections and Libraries
Data Access; storage, navigation, management, mining tools, curation, privacy
Computational Resources
Supercomputers
Clouds, Grids, Clusters
Visualization
Compute services
Data Centers
Networking
Campus, national, international networks
Research and experimental networks
End-to-end throughput
Cybersecurity
Software
Applications, middleware
Software development and support
Cybersecurity: access, authorization, authentication
Maintainability, sustainability, and extensibility

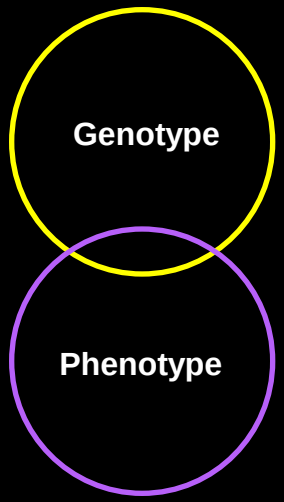
The Design of Facile, Seamless Cross-Domain Data Exchange Formats for Large Scale Biomedical Data

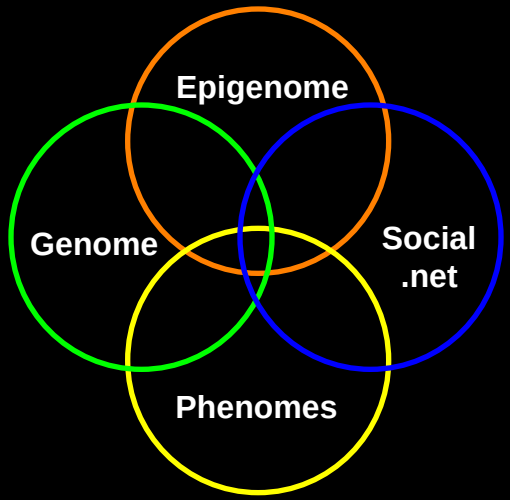


Silos Subvert Solutions



Rich Data Will Drive Clinical Profiling to 'Interpreted Phenotypes'





Observed Phenotype	Interpreted Phenotype and Phenomes
• clinical annotation • EHR data mining	• clinical annotation • iPOPs + • large scale data analytics for "*robustness of match*" of observed clinical phenotype + iPOP profile + curated literature as a multi-dimensional matrix

The Design Challenge for Next Generation HIT Systems

- today EHRs not designed to support secondary use of data to inform research/translational medicine
- lack of harmonized data standards in different disciplines/delivery systems as handicap to data meta-analytics outside of original capture institution
- urgent need for new integration models for diverse data

Healthcare IT News February 2012

Lessons from the UK

Whither public HIEs?

BY MIKE MILIARD, *Managing Editor*

LONDON – Some sobering news came from across the pond this past year. On September 22, England's Department of Health announced it would finally scrap the country's decade-long, problem-plagued health information technology initiative, the National Programme for IT (NPfIT).

its government-led approach, By hand-picking vendors and following a one-size-fits-all nationwide strategy – and especially by giving short shrift to the needs and feedback of physicians – NPfIT, however well-intentioned, was bound to fail.

"Labour's IT programme let down the NHS and wasted taxpayers' money by imposing a top-down IT system on the local NHS, which didn't fit their needs," said Andrew Lansley,

Some have predicted that the U.K.'s problems with top-down information exchange will soon be echoed here in the U.S.

- **22 September 2011 announcement by NHS to terminate decade long HIT initiative with sunk cost of £6.5 billion of planned £11 billion**
- **challenge of top-down, one size-fits-all approach**

Health IT: A Paleolithic (Pre-Internet) Endeavor Ready for Disruption: Making "Meaningful Use" Meaningful

- proliferation of over 700 EMR vendors with 1750 distinct certified products
- the vendor trap (K. D Mandl, I.S. Kohane, NEJM (2012) 336, 2240)
  - major barriers to use of common open-source systems for sharing population-level data and analytics
- import large scale web-based platforms and secure cloud-based storage from other industries
  - process automation and quality metrics
  - care coordination, patient engagement and reporting
- aggregated EMR data and longitudinal tracking of individuals as rich substrate to inform research/translational trials on outcomes

Collaborative Clinical Connectivity Inter-Operability and Open Source Technologies

The Design Challenge for Next Generation HIT Systems

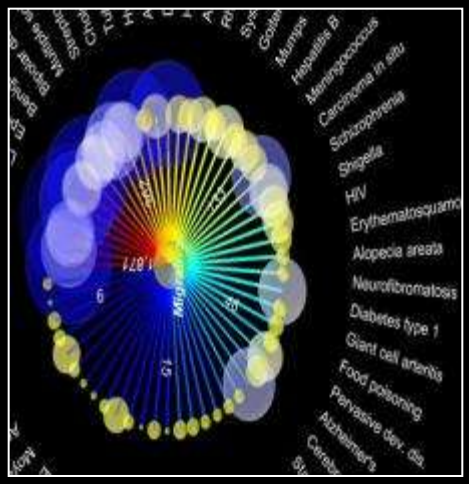
- urgent need for new integration models for diverse data
  - iPOPs
  - current and planned clinical trials
  - observational data from primary care provider and patient self-reported data
  - SEER (surveillance, epidemiology and end results) data
  - m.health/sensor net remote data monitoring
  - payor data and outcomes

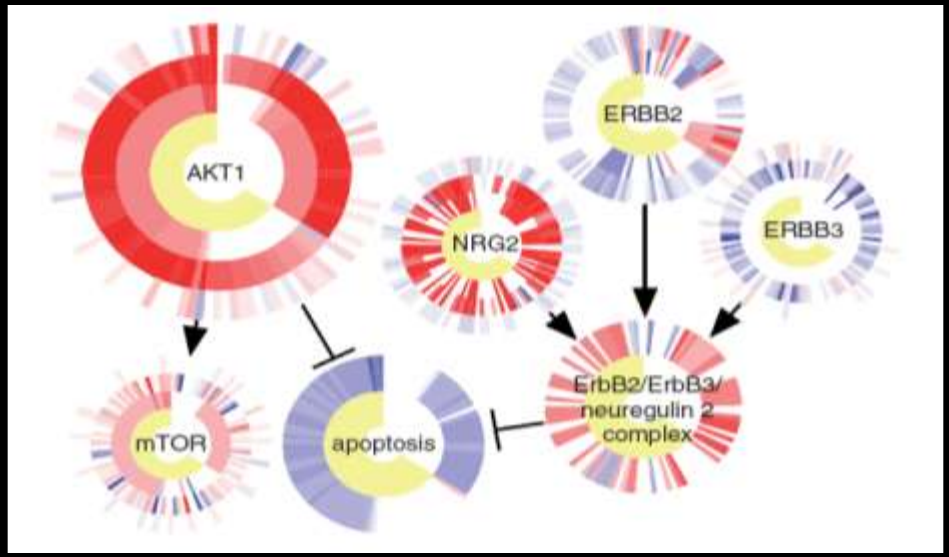
The Growing Education and Knowledge Gaps in Comprehension of Molecular Medicine Concepts Among Healthcare Professionals

Overcoming Gaps in Physician Knowledge of Molecular Medicine and a Paper-Centric Healthcare System

- 90% of Americans lack confidence in their clinicians ability to understand and use genetic information
  _ http://www.cogentresearch.com/news/Press%20Releases/CGAT_2010
- professional cultural vulnerability/reluctance to acknowledge
- refuge in outdated SOC/guidelines that fail to integrate much new molecular profiling data
- protracted deliberations by professional societies/boards
- less than 4% of 8967 ACGME programs relate to genetic expertise (JAMA 2011 306, 1015)
- MD curriculum/CME challenges
- generational gap in IT use/facileness and resistance to computerized decision-support tools

Integration of iOmics Data Into Electronic Health Records and Clinical Decisions





What Is?
The Evolution of Computation Capabilities for Natural Language Q&A in Large Unstructured Datasets

Jeopardy 16 February 2011

- IBM's Watson
  - 2880 CPUs
  - natural language questions
- prelude to Q&A systems for biomedicine beyond keyword IR searches

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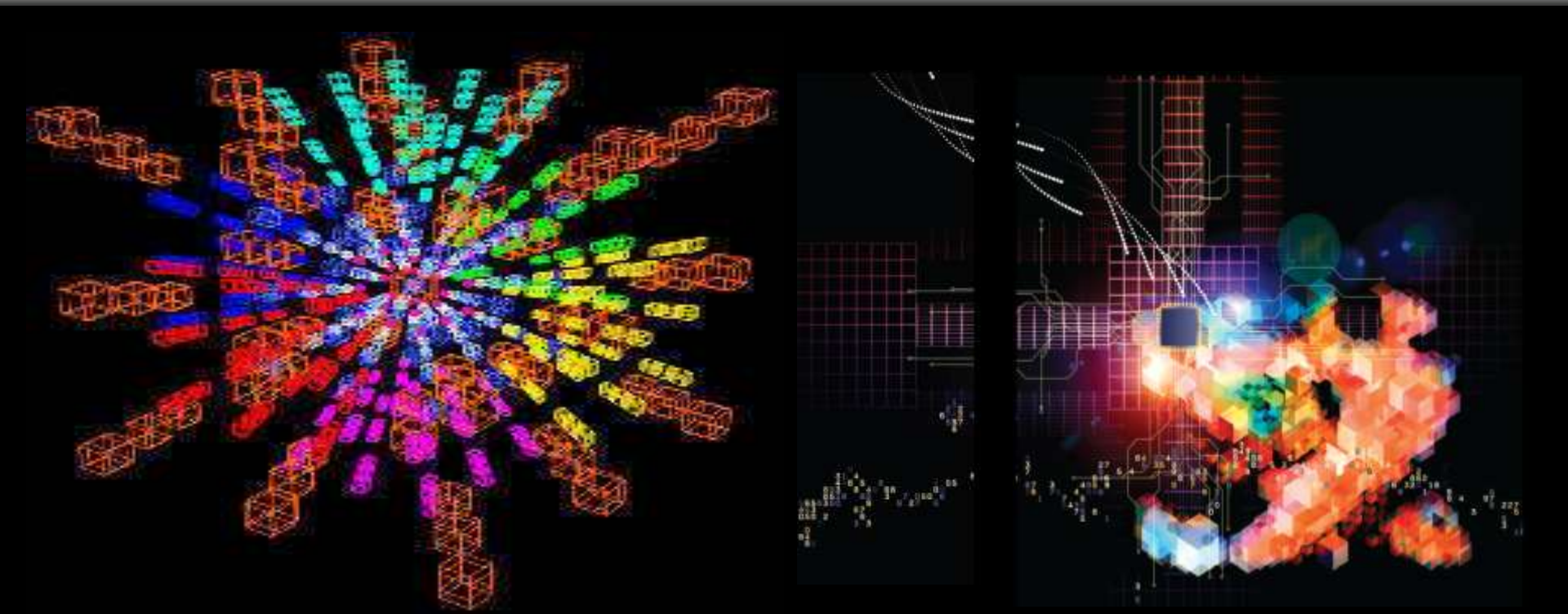
Assembly, Annotation, Analysis, Storage and Curation of Large iPOP Datasets

- don’t know future value of current data
- what can we ignore or discard?
- important dots yet to be identified can’t be connected
- data provenance, authenticity and durability
- dynamic curation and ID of meaningful dots and connections
- traditional models of collect, winnow and dissemble are ill-suited for dynamic analysis of big data

INTELLIGENCE AT INGESTION

INTELLIGENT STORAGE TECHNOLOGIES

Context: Data Finding Data



Feature Extraction and Classification

Context Analysis

Persistent Context

- **Relevance Detection**
- **Situational Awareness**
- **Intelligence**

Rapid, Informed Decisions

21st Century Knowledge Networks versus 20th Century Organizations


CHANGE
is good
you go first

Changing Minds and Changing Cultures: The Barriers of Entrenched Behaviors and Current Reward Structures

- re-engineering a complex ecosystem approaching 20% of GDP
- perverse incentives
  - academic research: lack of accountability and poor/slow translation
  - clinical: do more, bill more
  - industry: the tyranny of Wall Street short termism
- current institutions, leadership and financial interests can't be expected "to vote themselves off the island"

Silos, Turf and Cultural Conservatism as Barriers to Change

- rethink
- recalibrate
- design

What is required?

What is sustainable?

The Evolution of an e.Health:m.Health Knowledge Ecosystem

reactive, episodic care	→	continuous care
reactive, symptoms-based care	→	proactive pre-emptive risk detection and mitigation
erratic and poor compliance	→	monitored compliance
centralized delivery locations	→	increasingly distributed PON systems
professional paternalism, high initial misdiagnosis and error	→	access and democratization of relevant information by consumers and engagement in care decisions
fragmented and uncoordinated practice data	→	integrated datasets and analytics to optimize risk ID/ mitigation and best practice guidelines

New Locations and New Services in Primary Healthcare

What Was

Will Be

From: S. Burrill

The Changing ‘Care Space’ in Healthcare Delivery

- from fixed, tethered, compartmentalized, provider-centric facilities

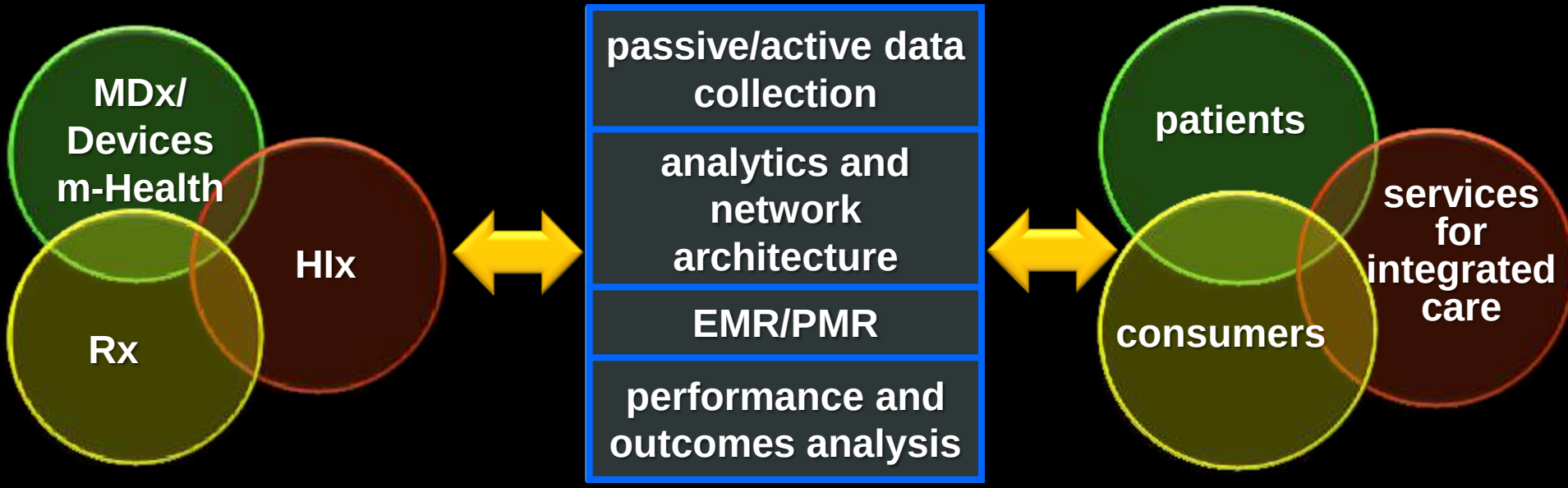
to

- distributed- and virtual-architectures connecting multiple providers, home, work and the internet
- from reactive, incident-centric, poorly coordinated and sequential referrals and inefficient post-incident monitoring

to

- pervasive, persistent monitoring of health status for pre-emptive risk mitigation and improved compliance/personal stewardship of health

A New Healthcare Ecosystem Arising From Technology and Market Convergence



Integrated Technology Platforms for Comprehensive Profiling and Remote, Real Time Monitoring

Data Mining and Integration Services

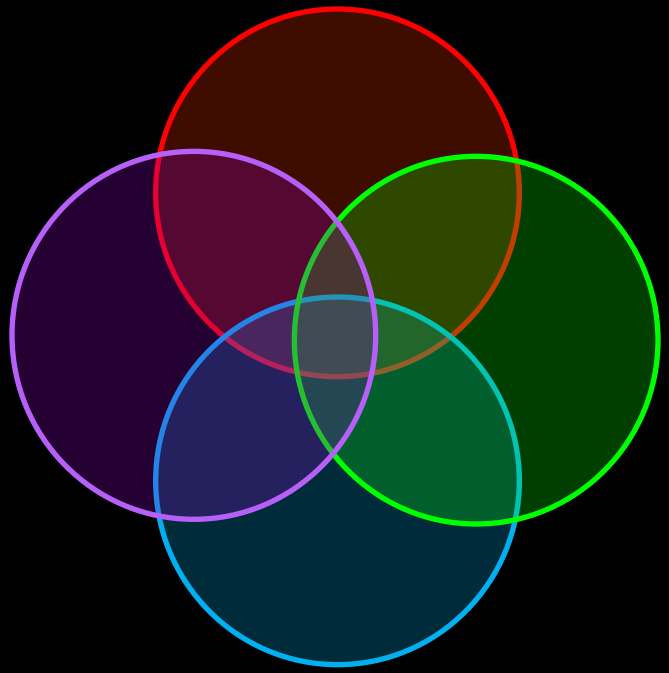
Increasingly Targeted Care and Efficient Use of Finite Resources

The Rise of Digital Healthcare

- sensors and m.health

device-based medicine

- remote health monitoring



molecular medicine

- iOmics
- iPOPs

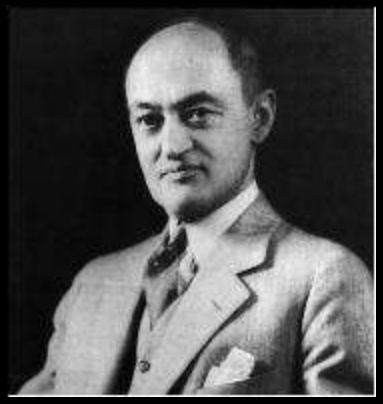
information-based healthcare

- m.health/e.health
- data integration and analytics
- decision-support tools

outcomes-based healthcare and sustaining health

new value propositions, new business models and services

Disruptive Technologies and Creative Destruction




- arise at margins of existing fields
  or
  convergence/fusion interstices of previously separate technical domains/markets
- importance typically denied by KOLs and market leaders with often fatal consequences

Disruptive Innovation in Healthcare

Convergence

- biomedicine, engineering, materials
- computing, telecommunications, social media

Consumerism

- engagement in health decisions
- responsibility for risk reduction and compliance
- remote health monitoring
- wellness premium

Cost Control

- precision diagnostics, rational Rx
- risk ID and mitigation
- data and evidence driven practice

Disruptive Innovation in Healthcare

Computational biomedicine

- big data analytics: discovery to care delivery
- m.health and e.health
- human: machine interactions

Competencies

- trans-disciplinary: cross-domain
- education and training

Competition

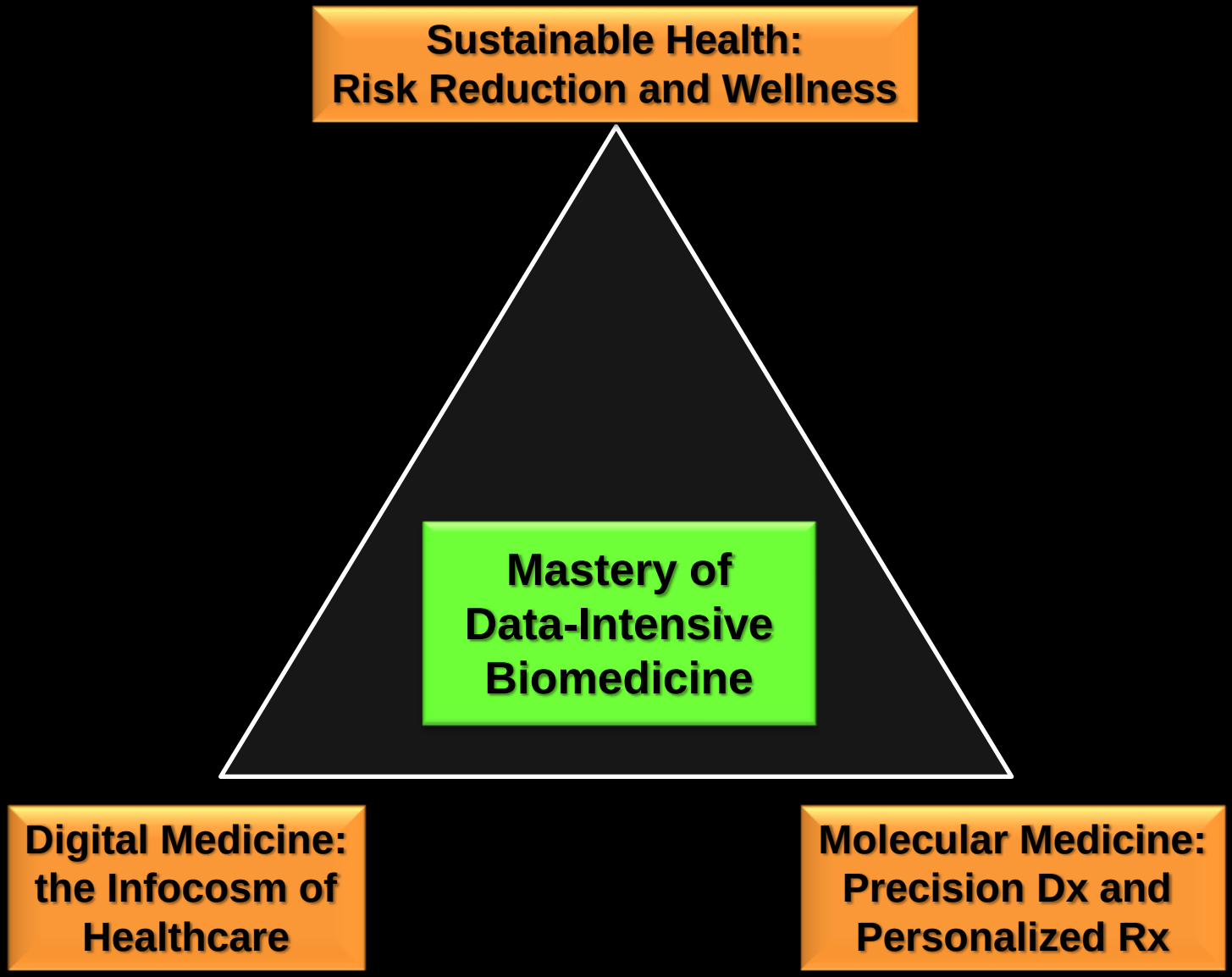
- new integrated services and business models
- reverse innovation (BRIC) countries
- new cross-domain coalitions and consortia

Disruptive Innovation in Healthcare

- convergence
- cost control
- competencies
- consumerism
- computational biomedicine
- competition

NEW VALUE PROPOSITIONS

Disruptive Innovation and Evolution of a New Ecosystems for Sustainable Health



Slides Available: http://casi.asu.edu/