The Complex Strategic Landscape for Precision Medicine

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The Complex Strategic Landscape for Precision Medicine

Cost

Complexity

Computing

Culture

Creative Destruction
(Comfort and Complacency)

Challenges Facing U.S. Healthcare

Balancing Infinite Demand versus Finite Resources

**From Volume-Based (Do More-Bill More)
Fee-for-Service to Value-Based Care**

**From Reactive, Episodic Interventions in Advanced Disease
to Proactive Identification of Disease Risk and Earlier Detection**

**Improving Clinical Outcomes at Lower Cost
and Optimizing Wellness**

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Improving Clinical Outcomes at Lower Cost-
and Optimizing Wellness

Value

Precision Medicine

Digital Medicine

The Demographics of an Aging Society: Clinical and Economic Challenges to U.S. Healthcare

wellness with longevity and high QOL

or
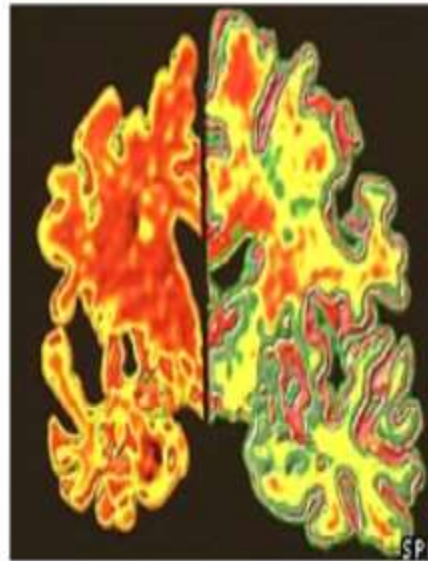
multiple co-morbidities and low QOL

?

?

Disease Burden:
Confronting the Largest Clinical Economic Disruptions and Threats to Sustainable Healthcare
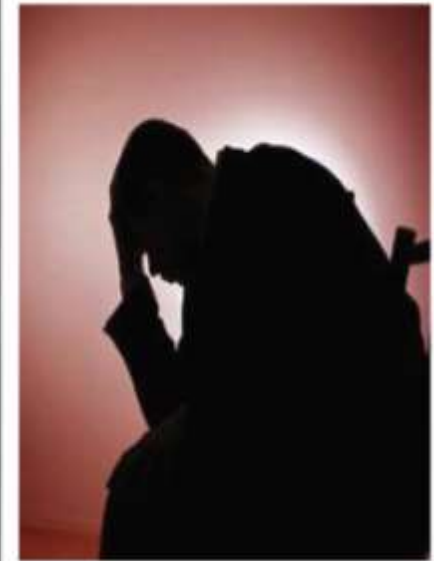
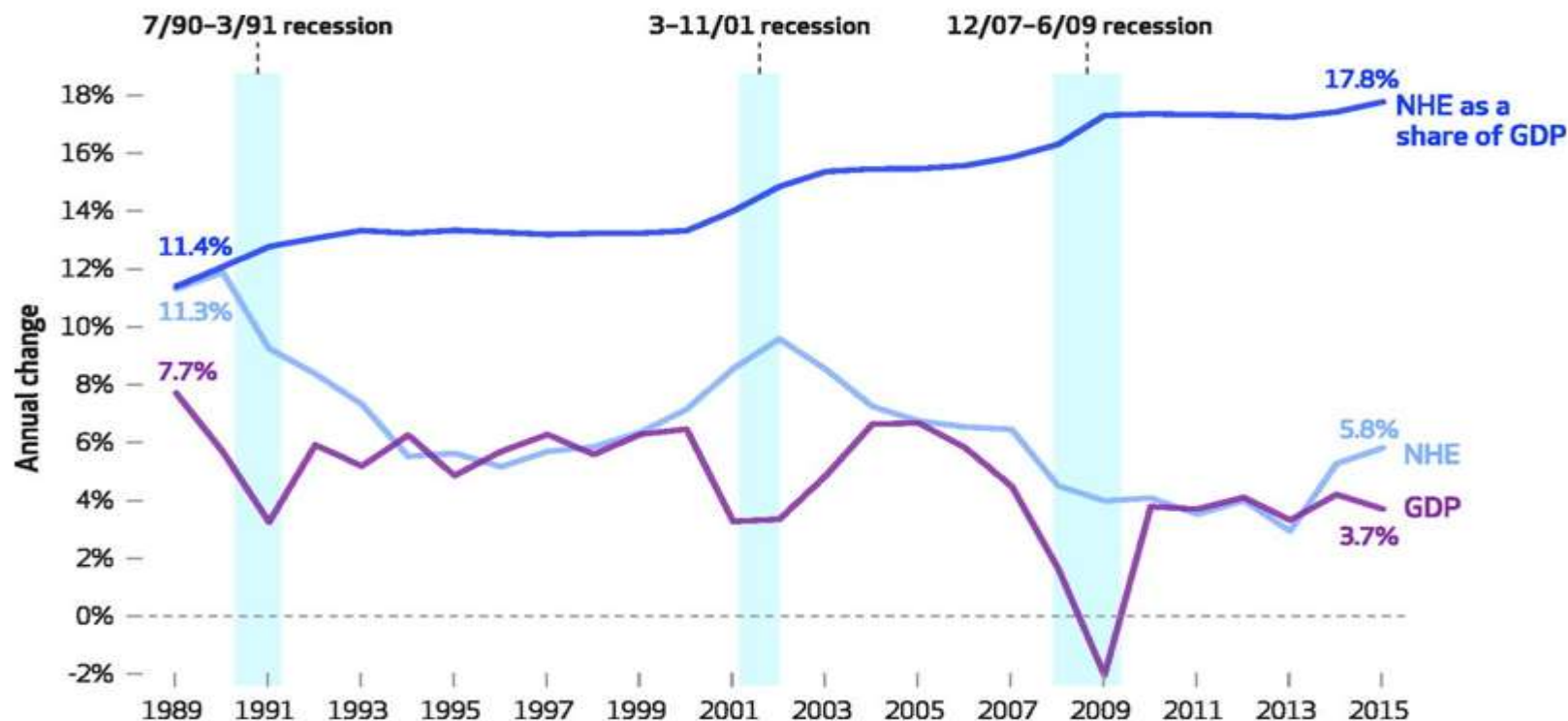| cancer | neurodegeneration | cardio-vascular/ metabolic disease | mental illness |

Cost

Health Spending Is Untethered From the Rest of the Economy: Growth in national health expenditures (NHE) and gross domestic product (GDP) and NHE as a share of GDP, 1989–2015
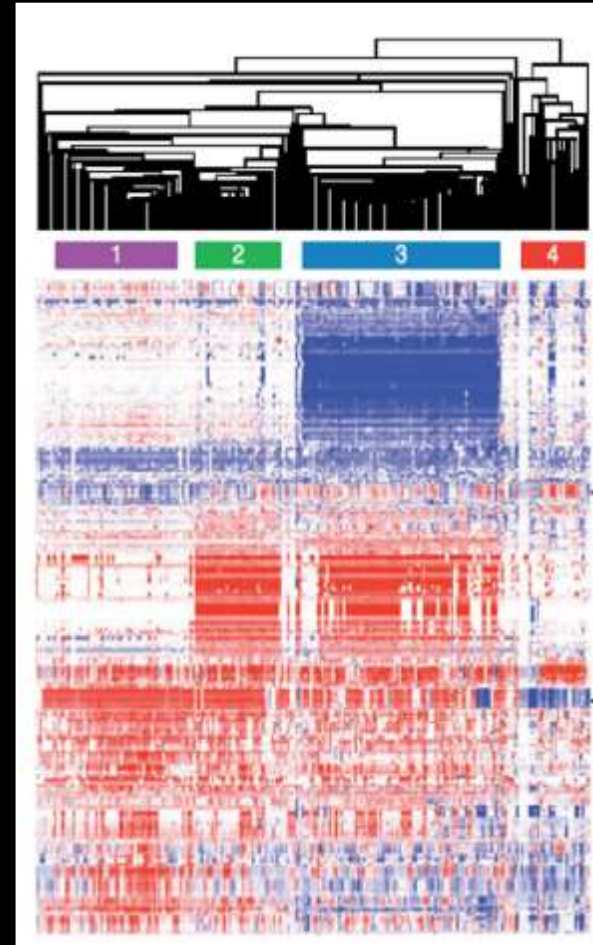
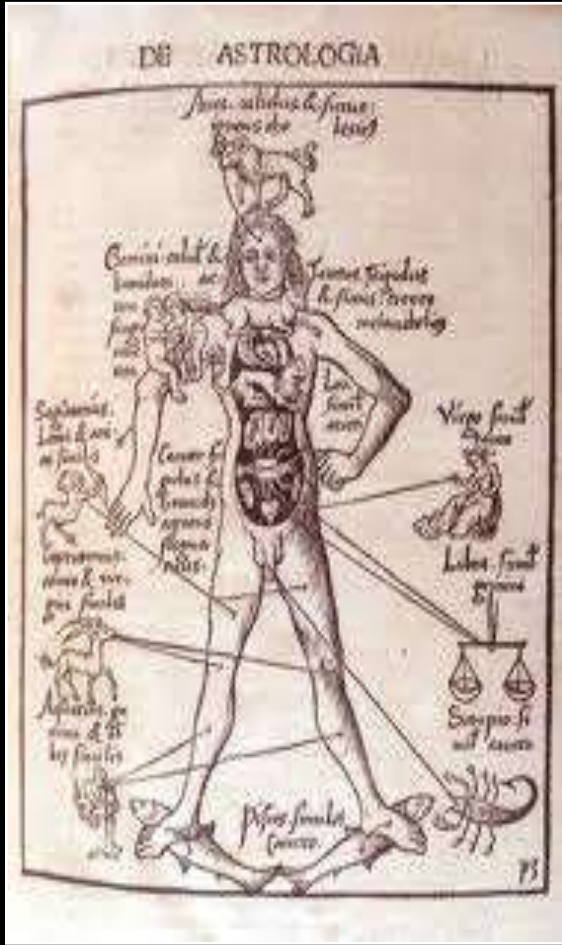**Health Affairs (2017) 17, 166-176**

- **$3.4 trillion dollar economy**
- **17.8% of GDP**
- **one in seven US workers employed in health sector**

Precision Medicine:
Not If, But…

- **what?**

- **when?**

- **how?**

- **who?**

- **value?**

The Path to Precision Medicine:
From Superstitions to Symptoms to (Molecular) Signatures

The Dangers of Techno-Optimism

Molecular medicine and information-based targeted healthcare.
G. Poste (1998) Nature Biotechnol. 16, p 19-21

Still Two Largely Separate Worlds

precision medicine

routine healthcare delivery and SOC

research
and
early clinical
adopters

slow incremental
adoption of
technological
advances

$10-25 billion
(estimated)

$3.2 trillion
(18% GDP)
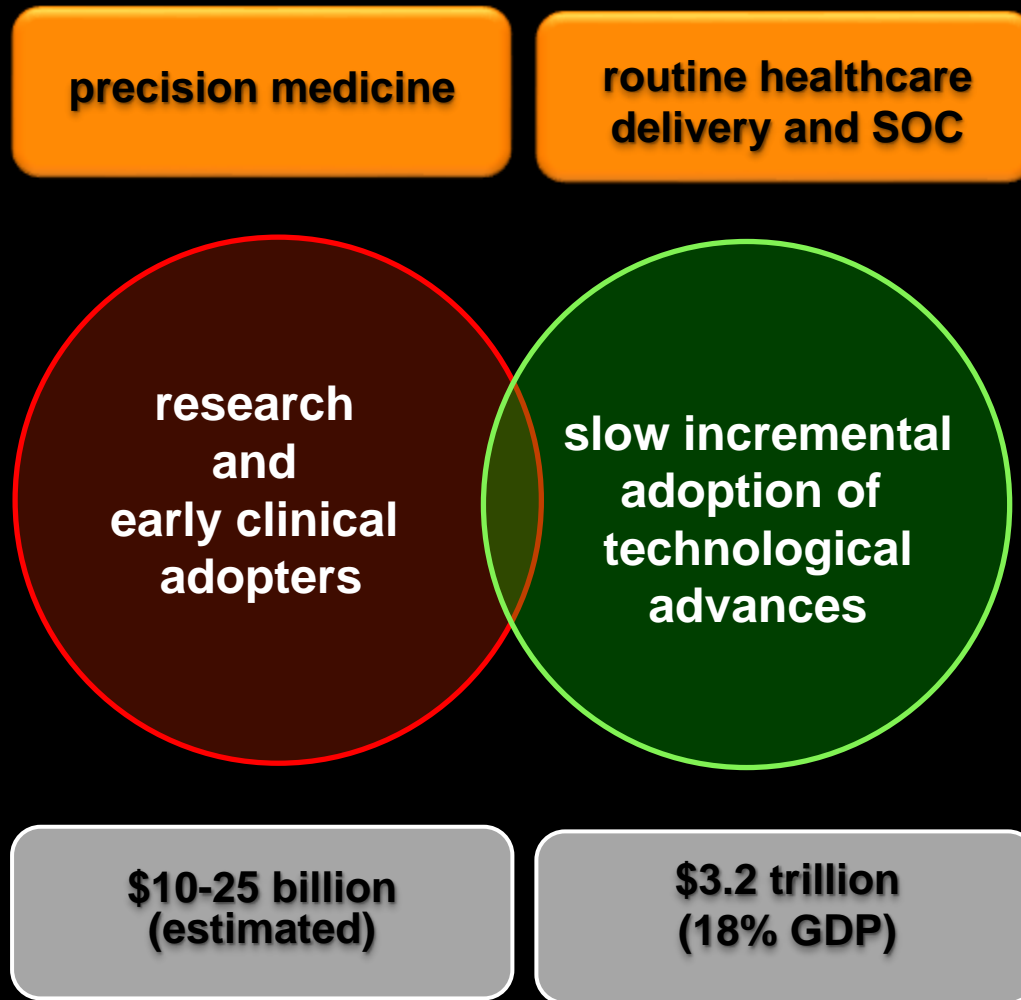
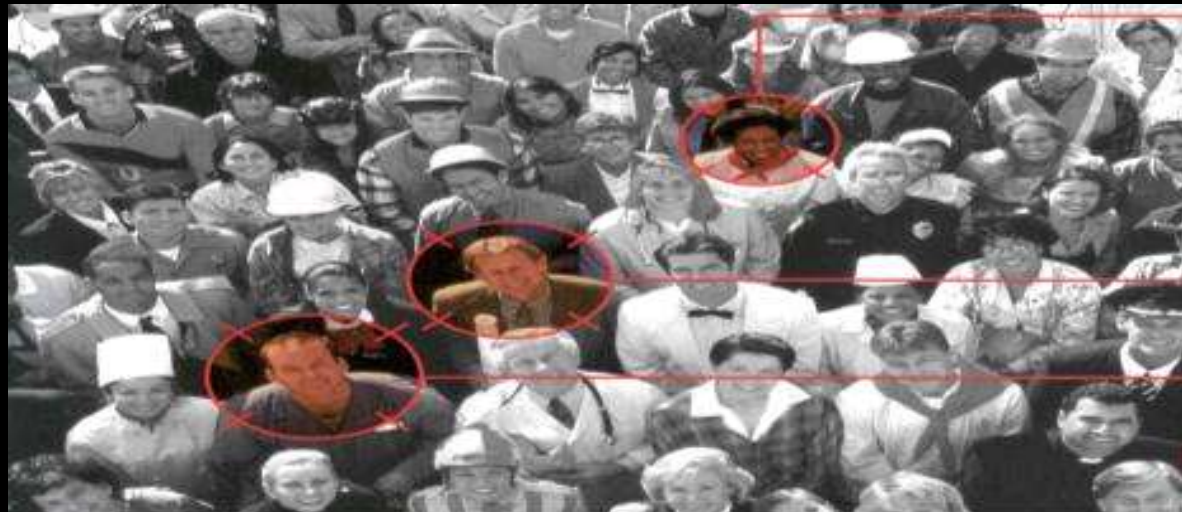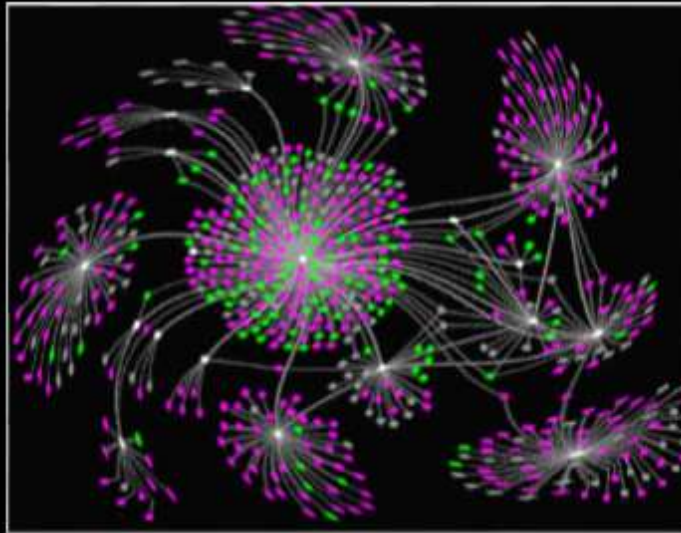# Precision Medicine:

(Epi)Genomics

**Causal Relationships Between
Molecular Signaling Network Disruptions and Disease**

- **terabytes per individual**
- **zettabyte – yottabyte
  population databases**

**Patient-Specific Signatures of Disease
or Predisposition to Disease**
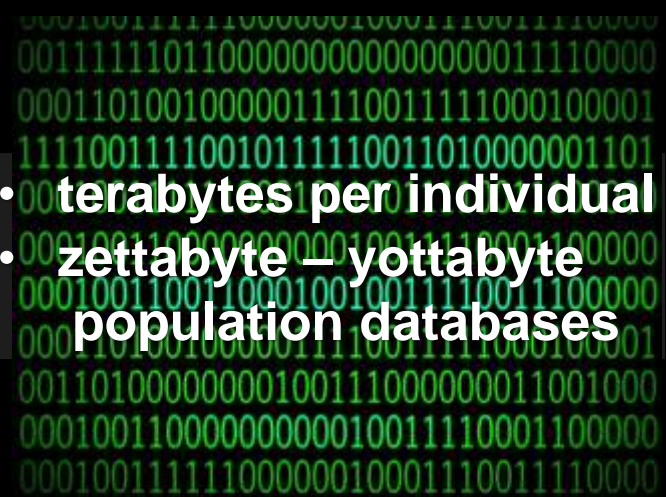
Big (Messy) Data

Precision Medicine and New Clinical Trial Designs

(2017) 377, 62

REVIEW ARTICLE

THE CHANGING FACE OF CLINICAL TRIALS
Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., and Janet Woodcock, M.D., *Editors*

Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both

Janet Woodcock, M.D., and Lisa M. LaVange, Ph.D.

(2017) 377, 405

REVIEW ARTICLE

THE CHANGING FACE OF CLINICAL TRIALS
Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., and Janet Woodcock, M.D., *Editors*

Evidence for Health Decision Making — Beyond Randomized, Controlled Trials

Thomas R. Frieden, M.D., M.P.H.

From RCT to Adaptive, Basket, Umbrella Trials and New Approaches to RWE Observational Trials and Registries

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(2017) 376, 2160

REVIEW ARTICLE

THE CHANGING FACE OF CLINICAL TRIALS
Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., and Janet Woodcock, M.D., *Editors*

Health Policy Trials

Joseph P. Newhouse, Ph.D., and Sharon-Lise T. Normand, Ph.D.

(2017) 376, 1350

REVIEW ARTICLE

THE CHANGING FACE OF CLINICAL TRIALS
Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., and Janet Woodcock, M.D., *Editors*

An FDA Viewpoint on Unique Considerations for Medical-Device Clinical Trials

Owen Faris, Ph.D., and Jeffrey Shuren, M.D., J.D.

Addressing the Biopharmaceutical Industry's Principal Pain Point

- **failure of clinical trials**
  - **unrealized opportunity cost**

- **cost of failed trials included in pricing of successful Rx**
  - **fuels political criticism about drug prices**

- **lack of predictive tools to differentiate responder (R) and non-responder (NR) patients**
  - **growing payer pressure for value-based reimbursement for guaranteed therapeutic outcomes**
  - **waste/risk from futile therapy in NR cohorts**

Monthly and Median Costs of Cancer Drugs at FDA Approval 1965-2016

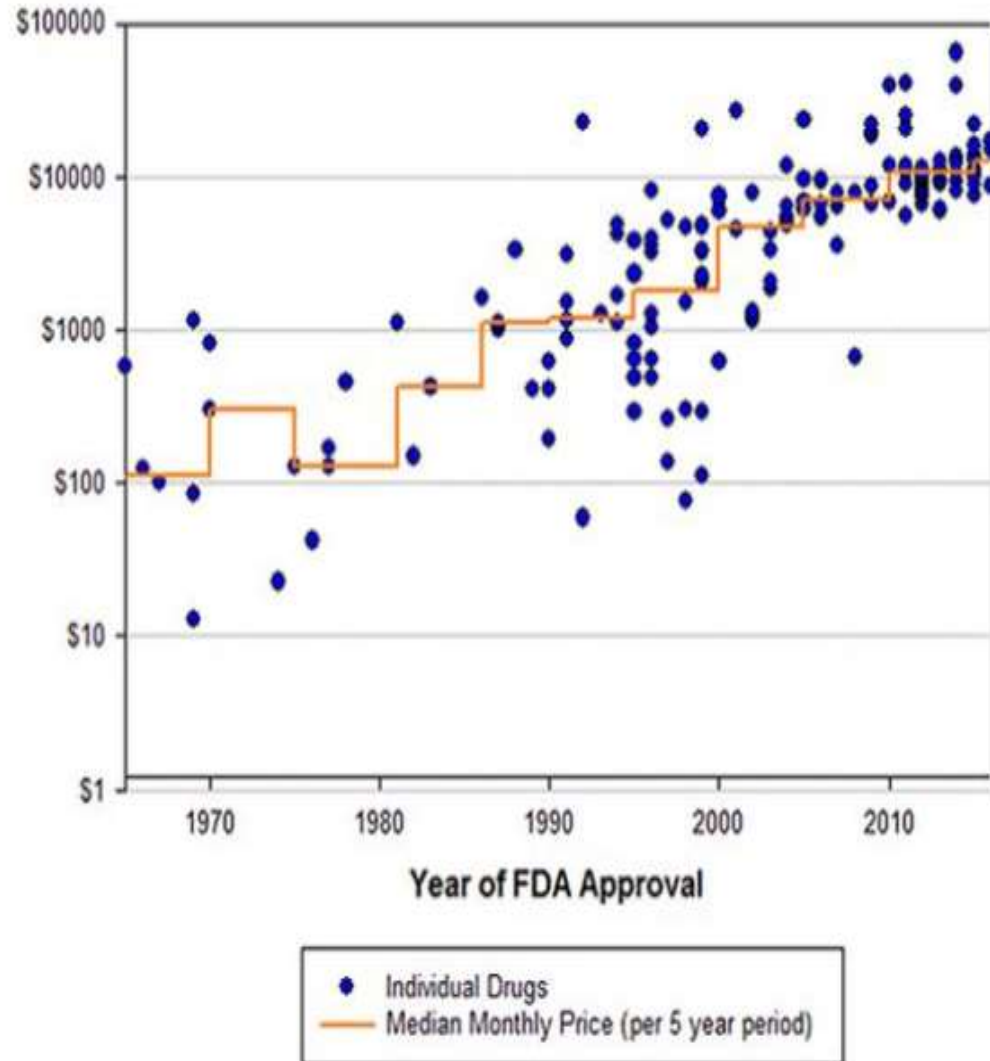Navigating the Coverage Experience and Financial Challenges for Cancer Patients:

Affordable Care Act Brings Improvements, But Challenges Remain

By JoAnn Volk and Sandy Ahn

Cancer Action Network™ American Cancer Society®

Georgetown University Health Policy Institute
CENTER ON HEALTH INSURANCE REFORMS

- Individual Drugs
- Median Monthly Price (per 5 year period)

Source: Peter B. Bach, MD, Memorial Sloan Kettering Cancer Center

What Constitutes a Meaningful Clinical Benefit?

- **71 FDA-approved Rx for solid tumors 2002 to 2012[a]**
  - **median PFS (2.1 months) and OS (2.3 months)**
- **47 Rx 2014-16[b]**
  - **only 19% met ASCO modest OS benefit criterion**
- **ESMO analysis of 226 randomized trials[c]**
  - **only 31% met meaningful benefit criteria**

a = T. Fojo et al. (2014) JAMA Otolaryngol. Head Neck Surg. 140, 1225
b = H. Kumar et al. (2016) JAMA Oncology 2, 1238
C = J. C. Del Paggio et al. (2017) Ann. Oncol. 28, 157

The Promise of Immunotherapy:
Is Widespread Adoption Economically Feasible?

What if your immune system could be taught to kill cancer?

Inside the brutally selective, hugely expensive, lifesaving trials of immunotherapy.

By Alice Park

- unit Rx cost (> $100K) before cost of clinical care

- escalating cost of combination Rx regimens (> $200K)

- extravagant cost of cell-based therapies ($500K - $1.5 million)

- 40-80% NR in most solid tumors

- TML, MSI, MMR as potential 'R' predictors

Hype Versus Hope - A Delicate Ethical Balance:
Come and Be Cured by Us: (Go Elsewhere at Your Peril)!

Impact of Pembrolizumab Dosing Regimen on Treatment Cost (75kg Patient)

- **2017 price $46.54/mg**
- **initial FDA approval 2mg/kg every 3 weeks**
  - **$121,000/yr.**
- **subsequent FDA approval 200mg dose every 3 weeks**
- **10mg/kg dose used in multiple publications**
  - **$586,000/yr.**

# Impact of Pembrolizumab Dosing Regimen on Treatment Cost (75kg Patient)

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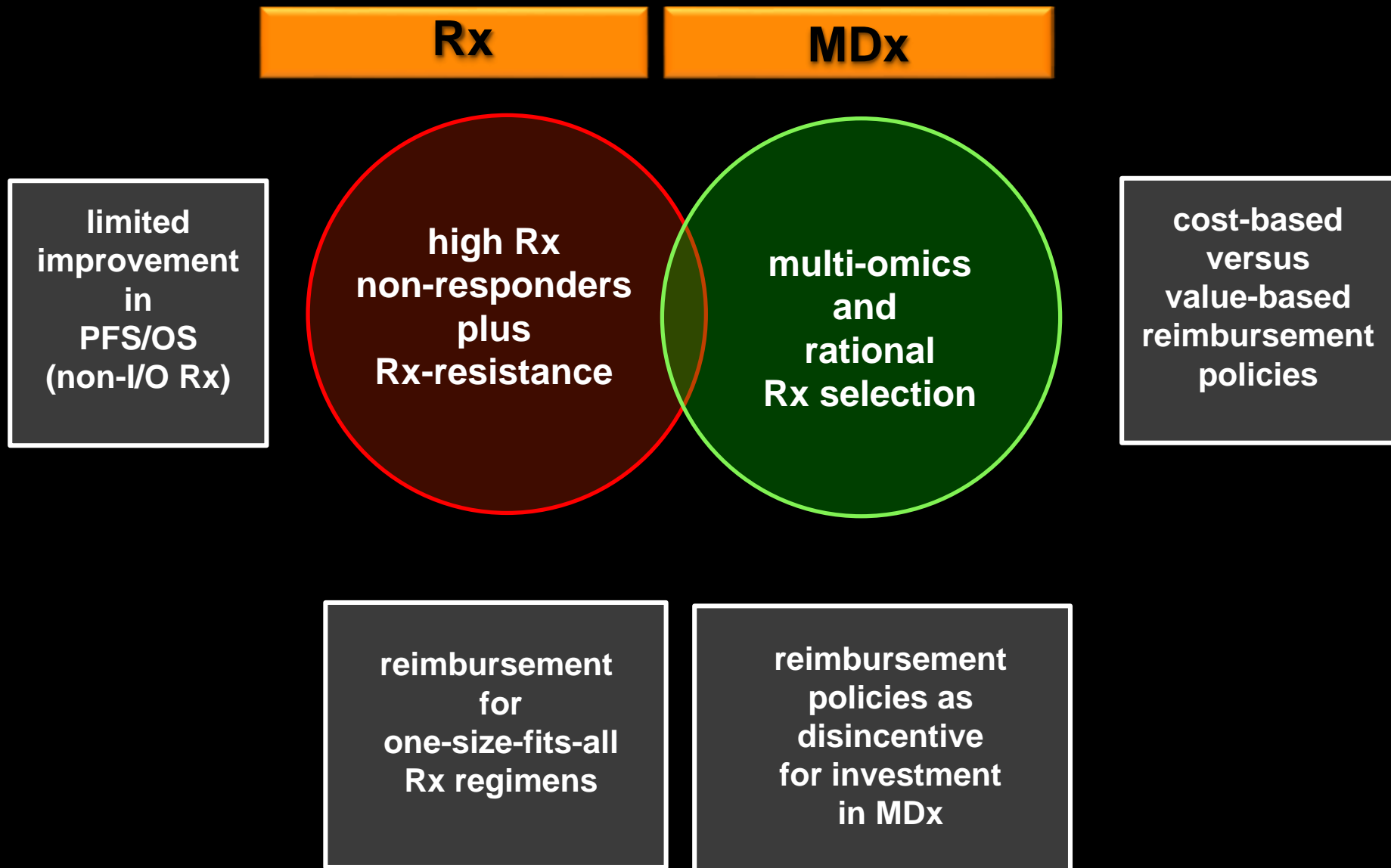 - $586,000/yr.

Pending I/O combinations: Aargh!!

"Unconscionable Price Increases and Price Gouging": The Biopharmaceutical Sector and Reputational Damage
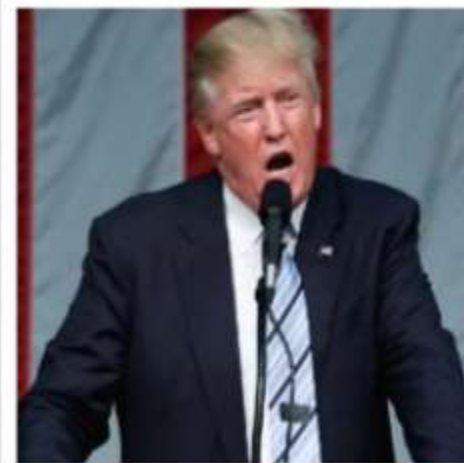
Precision Medicine and Predictive Identification of Rx Responder (R) and Non-Responder (NR) Patients

- **the single most important opportunity for the Rx industry in confronting political attacks about pricing?**

- **high cost immunotherapy as the inflection point?**

- **proactive industry engagement or imposition by payers?**

Conflicts and Contrasts in Reimbursement Policies for Therapeutics (Rx) and Molecular Diagnostics (MDx) in Oncology

Rx

MDx

limited
improvement
in
PFS/OS
(non-I/O Rx)

high Rx
non-responders
plus
Rx-resistance

multi-omics
and
rational
Rx selection

cost-based
versus
value-based
reimbursement
policies

reimbursement
for
one-size-fits-all
Rx regimens

reimbursement
policies as
disincentive
for investment
in MDx

Multigene Test Reimbursement Policies for Five Largest US Private Insurers (Enrollment 112 Million Lives)

Payer	# Policies	# Tests Included	% Policies Covering All Included Tests	% Policies Covering Some But Not all Included Tests	% Policies Covering None of Included Tests
1	7	48	43	29	29
2	15	116	13	27	60
3	4	40	25	50	25
4	15	54	13	13	73
5	14	55	29	36	36
Total	55	313	22	27	51

Adapted from: K.A. Phillips et al (2017) Nature Biotechnol. 35, 616

Policy Options to Incentivize Development of Diagnostic Assays to Identify Rx Responders (R) and Non-Responders (NR)

- **impose progressive Rx price reduction over five year post-launch period until R-NR assay introduced**

  - **annual reduction based on projected cost of documented futile Rx in NR patients**

- **payers guarantee premium pricing and formulary placement for positive outcomes in R patients**

- **accelerated regulatory review for Rx submitted with companion Dx (CoDx) versus Rx without CoDx**

Complexity

Ignoring Biological Complexity

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

Large Scale Genome Sequencing Projects: Siloed Data or Purposeful Integration with Multi-Omics and Phenotypic Data?

Individual Variation, (Epi)Genome Complexity and the Challenge of Genotype-Phenotype Predictions
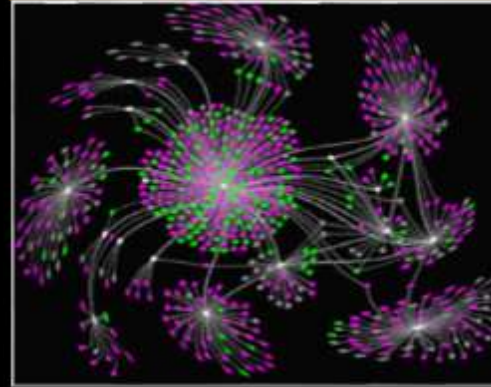
Junk No More: Pervasive Transcription

- alternate transcription /translation/ (co)splicing
- SNPs, CNVs
- pseudogenes
- indels, SVs
- phasing
- epistasis
- imprinting
- cis-and trans regulation
- RNA universe
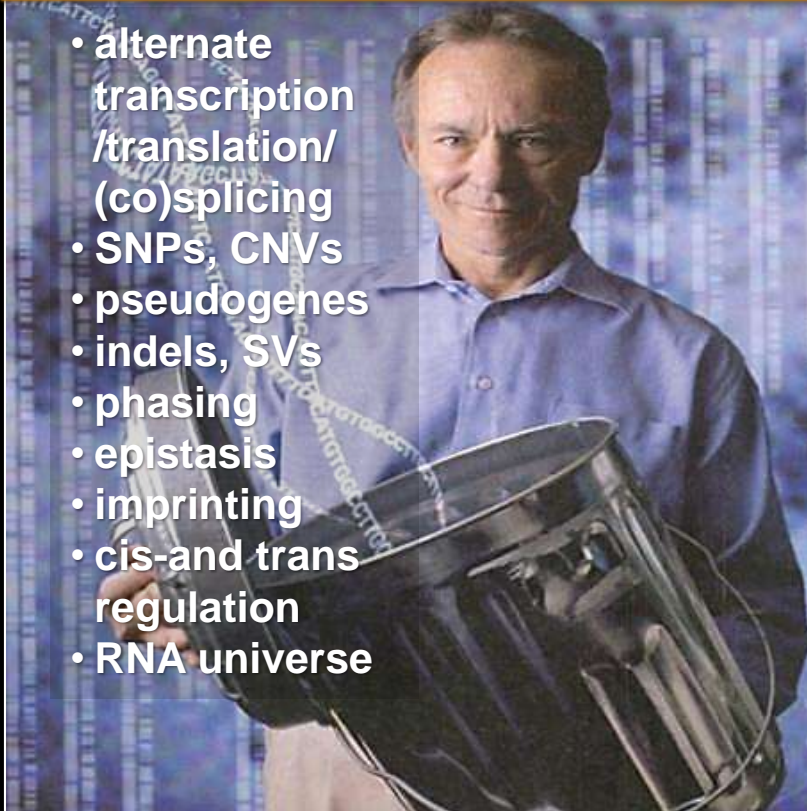
(epi)genome organizational and regulatory complexity

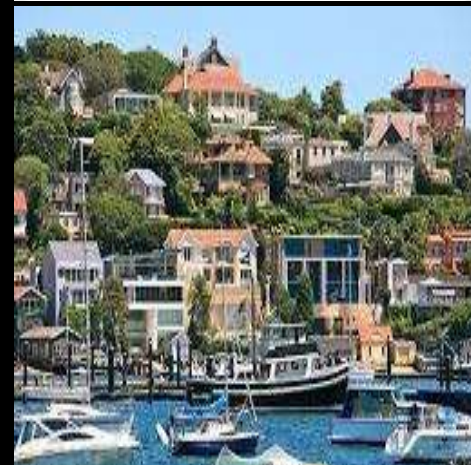## Cell-specific Molecular Interaction Networks

Perturbed Networks and Disease

(Epi)Genome Plus Environment (Exposome) Determines the Dynamics of Cellular (Information) Signaling Networks (System States)

Longitudinal Quantitative Data: A Major Knowledge Gap in Patient Histories

Behavior

Environment

An Emerging 'Omnigenic' Model for Epistatic Gene Networks in Driving Complex Phenotypes
A. Boyle et al. (2017) Cell 169, 1177

- consistent ID of alterations in a modest number of genes/pathways and/or their regulation in disease
  - "core genes", "drivers"
  - role in disease predisposition/onset
- variants in multiple 'peripheral' genes with non-zero effects affect penetrance of core/driver gene sets

An Emerging 'Omnigenic' Model for Epistatic Gene Networks in Driving Complex Phenotypes
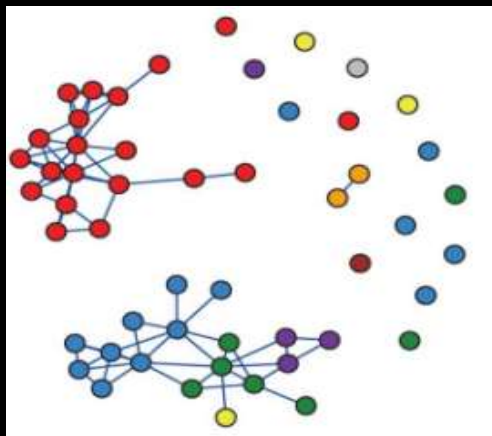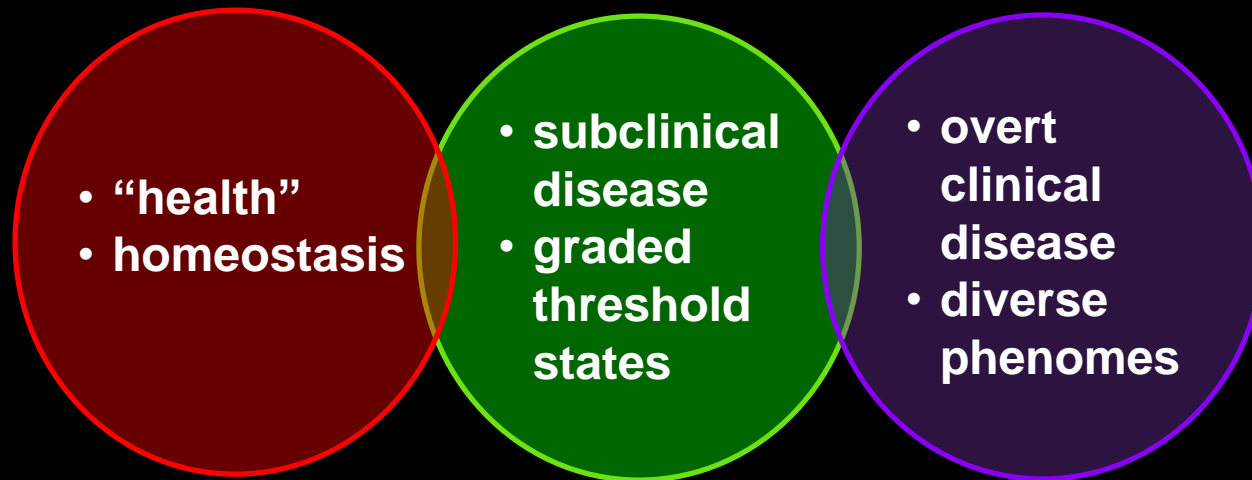## A. Boyle et al. (2017) Cell 169, 1177

- **dynamic shifts in composition/modularity of molecular networks/subnetworks engages different collections of peripheral (modulating) genes**

- **resulting spectrum of overlapping disease phenotypes based on different core-peripheral gene combinations**
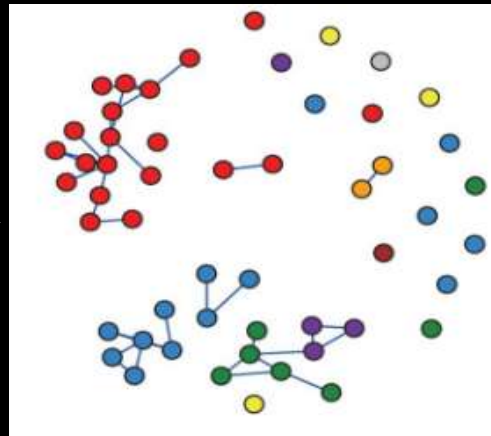
It's The Network Stupid!
Deconvolution of the Topology and Regulatory Dynamics of Molecular (Information) Networks
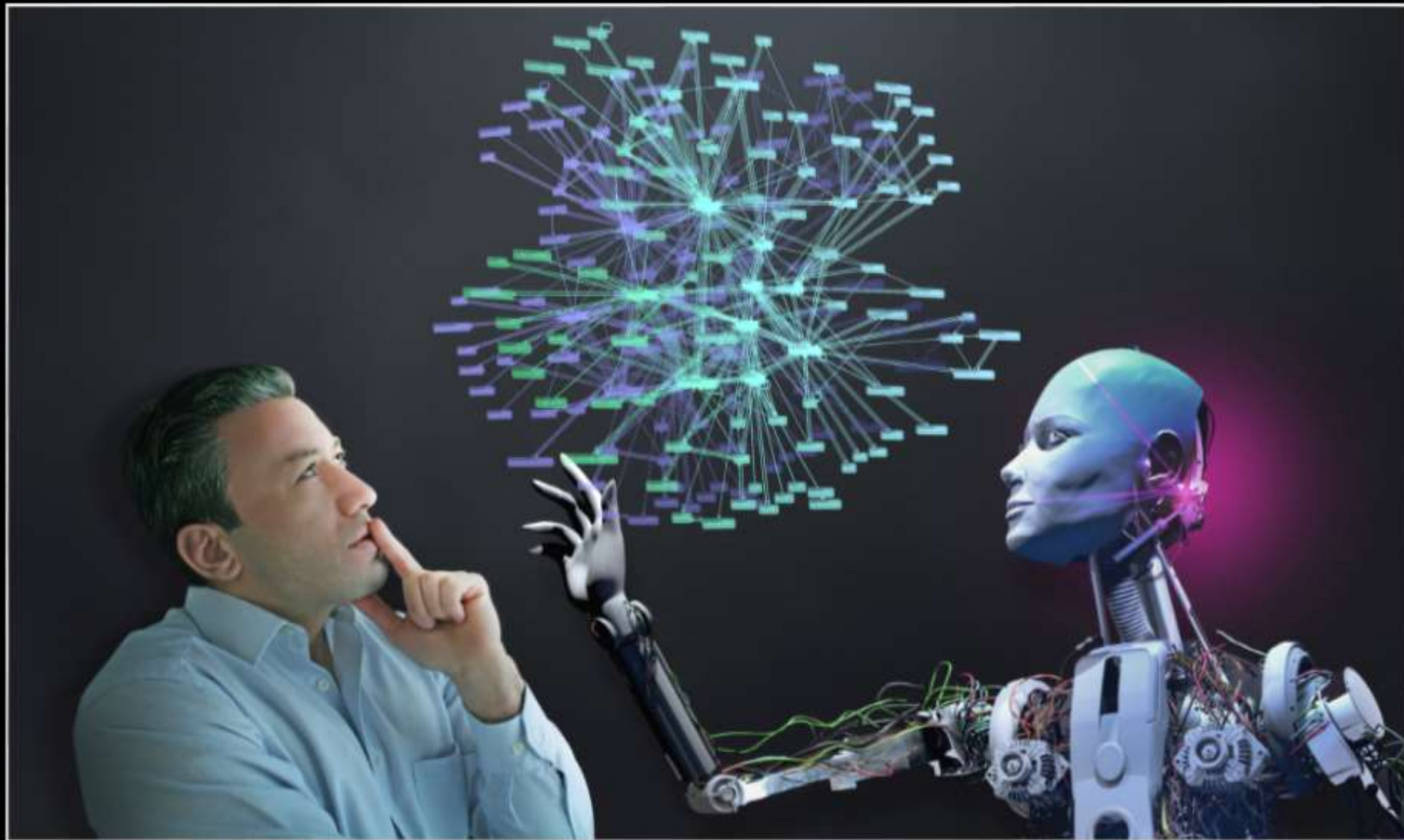
Understanding Network Organization and Regulatory Dynamics in Complex Adaptive Systems

- **"health"**
- **homeostasis**

- **subclinical disease**
- **graded threshold states**

- **overt clinical disease**
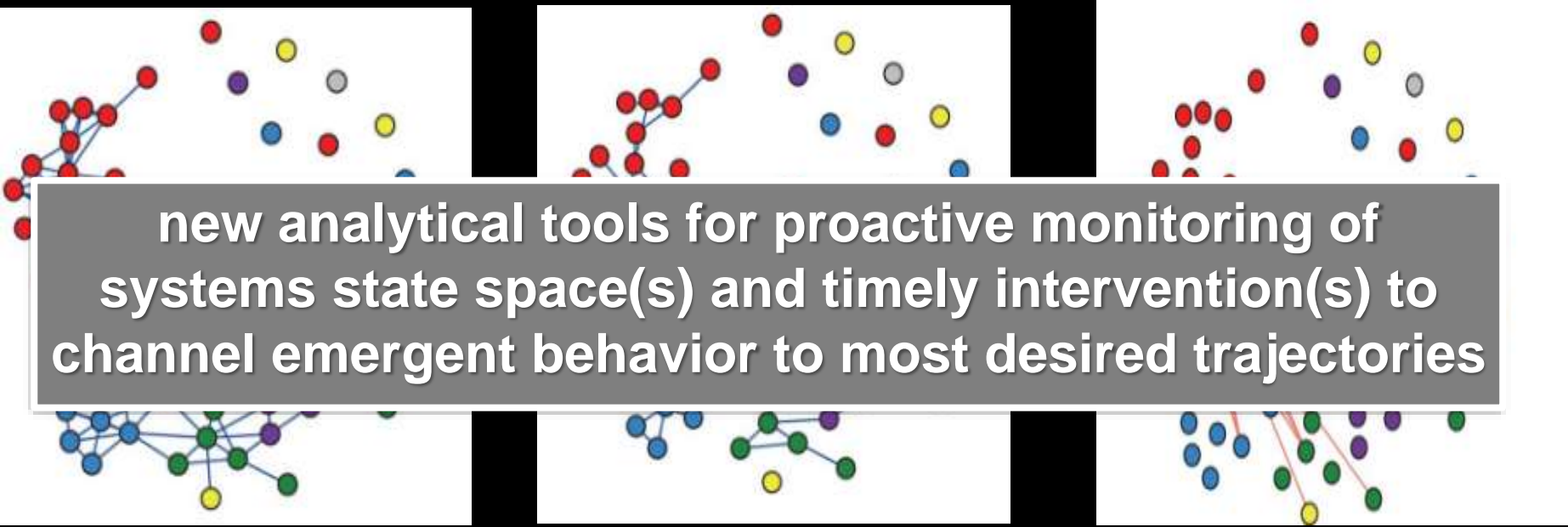- **diverse phenomes**

X
(health)

X´
(subclinical disease)
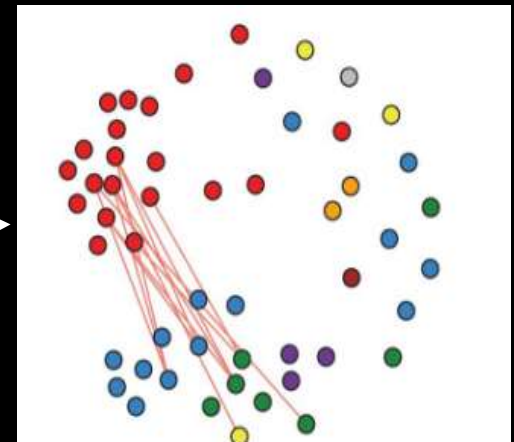
X (d)
(rational therapy)

Understanding Network Organization and Regulatory Dynamics in Complex Adaptive Systems

new analytical tools for proactive monitoring of systems state space(s) and timely intervention(s) to channel emergent behavior to most desired trajectories

X
(health)

X´
(subclinical disease)

X (d)
(rational therapy)

Are We Approaching the End of Identification of New Rx Targets Associated with the Coding Genome?

Will Future MDx and Rx Discovery Be More Productive By Identification of Novel Targets in Non-Coding Regulatory Elements (Regulome)?

Nature (2017) 547, 55

Recurrent and functional regulatory mutations in breast cancer

Esther Rheinbay, Prasanna Parasuraman, Jonna Grimsby, Grace Tiao, Jesse M. Engreitz, Jaegil Kim, Michael S. Lawrence, Amaro Taylor-Weiner, Sergio Rodriguez-Cuevas, Mara Rosenberg, Julian Hess, Chip Stewart, Yosef E. Maruvka, Petar Stojanov, Maria L. Cortes, Sara Seepo, Carrie Cibulskis, Adam Tracy, Trevor J. Pugh, Jesse Lee, Zongli Zheng, Leif W. Ellisen, A. John Iafrate, Jesse S. Boehm, Stacey B. Gabriel, Matthew Meyerson, Todd R. Golub, Jose Baselga, Alfredo Hidalgo-Miranda, Toshi Shioda, Andre Bernards, Eric S. Lander & Gad Getz

Genomic analysis of tumours has led to the identification of hundreds of cancer genes on the basis of the presence of mutations in protein-coding regions. By contrast, much less is known about cancer-causing mutations in non-coding regions. Here we perform deep sequencing in 360 primary breast cancers and develop computational methods to identify significantly mutated promoters. Clear signals are found in the promoters of three genes. FOXA1, a known driver of hormone-receptor positive breast cancer, harbours a mutational hotspot in its promoter leading to overexpression through increased E2F binding. RMRP and NEAT1, two non-coding RNA genes, carry mutations that affect protein binding to their promoters and alter expression levels. Our study shows that promoter regions harbour recurrent mutations in cancer with functional consequences and that the mutations occur at similar frequencies as in coding regions. Power analyses indicate that more such regions remain to be discovered through deep sequencing of adequately sized cohorts of patients.

J. Hematol. Oncol. (2017) 10, 107

An imprinted non-coding genomic cluster at 14q32 defines clinically relevant molecular subtypes in osteosarcoma across multiple independent datasets

Katherine E. Hill[2,4], Andrew D. Kelly[5], Marieke L. Kuijjer[3], William Barry[3], Ahmed Rattani[15], Cassandra C. Garbutt[1], Haydn Kissick[16], Katherine Janeway[11], Antonio Perez-Atayde[12], Jeffrey Goldsmith[12], Mark C. Gebhardt[13], Mohamed S. Arredouani[14], Greg Cote[6], Francis Hornicek[1], Edwin Choy[6], Zhenfeng Duan[1], John Quackenbush[3], Benjamin Haibe-Kains[7,8,9,10] and Dimitrios Spentzos[1,2*]

Genome Research (2017) 27, 1050

High-confidence coding and noncoding transcriptome maps

Bo-Hyun You,[1] Sang-Ho Yoon,[1] and Jin-Wu Nam[1,2,3]

[1]Department of Life Science, College of Natural Sciences, Hanyang University, Seoul 133791, Republic of Korea; [2]Research Institute for Convergence of Basic Sciences, Hanyang University, Seoul 133791, Republic of Korea; [3]Research Institute for Natural Sciences, Hanyang University, Seoul 133791, Republic of Korea

The advent of high-throughput RNA sequencing (RNA-seq) has led to the discovery of unprecedentedly immense transcriptomes encoded by eukaryotic genomes. However, the transcriptome maps are still incomplete partly because they were mostly reconstructed based on RNA-seq reads that lack their orientations (known as unstranded reads) and certain boundary information. Methods to expand the usability of unstranded RNA-seq data by predetermining the orientation of the reads and precisely determining the boundaries of assembled transcripts could significantly benefit the quality of the resulting transcriptome maps. Here, we present a high-performing transcriptome assembly pipeline, called CAFE, that significantly improves the original assemblies, respectively assembled with stranded and/or unstranded RNA-seq data, by orienting unstranded reads using the maximum likelihood estimation and by integrating information about transcription start sites and cleavage and polyadenylation sites. Applying large-scale transcriptomic data comprising 230 billion RNA-seq reads from the ENCODE, Human BodyMap 2.0, The Cancer Genome Atlas, and GTEx projects, CAFE enabled us to predict the directions of about 220 billion unstranded reads, which led to the construction of more accurate transcriptome maps, comparable to the manually curated map, and a comprehensive lncRNA catalog that includes thousands of novel lncRNAs. Our pipeline should not only help to build comprehensive, precise transcriptome maps from complex genomes but also to expand the universe of noncoding genomes.

Nature Genetics (2017) 49, 825

Recurrent noncoding regulatory mutations in pancreatic ductal adenocarcinoma

Michael E Feigin[1,2,22], Tyler Garvin[3,22], Peter Bailey[4], Nicola Waddell[5,6], David K Chang[4,7−9], David R Kelley[10], Shimin Shuai[11], Steven Gallinger[12,13], John D McPherson[14,21], Sean M Grimmond[4,6,21], Ekta Khurana[13], Lincoln D Stein[11,16], Andrew V Biankin[4,9,20], Michael C Schatz[1,17,18] & David A Tuveson[1,2,19]
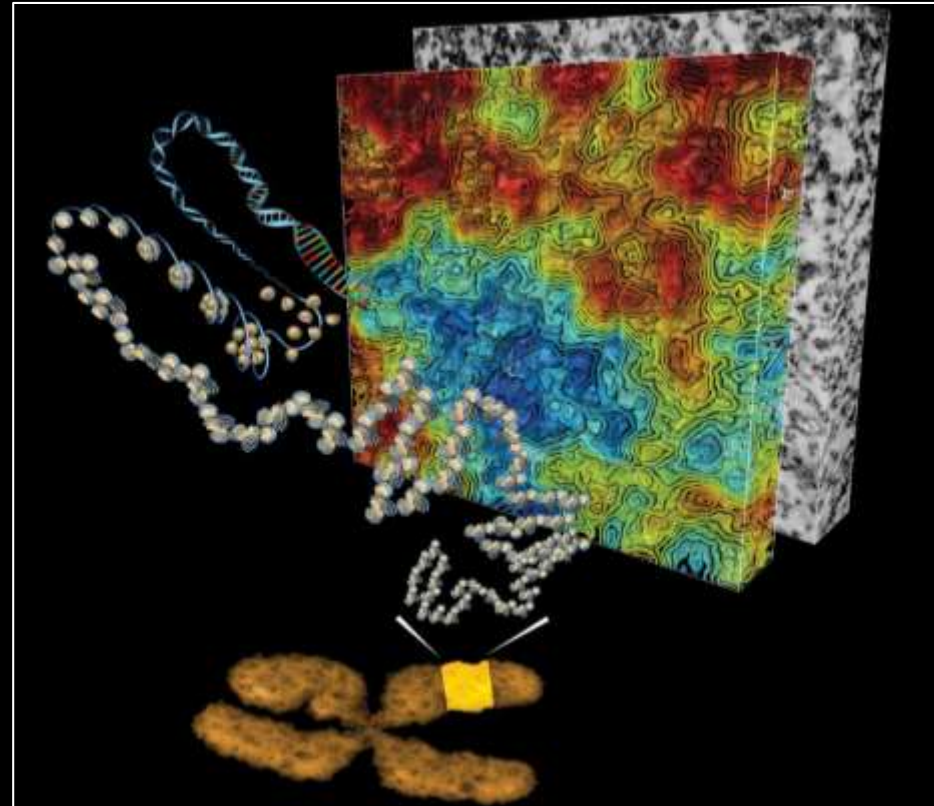
Defining Short- and Long-Range Cis- and Trans- Regulation of Gene Networks

Chromosomal Neighborhoods: Understanding the 3-D and 4-D Genome

ChromEMT Mapping of Chromatin Ultrastructure and DNA Packing
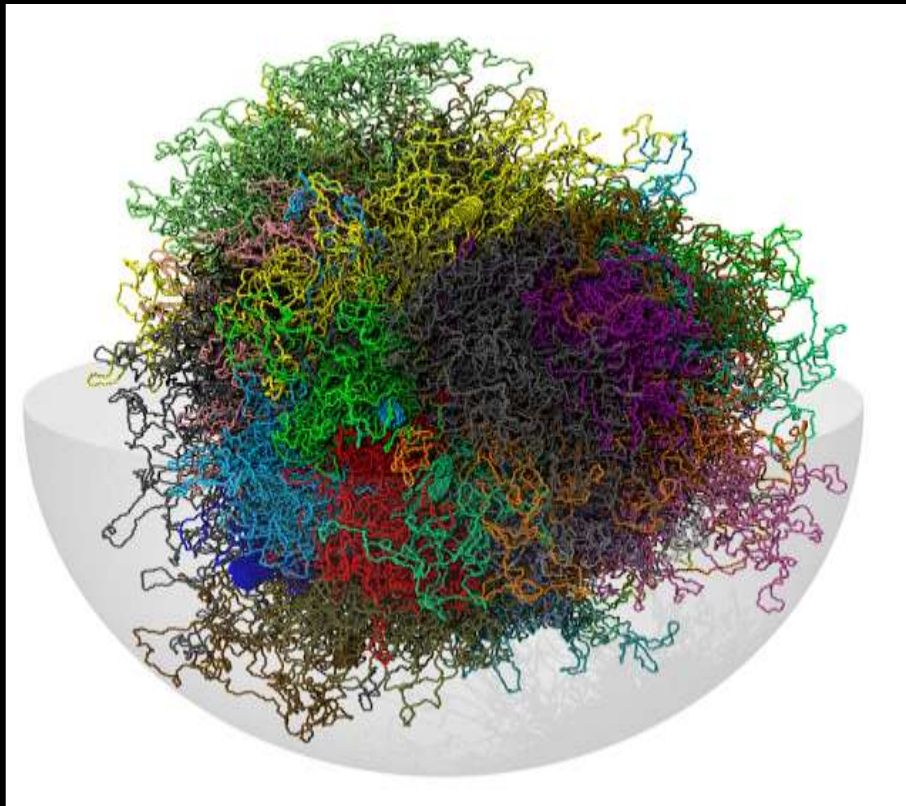
From: International School of Advanced Studies (SISSA) [October 26, 2016]

From: H. D. Ou et al. (2017) Science eaaag.0025

The Deconvolution of Biological Complexity: The Shift from Reductionism to Systems-Based Concepts

- **fifty years of reductionist biology**

- **vital legacy but now ill-suited to address the daunting complexity of biological network dynamics in physiology and pathology**

- **big biology (analogy with big physics)**

  – **multi-disciplinary, multi-institutional, multi-sector**

  – **increased investment and dependency on methods from industry sectors hitherto uninvolved in healthcare**
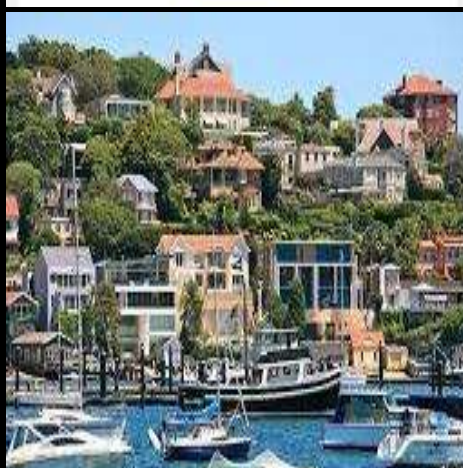
Convergence

Convergence of Advances in Biomedicine, Materials Science, Engineering, Telecommunications, Advanced Computing and Data Science

Blurring the Boundaries of Biomedicine

Most Events That Affect Our Health Occur Outside of the Healthcare System And Are Not Monitored

## Need for Continuity of Care Record: From Womb to Tomb

Behavior

Environment

Precision Medicine:
Healthcare Beyond The Clinic

- **daily decisions by individuals have greater effects on their health than decisions controlled by the healthcare system**

- **building HIT systems to better monitor health status and treatment adherence**

Microbiome Profiling:
The Gut-Immune-Brain Axis in Health and Disease
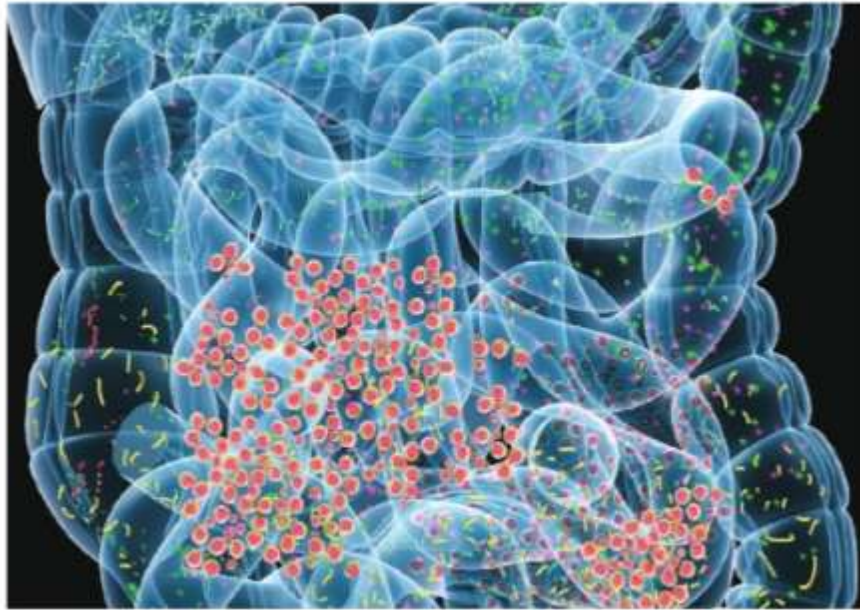
- **influence of microbial metabolites**
  - **nutrition**
  - **obesity**
  - **brain function/mood**
  - **drug metabolism**
  - **autoimmunity; immune system responsiveness**

Personal, Dense, Dynamic Data Clouds: Comprehensive Profiling of Health Status of 108 Individuals Over 9 Months

N. D. Price et al. (2017) Nature Biotechnology 35, 747
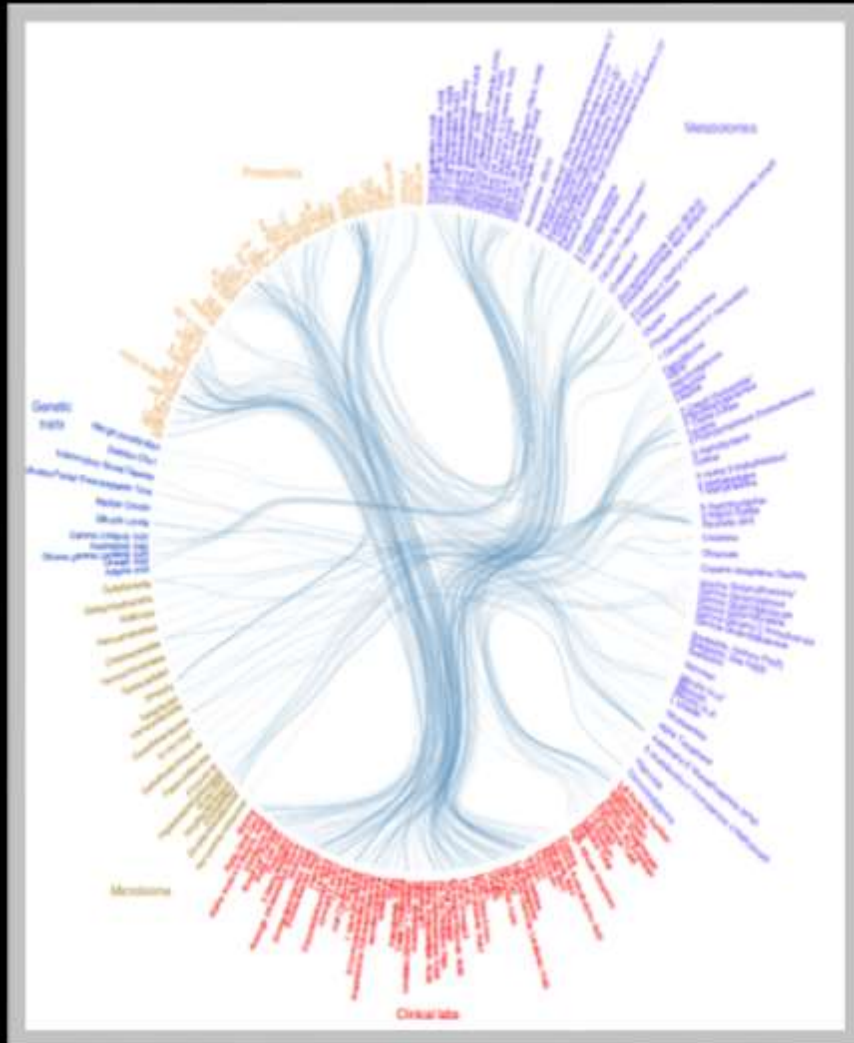
- **WGS**

- **daily physical and sleep activities**

- **3 month blood, saliva, urine and stool analysis**

- **643 metabolites**

- **262 proteins**

- **cost**

- **scalability**

- **data interpretation**

- **clinical utility**

Science (2017) 357, 345

BIOMEDICINE

'Scientific wellness' study divides researchers

Famed biologist's spinoff company sells personalized health monitoring and coaching

By Ryan Cross

eroy "Lee" Hood is one of biolog[y's] living legends. Now 78 years old,

ports in the August issue of *Nature Biotechnology* that dozens of the participants turned out to have undiscovered health risks, including prediabetes and low vitamin D, which the coaching helped them address.

Hood says the findings justify commercializing the monitoring, in a service costing thousands of dollars a year. But some colleagues disagree. The effort takes health monitoring "to new heights, or depths, depending on how you look at it," says Eric Topol, director of the Scripps Translational Science Institute in San Diego, California.

"[Brings] health monitoring to new heights or depths, depending on how you look at it."
  - Eric Topol, Scripps Institute

"when you link it [profiling] to companies offering this as a service, that is where we start getting into trouble."
  - Jonathan Berg, UNC

"…lack of sparkling findings. All these tests cost a lot of money and it's not exactly clear what we are getting out of them."
  - Atul Butte, UCSF

Berg, a physician scientist who studies cancer and genetics at the University of North Carolina School of Medicine in Chapel Hill, considered that project "thrilling." But, he adds, "when you link it to companies offering this as a service, that is where we start getting into trouble."

The problem, Berg says, is that "we don't have any idea at all how this information should be used clinically." Topol agrees, noting that he had comparable concerns about a similar barrage of tests on presumably healthy people, including genome sequencing and a full-body MRI scan, from a company launched by another genome legend, J. Craig Venter.

Arivale
Your scientific path to wellness

Entrepreneur Clayton Lewis (left) and biologist Leroy Hood (right) offer a data-heavy approach to health monitoring through their company, Arivale.

Invasion of the Body Trackers:
Expanding the "Care Space" in Healthcare

Smartphones, Wearables, Devices and Digital Services

M4: Making Medicine More Mobile

Remote Health Status Monitoring
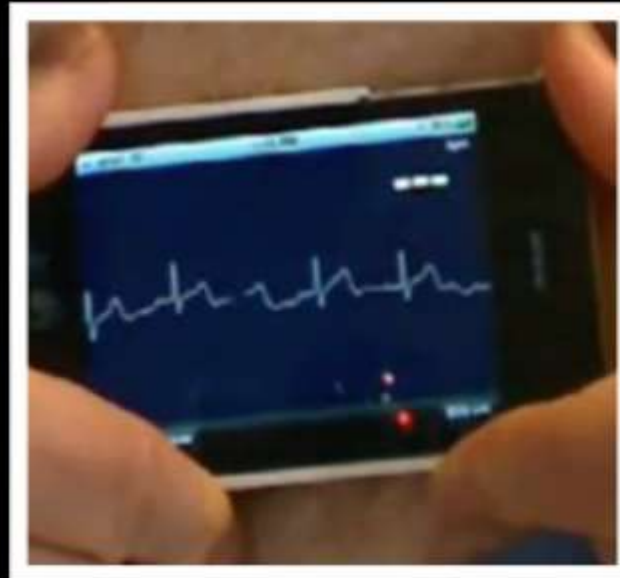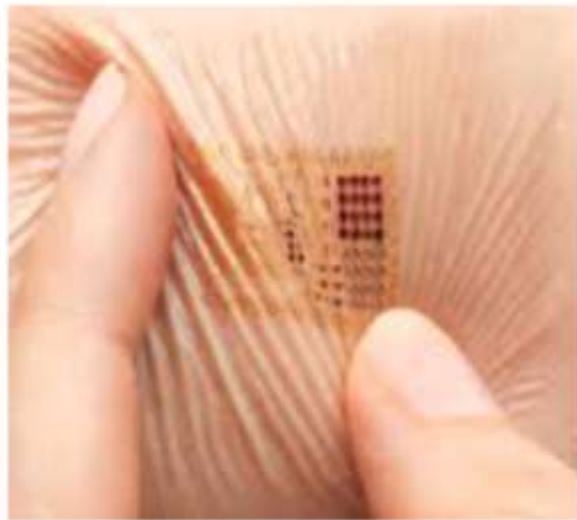
Wearables and Tracking Physical Activities

Nature (2017) 547, 13
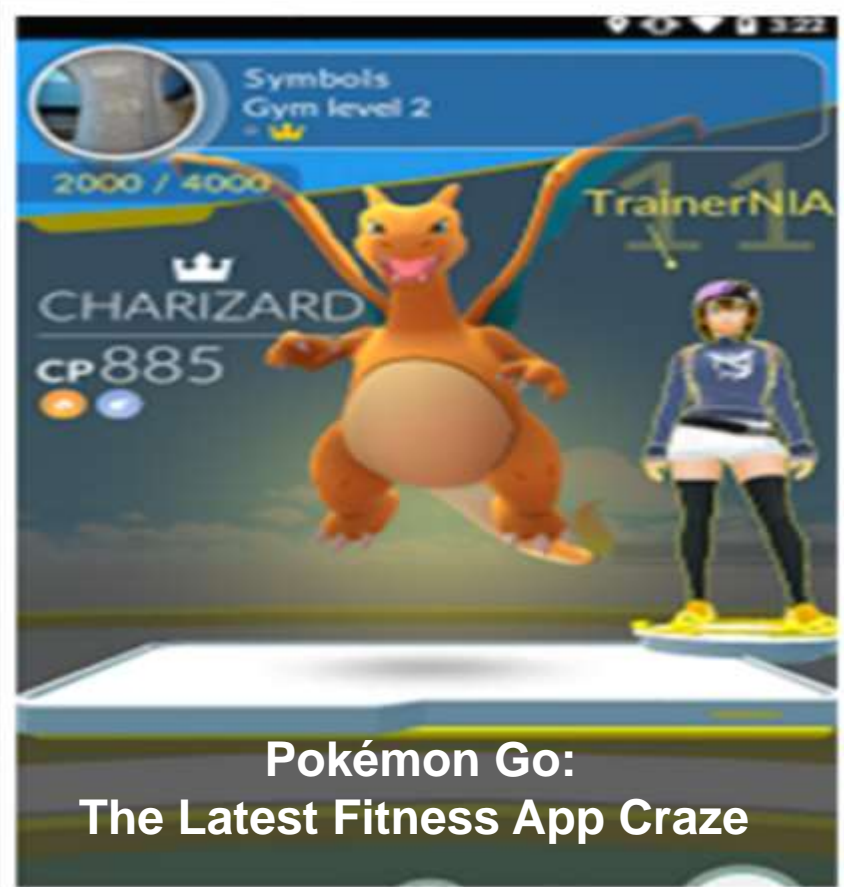
Pokémon Go:
The Latest Fitness App Craze

Gray Technologies and Aging in Place:
Independent But Monitored Living for Aging Populations

Rx adherence

cognitive stimulation

in home support and reduced readmissions

reduced office visits

Digital Assistants and Support Robots in Healthcare
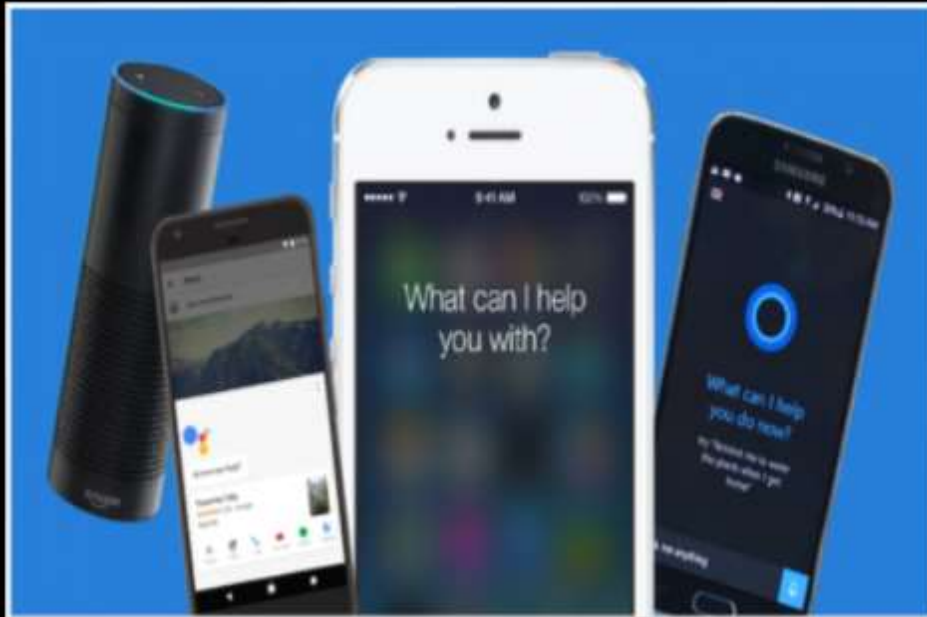
AORTA Technologies:
Always-on-Real-Time Access for Health Status Monitoring

- better real time patient-specific data and decision-support tools

- new patterns (touch points) of patient engagement with the health system

  - extend reach and continuity in care

  - ability to monitor larger number of patients

- each individual becomes their own control

Mobile Apps, Wearables, Sensors and Continuous Health Status Monitoring

- who sets the standards?

- who integrates and interprets the data?

- who pays?

- who consents?

- who owns the data?

An Apps-Based Information Economy in Healthcare

- **lack of developer access to high quality healthcare data to validate App platforms**

- **accuracy, reliability, security and privacy**

- **FDA focus on Apps that transform phone/tablet into a regulated medical device**

- **renewed FTC interest on Apps making unsubstantiated claims**

Computing

Precision Medicine and Digital Medicine: Evolving Inter-Dependencies

Individual Data

Population Databanks
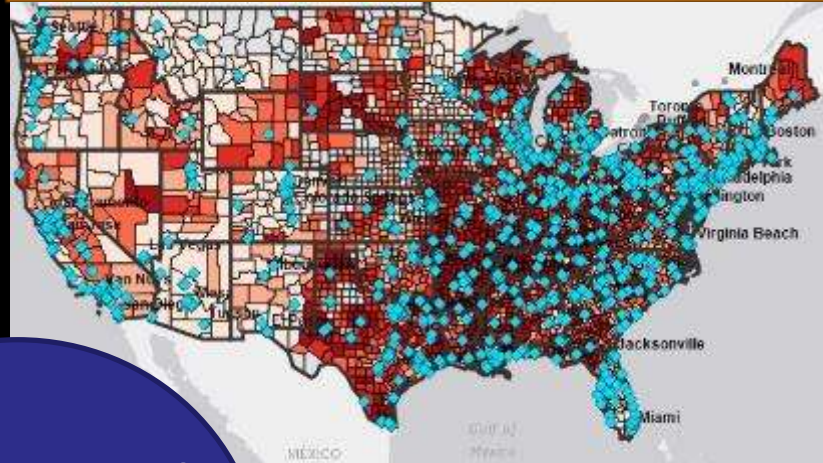
integration and analysis of large scale, diverse data

matching individual profiles to "best matched" cohorts for clinical decisions

Social Spaces and Behavior Become Quantifiable

- **who knows why people do what they do?**
    - **the fact is that they do!**

- **these activities can now be traced and measured with unprecedented precision**

- **with sufficient data, the numbers reveal increasingly predictable behavior and individual risk patterns**

- **new ethical and legal issues**
    - **consent, privacy, surveillance, security**

Population Health Research and Precision Medicine: Blurring the Boundaries Between Research and Clinical Care

- **every encounter (clinical and non-clinical) is a data point**

- **every individual is a data node**

- **every individual is a research asset**

- **every individual is their own control**

"I don't think of Humana so much as an insurance company as an IT company who is helping us with the data that we need in order to deal with our population health tools."

Dr. Roy Beveridge, M.D.

CMO, Humana

Cited in Fierce Healthcare 9 May 2017

Now Comes the Hard Part!

Driving Precision Medicine and Large Scale Data Analytics into Routine Clinical Practice

The Problem With Real World Data is the Real World

HELL IS THE PLACE WHERE NOTHING CONNECTS — T.S. ELIOT
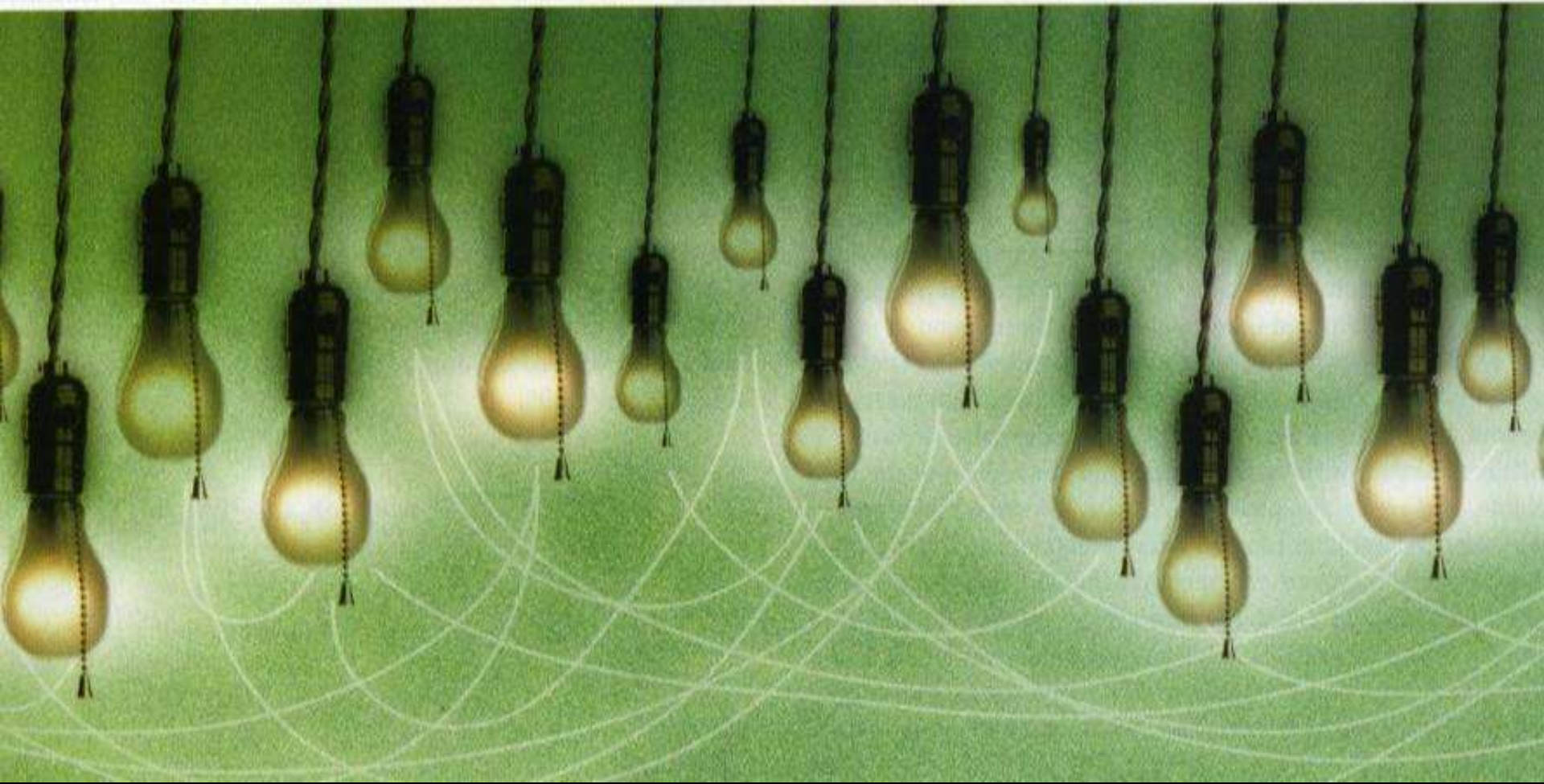
HELL IS THE PLACE WHERE NOTHING CONNECTS — T.S. ELIOT

**Welcome to
The World of
Biomedical Research
and
Healthcare Information Systems**

The Worst Supply Chain in Society: The Health Information Supply Chain

- slow transition from paper to electronic systems

- fragmented, disconnected, incomplete and inaccurate data

- incompatible data formats as barrier to data integration and sharing

- EMR integration of new data classes (multi-omics)

- legislative barriers to data transfer based on well intentioned privacy protections (HIPAA)

- organizational, economic and cultural barriers to open data sharing

Culture
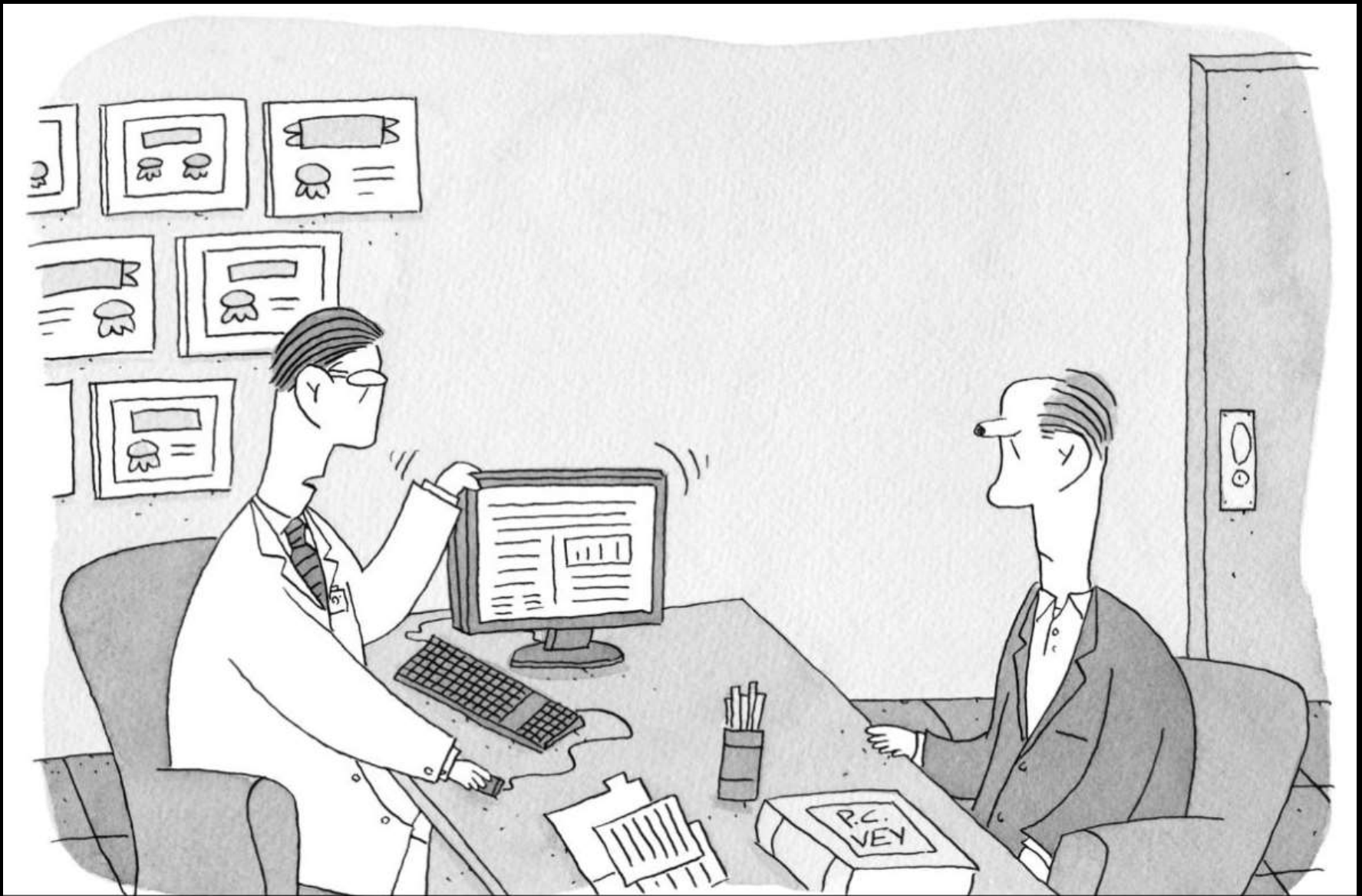
"So, as you can see, health care is so complicated you may never get well."

Adapting to the Rise of Large Scale, Data-Intensive Biomedicine
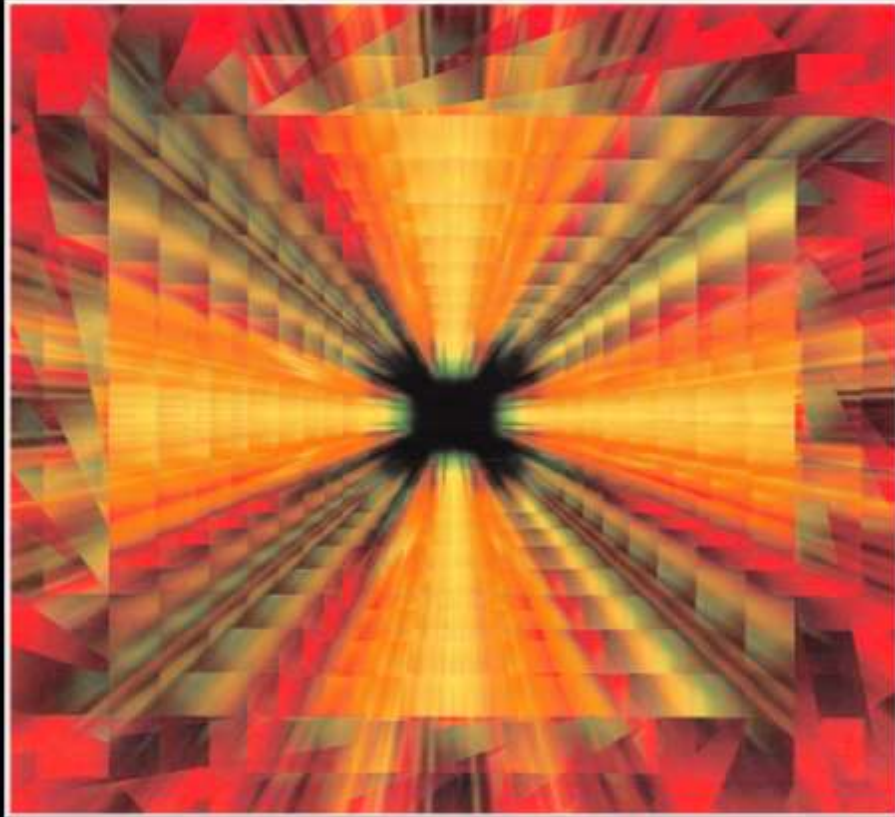
- **exponential technology acceleration**
- **technology convergence: the exponential of the exponentials**
- **scale: major implications for investment, organization and culture**

The Cultural, Organizational and Economic Implications of the Evolution of Large Scale, Data-Intensive Biomedicine

'S4'

- silos
- single discipline
- single investigator
- single institution

'M4'

- matrix networks
- multi-disciplinary
- multi-investigator
- multi-institutional
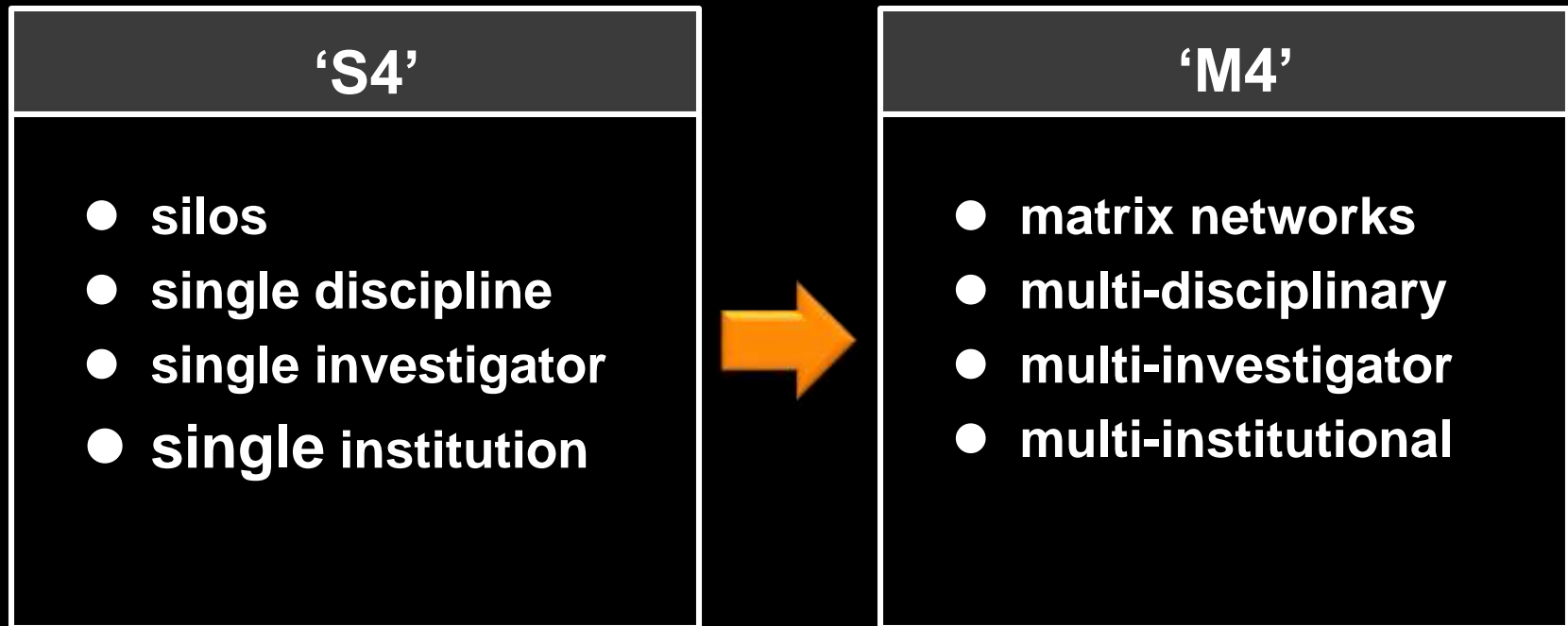
Recognizing the Importance of Scale: Multidisciplinary, Multi-Institutional, Multi-Sector Collaborations and Knowledge Networks

FasterCures

consortia-pedia

An In-Depth Look at the Research-by-Consortium Trend in Medical Research and Development

Science Translational Medicine
(2014, 6, 242cm6)

COLLABORATIVE ENVIRONMENTS

Consortium Sandbox:
Building and Sharing Resources

Mark D. Lim

Some common challenges of biomedical product translation—scientific, regulatory, adoption, and reimbursement—can best be addressed by the broad sharing of resources or tools. But, such aids remain undeveloped because the undertaking requires expertise from multiple research sectors as well as validation across organizations. Biomedical resource development can benefit from directed consortia—a partnership framework that provides neutral and temporary collaborative environments for several, oftentimes competing, organizations and leverages the aggregated intellect and resources of stakeholders so as to create versatile solutions. By analyzing 369 biomedical research consortia, we tracked consortia growth around the world and gained insight into how this partnership model advances biomedical research. Our analyses suggest that research-by-consortium provides benefit to biomedical science, but the model needs further optimization before it can be fully integrated into the biomedical research pipeline.

Cornerstones of Collaboration
FOUNDATION-LED PARTNERSHIPS TO ACCELERATE R&D

FasterCures

A Pending Transition in Research Methods and Clinical Care Decisions?
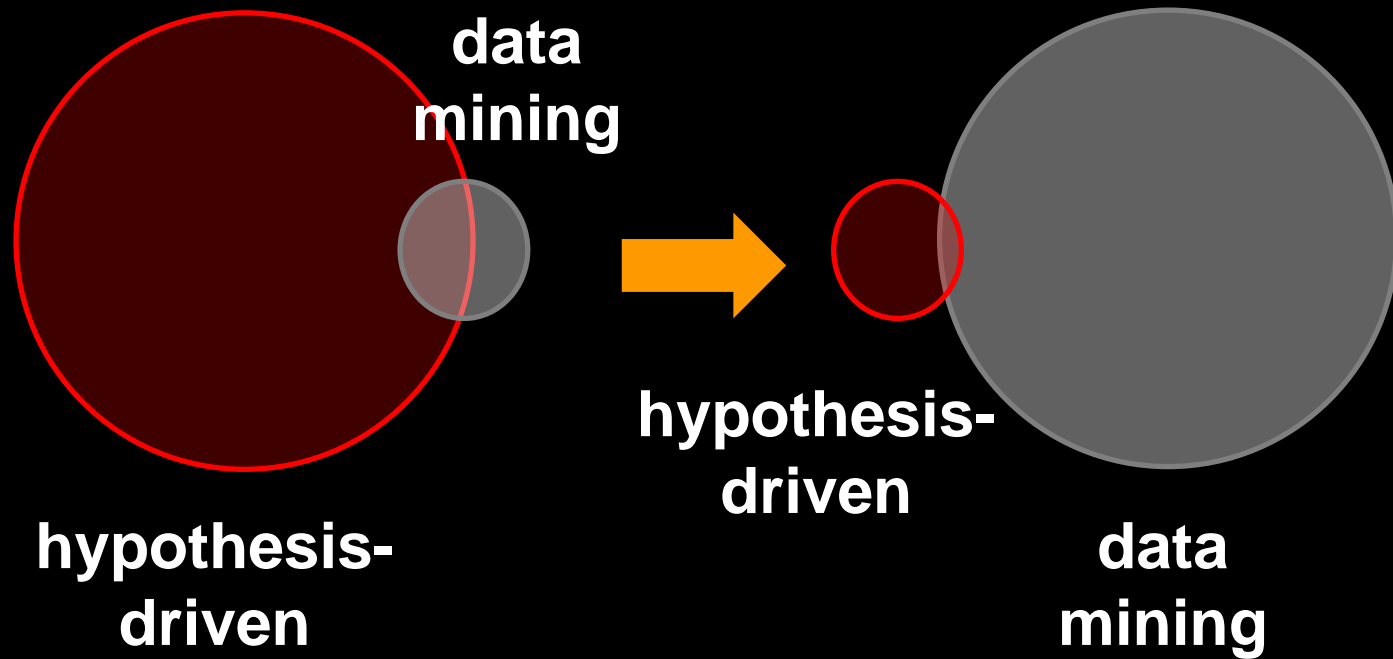
Cultural Barriers to Systems-Based, Data-Intensive Biomedical Research and Clinical Care

- biomedical communities largely untrained in quantitative data methods and analytics, statistics, computing and data science

- predominance of descriptive, unstandardized, qualitative data generated in fragmented expertise silos

- skepticism about premature, unrealized claims of the transformative impact of "-Omics" platforms

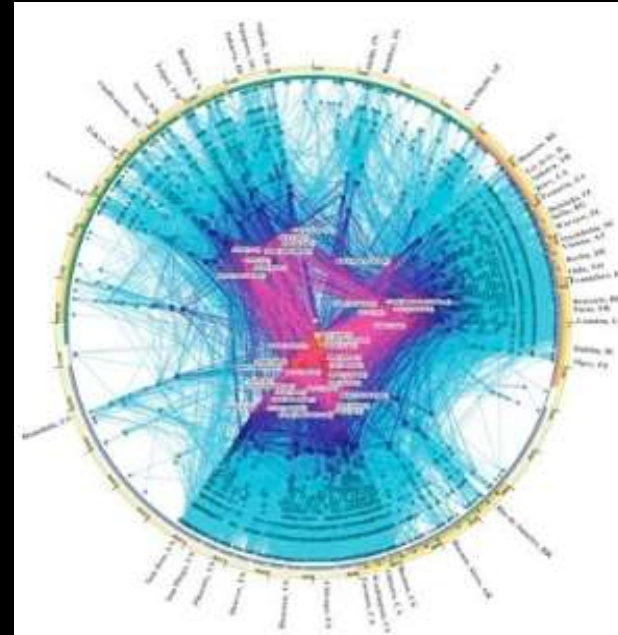- personal and institutional reluctance for data sharing

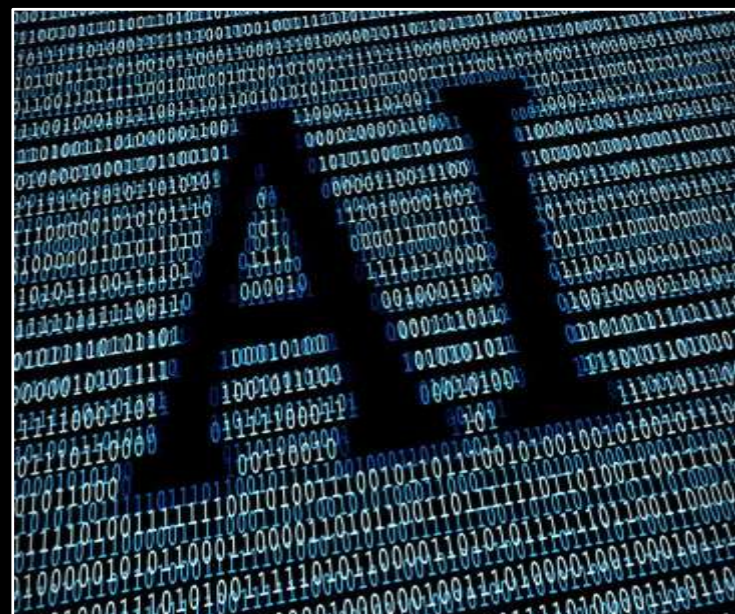# The Emergence of Big Data Changes the Questions That Can Be Asked

Isolated Data

Complex Networked Data

Complex Computational Data

The Future Issue
FORTUNE
The Doctor Will See You Now
INSIDE THE DIGITAL HEALTH REVOLUTION & HOW IT WILL CHANGE YOUR LIFE P. 90

The Future of
**Television
Food
Finance
Security
Fashion**
AND THE
41 Companies
THAT ARE CREATING TOMORROW TODAY

What Prediction Markets Can Tell Us About *Trump's Next Move* P. 10

Newsweek.
THE DOCTOR WILL SEE YOU NOW
HOW AI IS GOING TO CURE OUR SICK HEALTH CARE SYSTEM

DEEP LEARNING

AI

Machine Learning and Image Analysis in Clinical Medicine

pathology	radiology	dermatology	ophthalmology
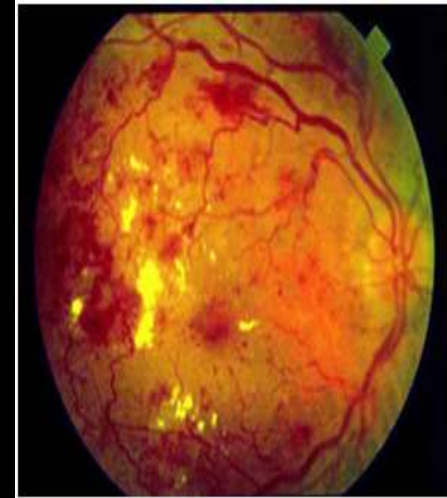
- **large scale training sets and classification parameters**

- **standardized, reproducible and scalable**

- **260 million images/day for $1000 GPU**

Artificial Intelligence, Pattern Analysis and Medical Practice

"I don't think any physician today
should be practicing without artificial intelligence
assisting in their practice.
It's just impossible (otherwise) to pick up on patterns,
to pick up on trends, to really monitor care."

Bernard J. Tyson
CEO, Kaiser Permanente
Cited in Forbes: The Future of Work
1 March 2017

Recent AI Investments in Drug Discovery

Biology and Medicine Meets Blockchain
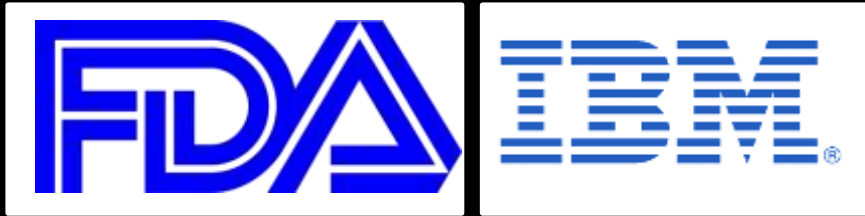
- **security of patient data**

- **improve efficiency of clinical trials**
- **user validation, proof of work, smart contracts**
- **supply chain tracking and anti-counterfeiting**

Cognitive Computing and Decision-Support Systems: Overcoming the "Bandwidth" Limits of Human Individuals

- **limits to experiences and perceptions**
- **limits to objective decision-making**
  - **escalating (paralyzing?) complexity**
  - **shorter time-to-act**
- **limits to individual expertise**
- **limits to sensory and cognitive capacities**

Complex Autonomous Systems and Automated Computational Decision Support Systems

Creative Disruption
Technology, Strategy and the Future of the Global Defense Industry

By Ben FitzGerald and Kelley Sayler

Foreword by the Honorable William J. Lynn III
and ADM James Stavridis, USN (Ret.)

THE DEFENSE SCIENCE BOARD REPORT ON
Technology and Innovation Enablers for Superiority in 2030

JUNE 2014

Deep Learning, Machine Intelligence, AI and Decision Control

"I Can't Let You Do That Dave"

Living in a World Where the Data Analytics and Interpretation Algorithms Are Obscure to the End User

- **ceding decision authority to computerized support systems**

- **culturally alien to professionals in their claimed expertise domain but they accept in all other aspects of their lives**

- **who will have the responsibility for validation and oversight of algorithms used in decision tree analytics for big data?**

  - **regulatory agencies and professional societies?**

  - **humans?**

  - **machines?**

"Explainable AI"

- **need to better characterize the evolution of decision algorithms**

  - **keeping humans in the loop**

- **deconvolution of how and why machine learning algorithms reach flawed conclusions**

- **concern over AI-directed manipulation of financial and social networks, advertising and personal data**

  - **implant bias and distrust**

  - **crime**

  - **broad national security issues related to data integrity and national cyber-vulnerabilities**
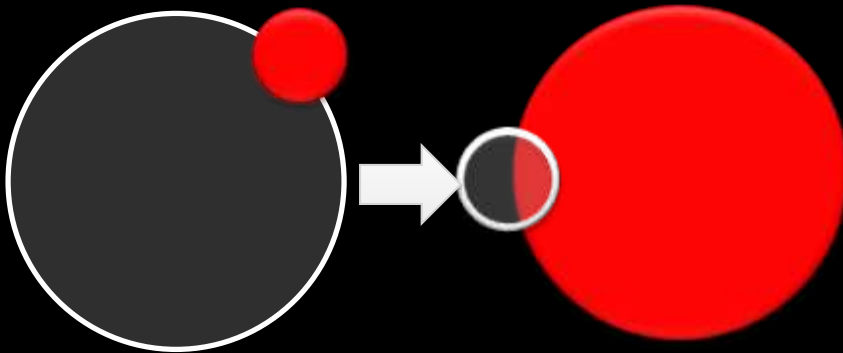
Creative Destruction

Schumpeterian Creative Destruction

- **comfort and complacency erode capabilities and competitiveness**

- **failure to see/adapt to disruptive forces and threats to the status quo**

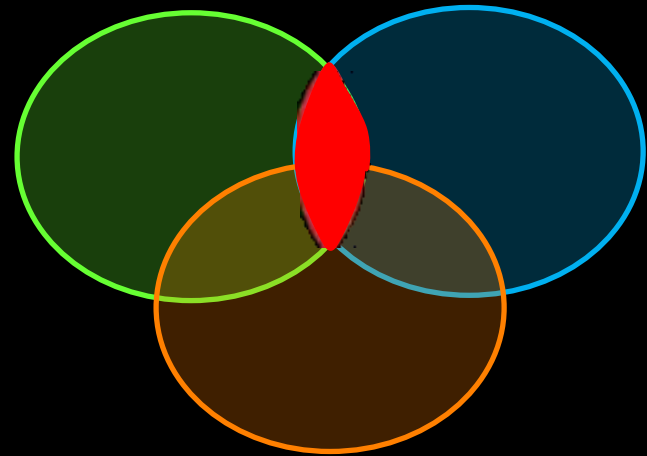- **technology as the most potent catalyst for industrial transformation and market disruption**

Technology Innovation and Creative Destruction

DNR: Is the Current Healthcare System Terminal?
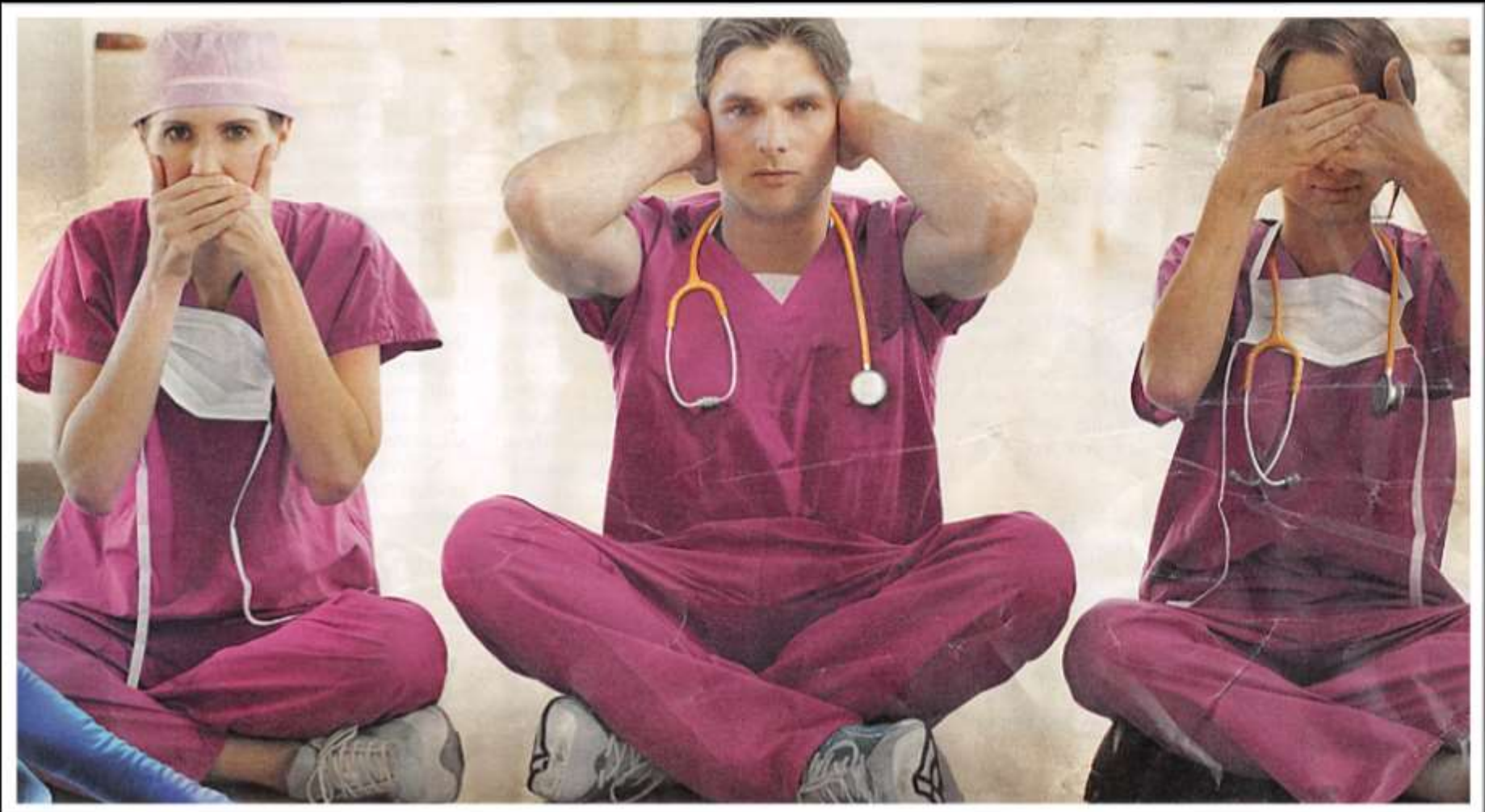
Denial   **Negativity**   **Resistance**

Biomedical Research and Healthcare Delivery: Ecosystems with Pervasive Embedded Inefficiencies Ripe for Creative Destruction
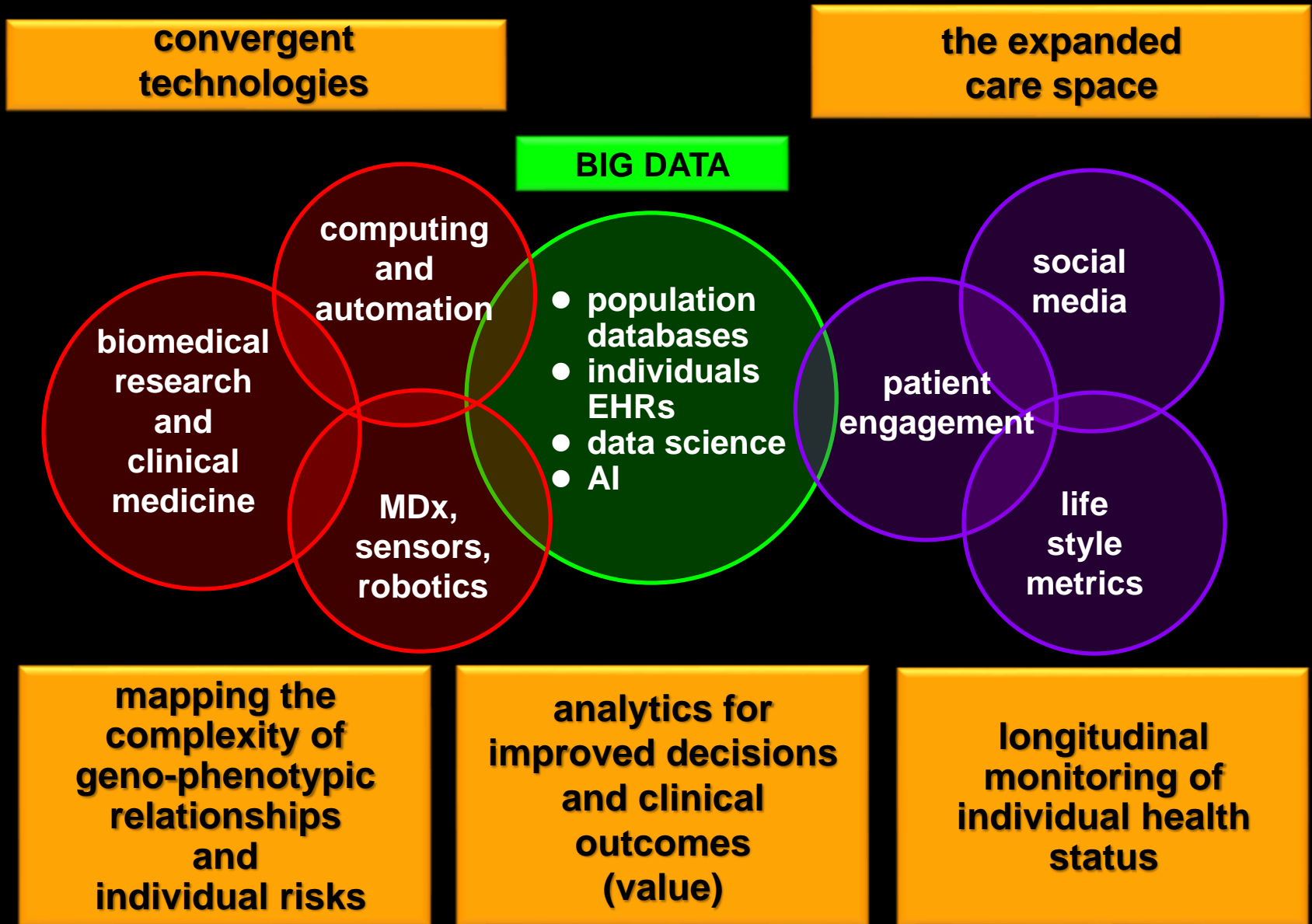
- slow translation of research for patient benefit

- unstainable cost of care

- fragmented, uncoordinated duplication, waste and administrative bloat

- poor use of available information

- slow adoption of advanced IT systems relative to other sectors

- public dissatisfaction and political turmoil over care access and affordability

The Co-Evolution of Precision Medicine and Learning Healthcare Information Systems

convergent technologies

the expanded care space

BIG DATA

computing and automation

biomedical research and clinical medicine

MDx, sensors, robotics

- **population databases**
- **individuals EHRs**
- **data science**
- **AI**

patient engagement

social media

life style metrics

mapping the complexity of geno-phenotypic relationships and individual risks

analytics for improved decisions and clinical outcomes (value)

longitudinal monitoring of individual health status

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