

# **Sustaining Healthcare Innovation in an Era of Constraint**

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**Gold Laboratory: Somalogic Symposium**  
**Boulder, Colorado 14 May 2010**

# Major Challenges in Healthcare

## Cost



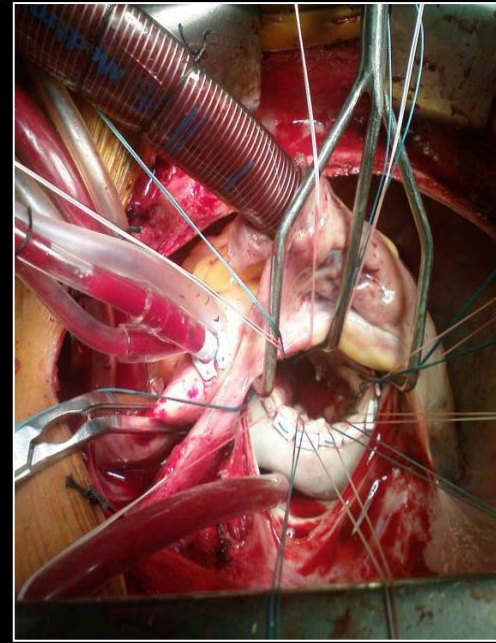
## Demographics



## Access



## Variation in Clinical Practice



# Major Challenges in Healthcare



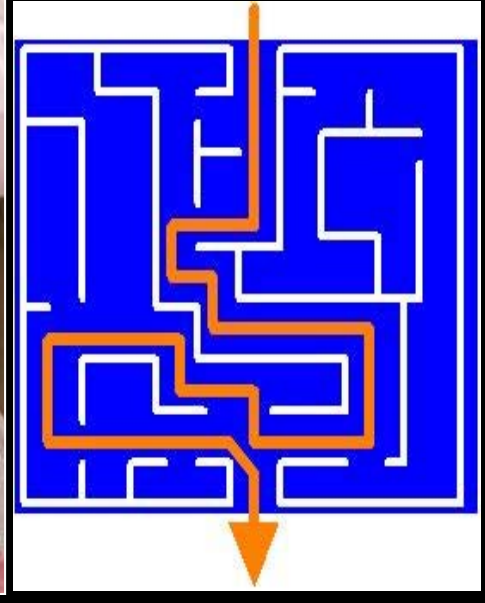
**Inefficient  
Use of  
Information**



**Fragmented  
Care Versus  
Integrated Care**



**Duplication,  
Defensive  
Medicine & Waste**



**Protracted  
Adoption of  
Innovation**

# Excessive Use of Services



**“If you lie down long enough,  
someone will scan you.”**

**Mike McCallister  
CEO, Humana**

**[www.forbes.com/2009/03/19](http://www.forbes.com/2009/03/19)**



# Fragmentation Versus Integration in Healthcare Delivery

## Physicians

- specialization and fee-for-service drives volume and siloed care provision
- lack of curriculum reform and propagation of anachronistic behavior/expectations

## Payors

- impenetrable thickets of eligibility/reimbursement criteria
- bloated administrative infrastructure to accommodate multiple payment channels

## Politicians

- boldness or timidity in healthcare reform?

## Patients

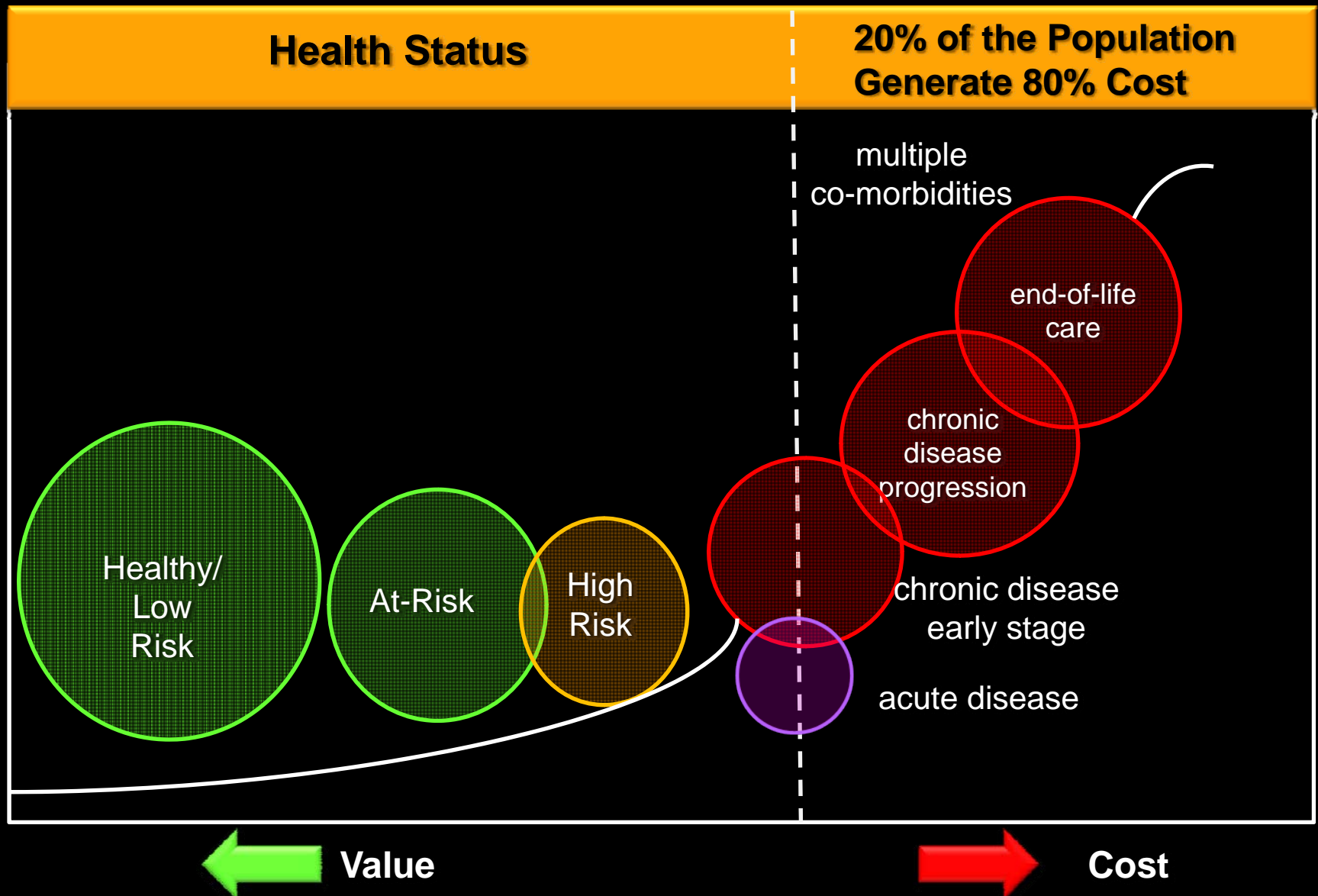
- confused and increasingly afraid

# Reasonable Expectations for Rational Healthcare

- what works?
- why it works?
- who it works for?
- what works best?
- when should it be used optimally?
- validated evidence
- mechanism of action
- personalized medicine
- comparative effectiveness
- best practice guidelines, standard-of-care and malpractice

**VALUE**

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

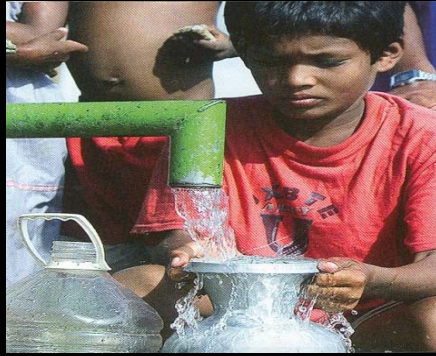


# New Value Propositions in Healthcare

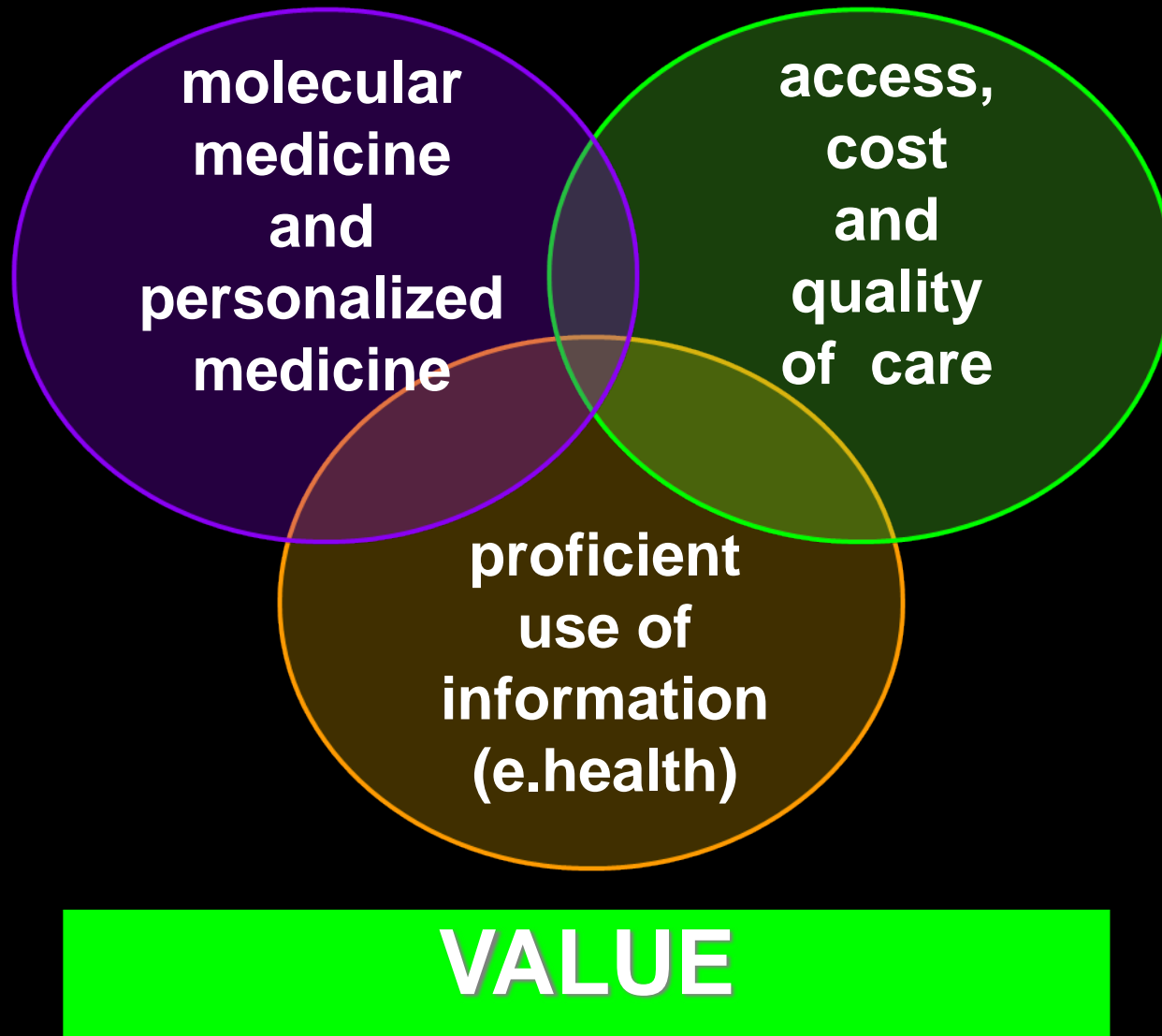
- **social and economic value of reducing disease burden will rise**
  - **earlier disease detection and mitigation**
  - **rational Rx and guaranteed outcomes**
  - **integrated care management of complex chronic diseases**
  - **extension of working life**
- **progressive shift from 'reactive' medicine to 'proactive' care and 'integrated' delivery**
  - **prospering in an era of increasing constraints**
  - **managing the limit(s) of society's willingness and ability to pay for innovation**



# Global Health: Understanding the Implications of Major Economic and Environmental Dislocations

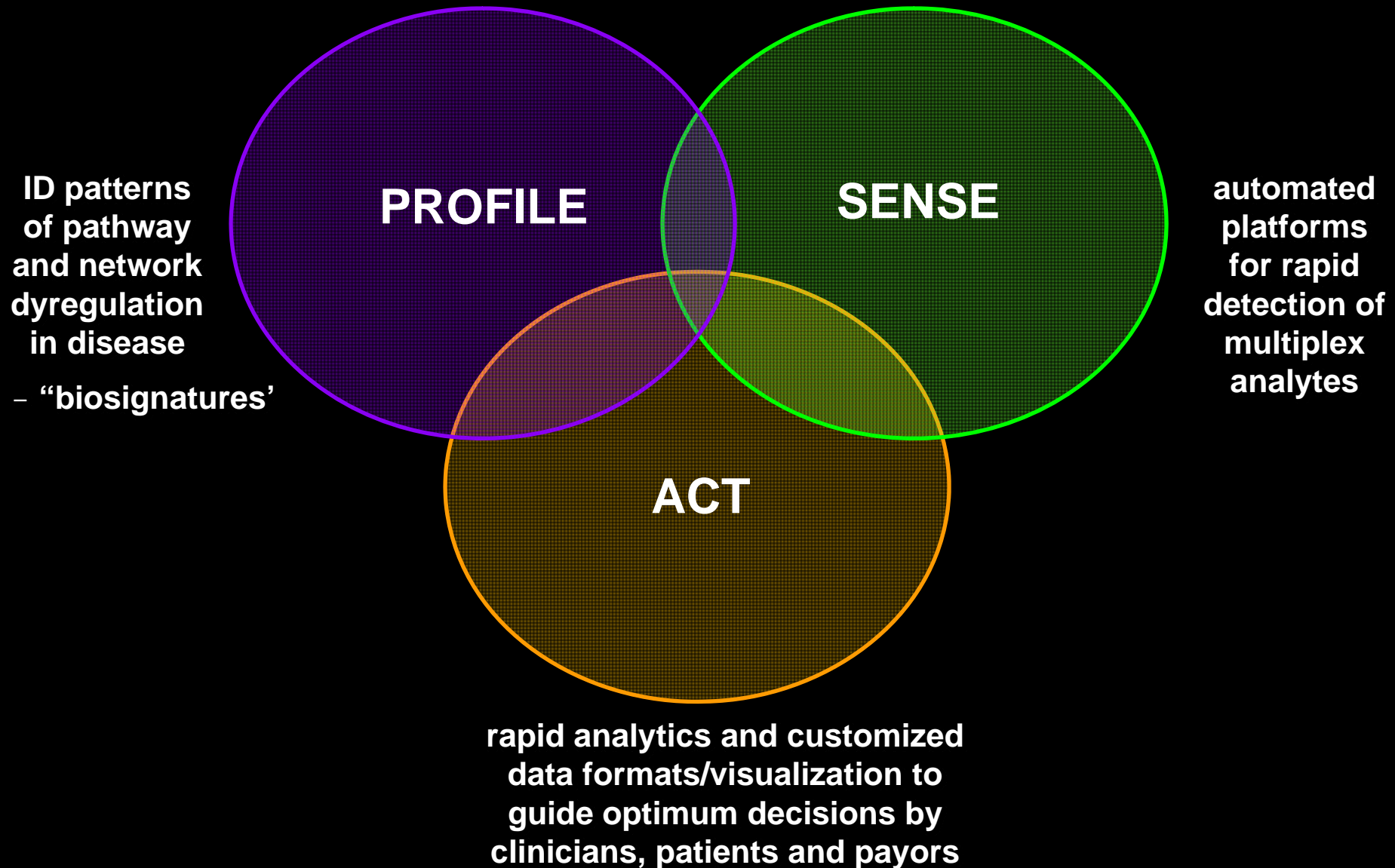


# The Three Convergent Forces Shaping the Evolution of Healthcare





# Mapping the Molecular Signatures of Disease



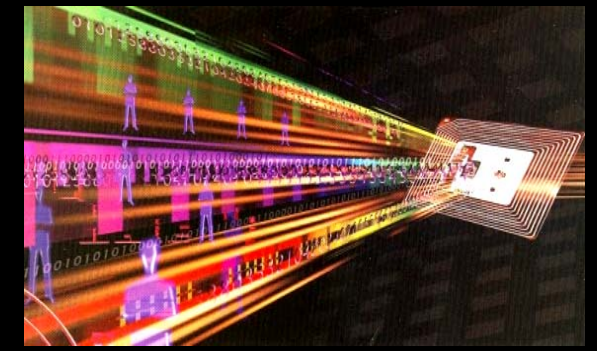
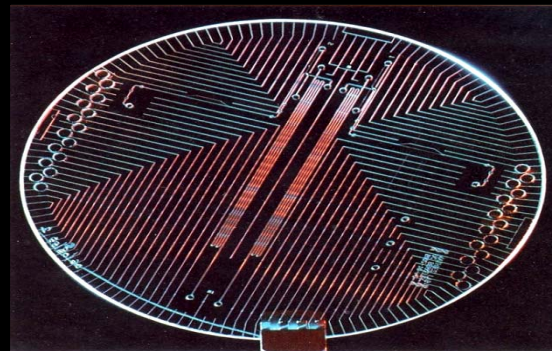
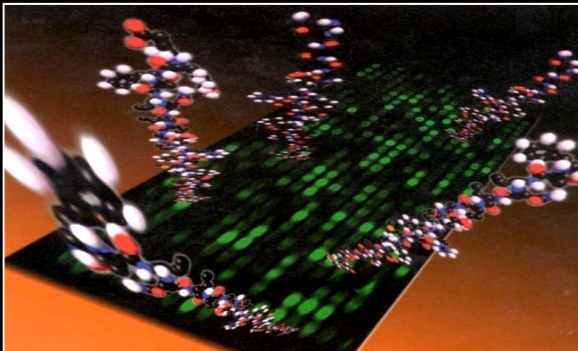
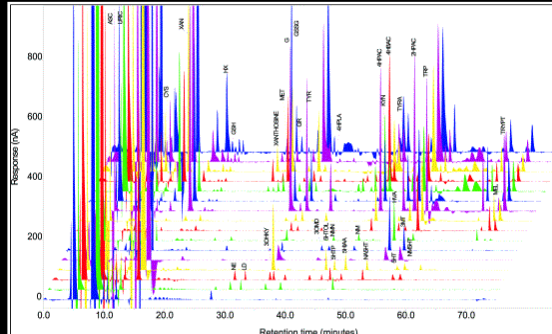
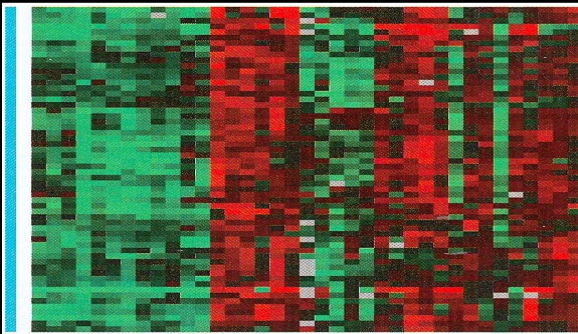
# Molecular Diagnostics and Miniaturized Devices: A Key Future Driver in the Healthcare Value Chain

## Complex Biosignature Profiling

genomics

proteomics

immunosignatures



## Signature Detection, Deconvolution and Multivariate Analysis

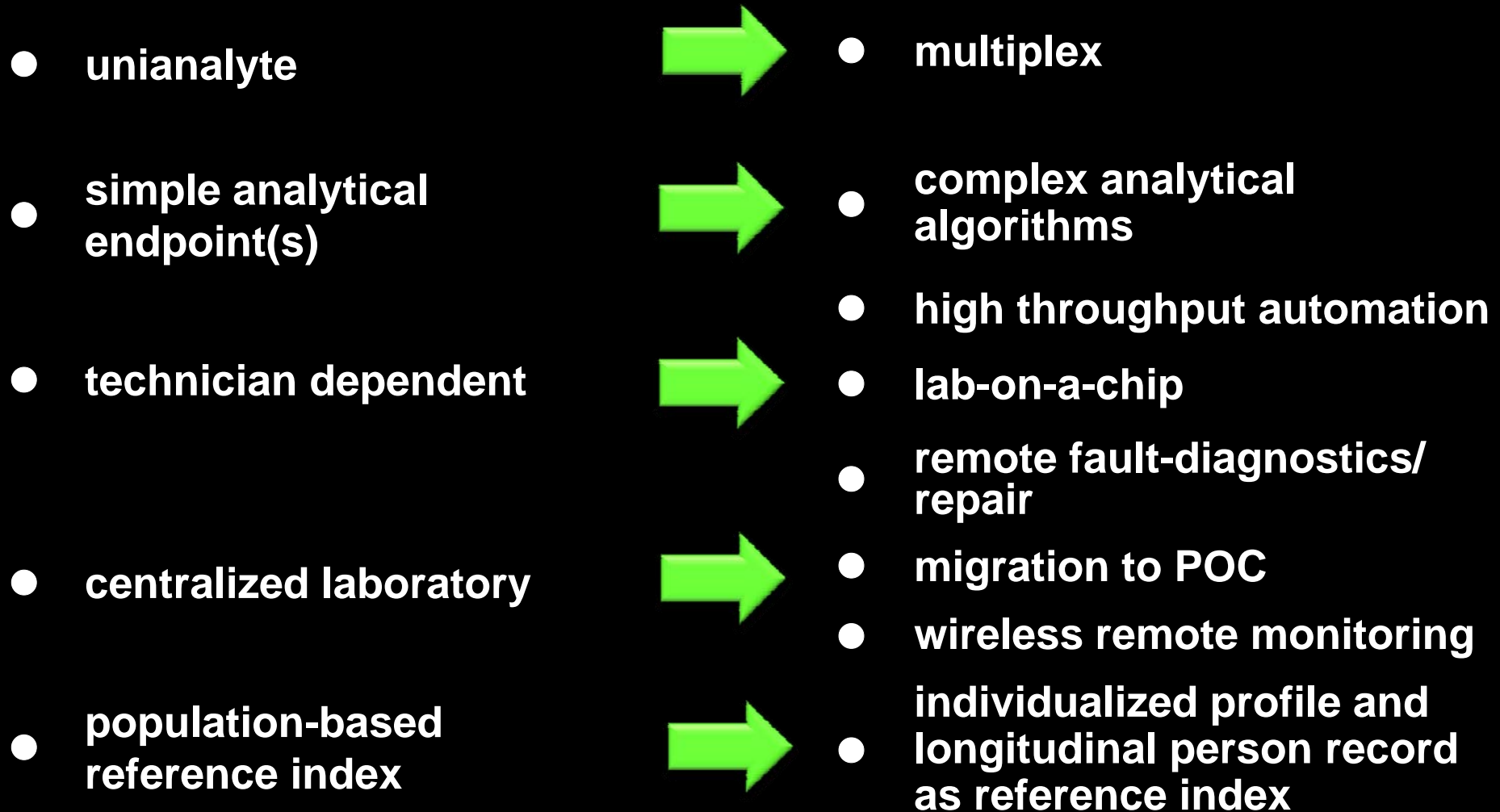
automated,  
high throughput  
multiplex assays

novel test formats  
and devices (POC)

new algorithms  
For complex  
signal/deconvolution



# Trends in Mapping Diagnostic Signatures of Health and Disease

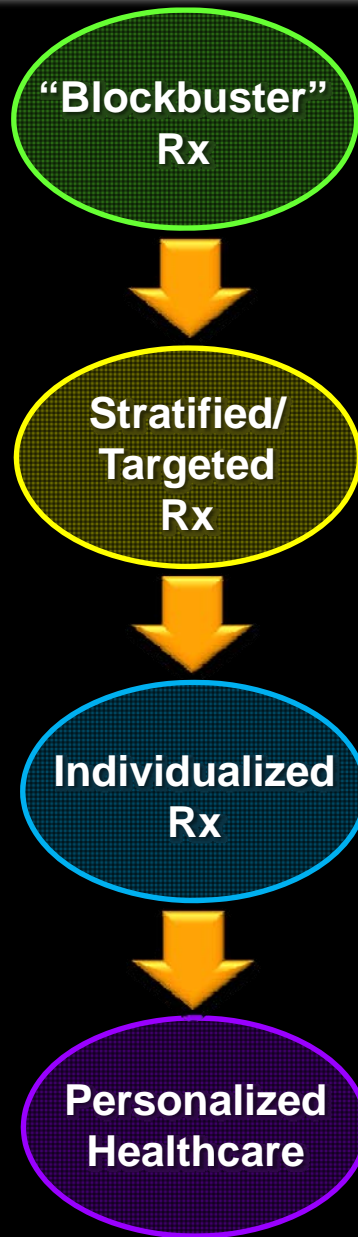


# The Value of Blood-Based Diagnostic Profiling

- **minimally invasive**
- **blood bathes all organs**
- **organ-specific ‘biosignatures’ detectable in blood**
- **facile routine tracking of disease progression and Rx responsiveness**
- **value of highly stable biomarkers for retrospective studies to correlate with clinical outcomes**
- **POC testing**



# The Evolving Market for (Bio)Pharmaceutical Therapies



- empirical “one-size-fits-all”
- population-based Rx
- Rx targeted to patient subgroups with common molecular pathology
- Dx-Rx combinations and Rx labeling
- individualized Rx
  - relevant disease subtype
  - AE risk profiling
  - compliance monitoring
- integrated framework of coordinated care and longitudinal care



# K-RAS Profiling and Anti-EGFR Monoclonal Antibody Therapy



- higher response in patients with K-RAS versus mutant-K-RAS
- estimated \$604 million/year savings (ASCO)

clinical guidelines



- regulatory endorsement in product labeling



- payor adoption

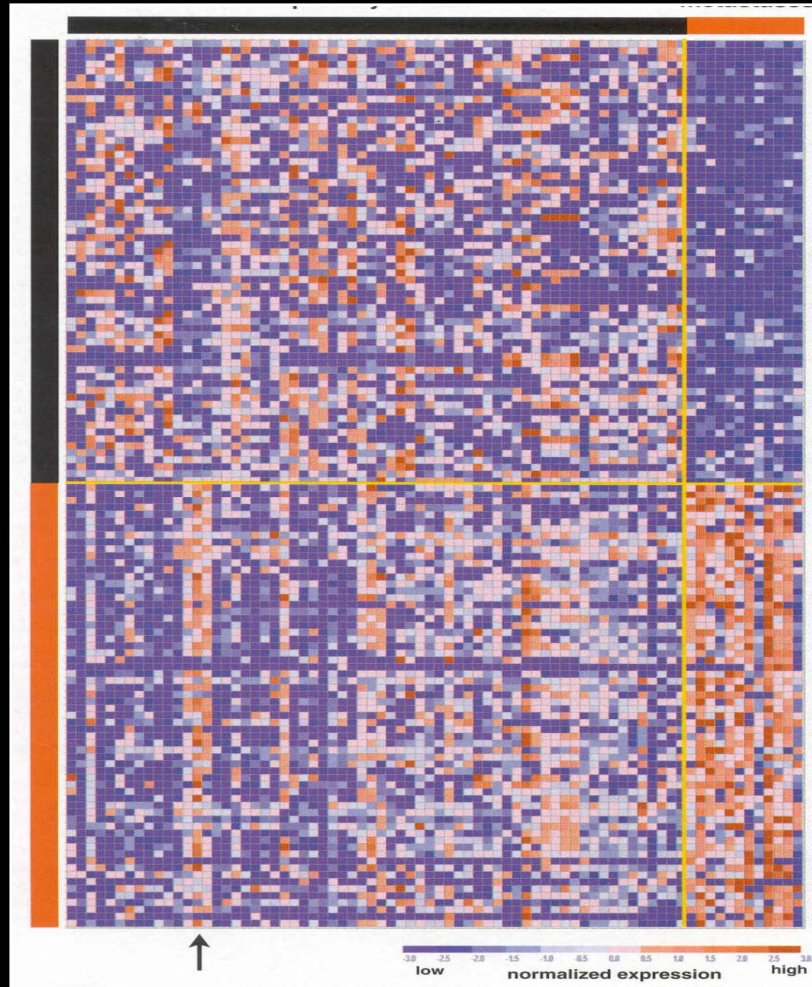
# **Molecular Medicine and Rational Therapeutics: Molecular Diagnostics and Targeted Rx**

- **opening era in linking disease molecular pathology to rational Rx**
- **increasing payor, regulatory and public pressures for reliable ID of Rx-responsive patients**
- **demand for Dx-Rx combinations will intensify**
- **Dx-Rx combination will become an obligate element of NDA/BLA submission and product labeling**
- **development of Dx-Rx combinations as intrinsic components of R&D programs for investigational Rx**

**Companion Therapeutics Selected by Precision Diagnostics**

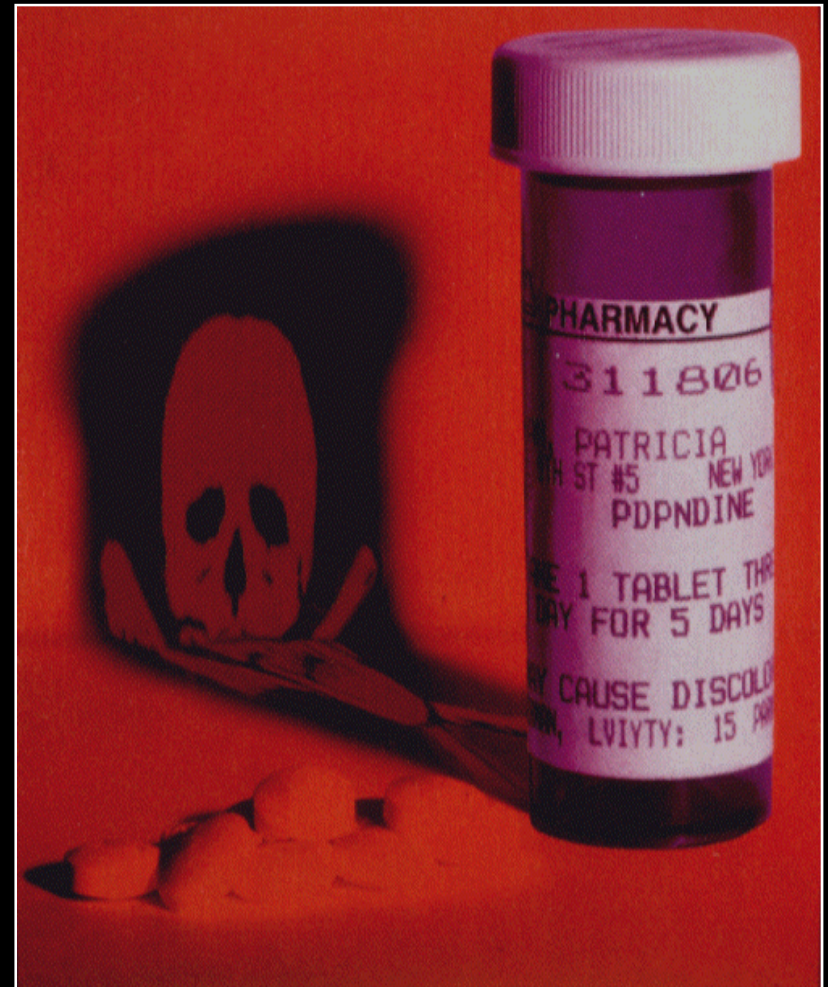
# From Pharmaceuticals to Pharmasuitables

**Disease Subtyping:**



**Right Rx for Right Disease**

**Individual  
Variation and AE risk**



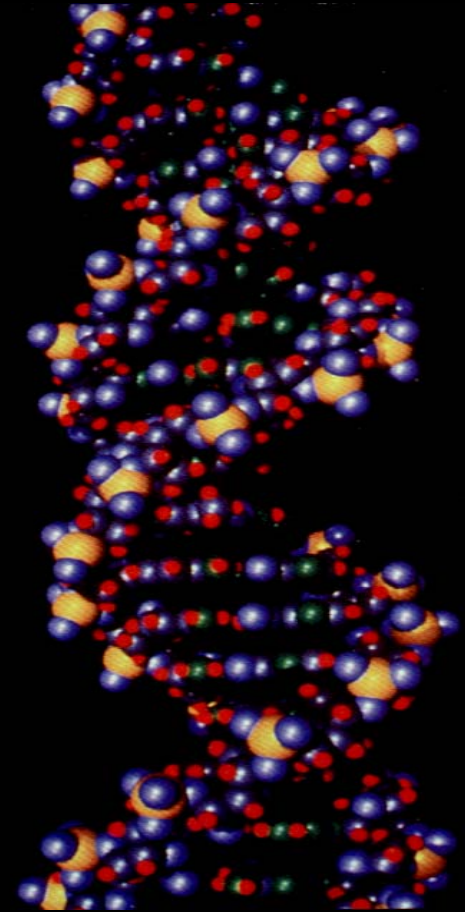
**Right Rx for Right Patient**

# **Molecular Diagnostics and Pharmacogenetic Profiling to Identify Individuals at Risk for Rx Adverse Events**

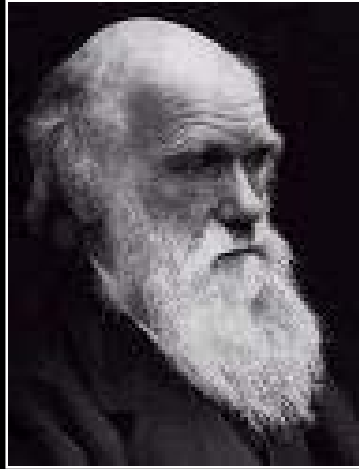
- **broader, more complex profiling platforms than MDx assays for ID of drug targets**
  - **number of isoforms for DMPK enzymes and scale of individual variation within populations**
- **ID of slow metabolizer genotypes**
- **unknown effects of genetic and environmental confounders in AD(M)E beyond genetic variation in drug-metabolism (I-III) repertoire**
- **growing recognition of importance of variation in HLA alleles as additional risk factor**
- **touching the third rail: race and ethnopharmacology-PC trumps rational science**



# The Hunt for Gene Loci Associated with Complex Human Diseases



# Mapping Human Diversity



**“Our ignorance of the laws of  
variation is profound”**

**Charles Darwin**

**CGCCME!CAGGCATGCA  
CAGTGCCAGGCATGCAT  
CATGCCAGME!GCACT  
TGCTAGGCATGCATGA  
TCATGCCAGTCATGCA**

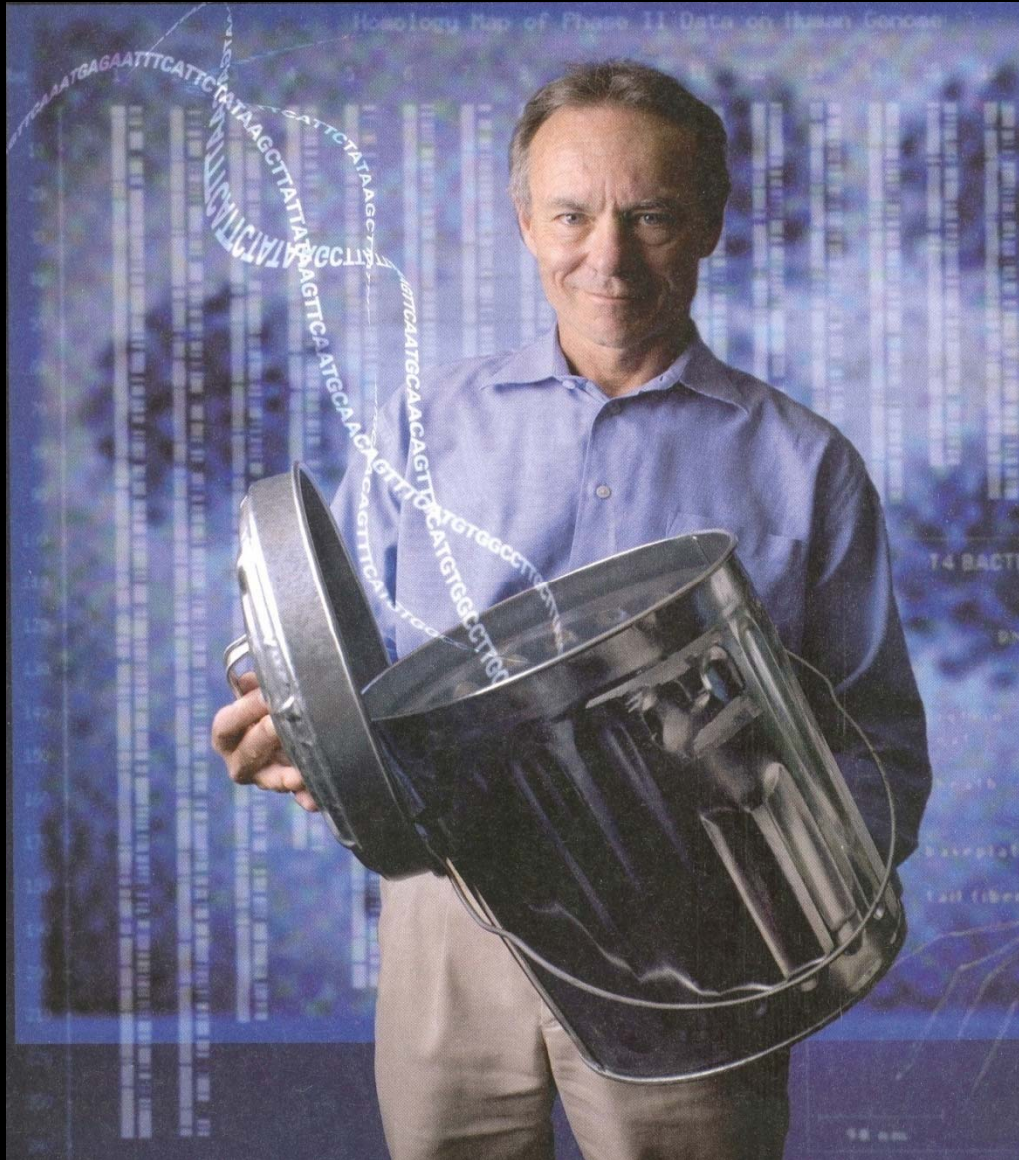
# **Disease Predisposition Risk Profiling for Common, Multigenic Late-Onset Disorders**

- **slower evolution than many predict**
- **Genome-Wide Association Studies (GWAS)**
  - **high cost and to date low yield in terms of clinically exploitable markers**
  - **disease origins from multiple low penetrance alleles versus small, dominant set of high penetrance alleles**
- **substantial ambiguities regarding probabilistic risk of overt disease**
  - **epistasis**
  - **epigenetics**
  - **environmental confounders**

**The premature quest to provide consumer genomic testing (CGx) for future risk of major diseases**

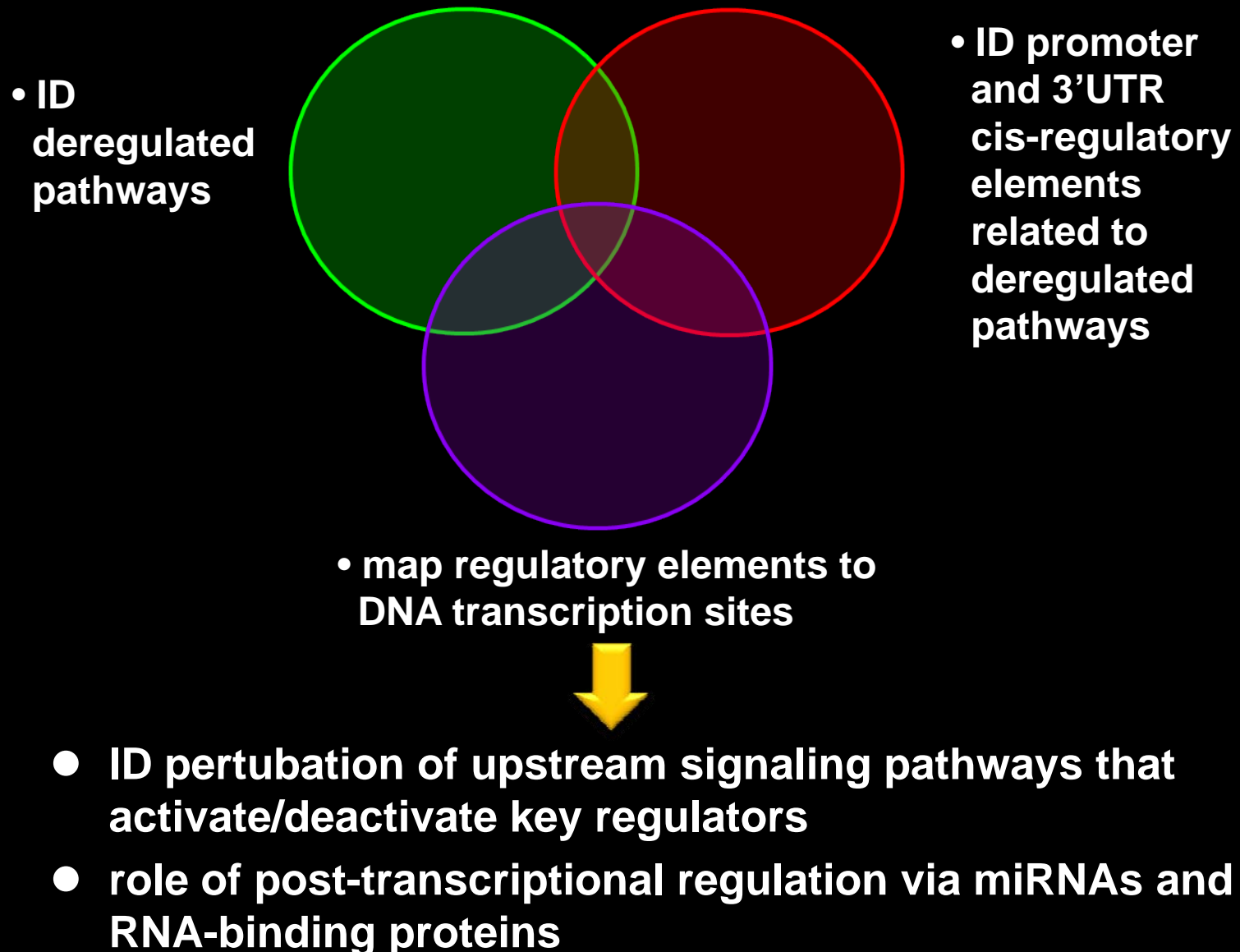


# Mapping the Complexity of Genome Organization



- recognition of increasing levels of organizational and regulatory complexity
  - haplotypes
  - CNV
  - indels
  - RNA universe
  - ‘dark’ elements
  - epistasis
  - epigenetics
  - nuclear compartmentalization and *trans*-expression

# Mapping Global Pathway and Network Regulatory Perturbations in Disease





# miRNAs Associated with Leukemia

Malignancy	miRNA	Regulation
CLL	miR-15a, miR-1G-1, miR-181a, let-7a, miR30d, miH-150, miR-92	Downregulation
Pediatric Burkitt's lymphoma, Hodgkin's lymphoma, diffuse large B cell lymphoma	miR-155, miR-17-92	Upregulation
Hodgkin's disease, Burkitt lymphoma cells	miR-9, let-7a	Upregulation
B cell malignancies	miR-143, miR-145	Downregulation
AML	miR-127, miR-154, miR-299, miR-323, miR-368, miR-370	Upregulation
AML	miR-221, miR-222	Downregulation
Hematopoietic malignancies	miR-203	Downregulation

From: M. Galasso et. al. (2010) Genome Medicine 2, 12

# The Race for Low Cost ( $\$ < 1000$ ) Whole Human Genome Sequencing



life  
technologies™



illumina®



454  
SEQUENCING Roche



IBM®



Electronic  
Bio  
Sciences



pb PACIFIC  
BIOSCIENCES™



Complete  
genomics



BioNanomatrix



ion torrent  
△ ★ △ ○ × □ + ≈



imagination at work



Helicos  
BioSciences Corporation

# **Translation of the Major Potential of Molecular Medicine into Routine Clinical Practice**

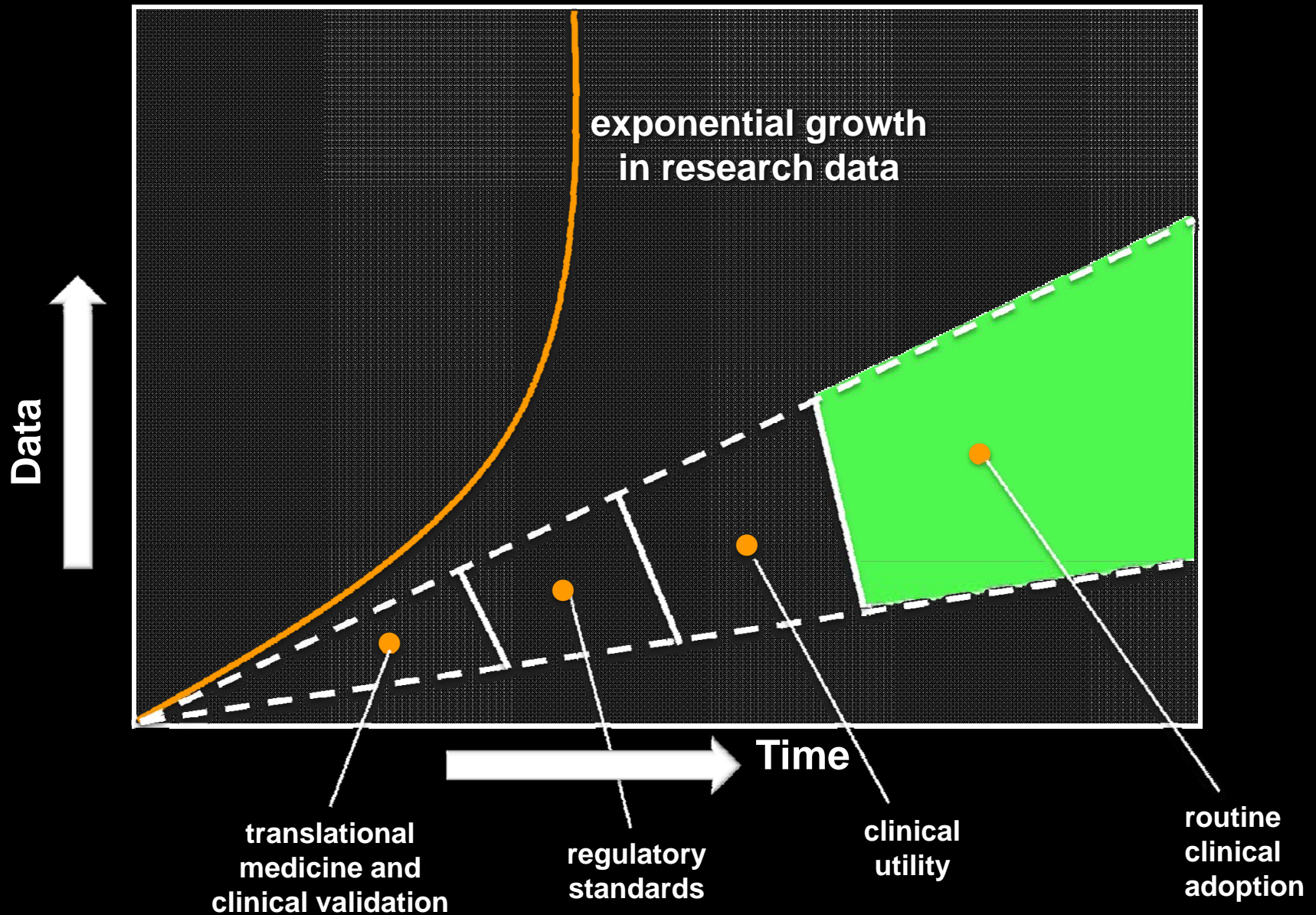
**A Complex Multi-Dimensional Challenge**

# **Knowledge and Evidence Doesn't Translate Easily into New (or Rational) Behaviors**

- **science (impact is too often unknown or abstract)**
- **industry (incremental timidity driven by short-term focus on markets and stock valuation)**
- **payors (cost control)**
- **physicians and healthcare professionals (status, revenue and recognition)**
- **patients (unaware and uninvolved in healthcare decisions)**
- **politicians (populism and short-term fixes)**

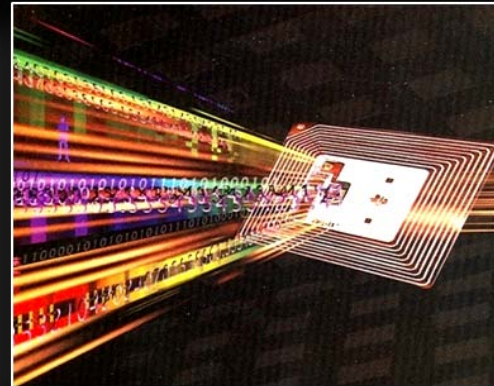
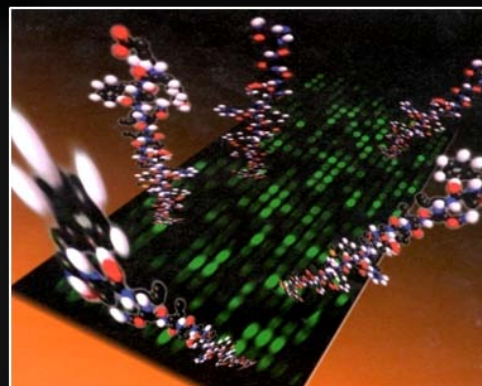
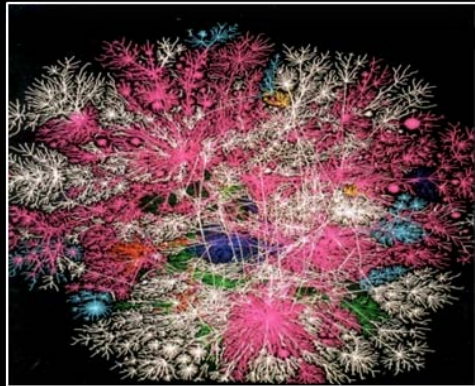
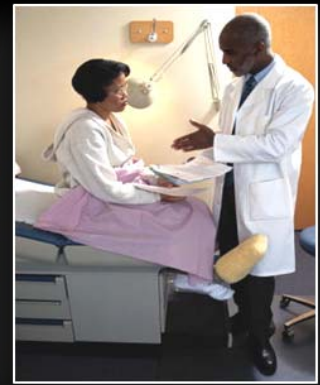
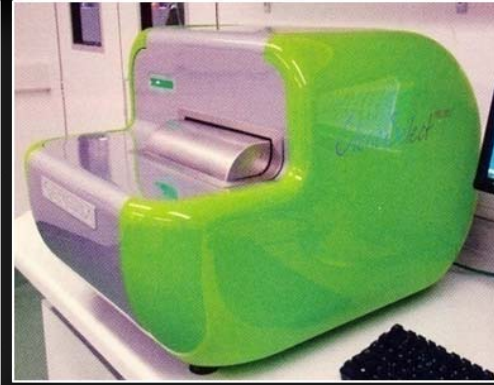
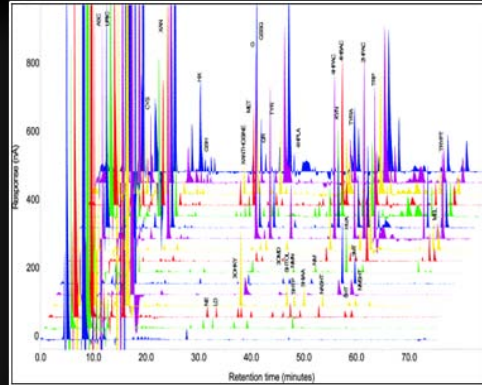
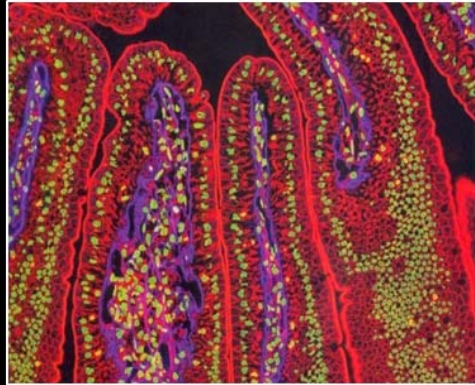
**The Pragmatic Challenge:  
Who Pays, Who Benefits and Who Decides?**

# The Trajectories for Molecular Medicine





# Identification and Validation of Disease-Associated Biomarkers: Obligate Need for a Systems-Based Approaches



**Biospecimens  
and  
Molecular  
Pathway  
Analysis**

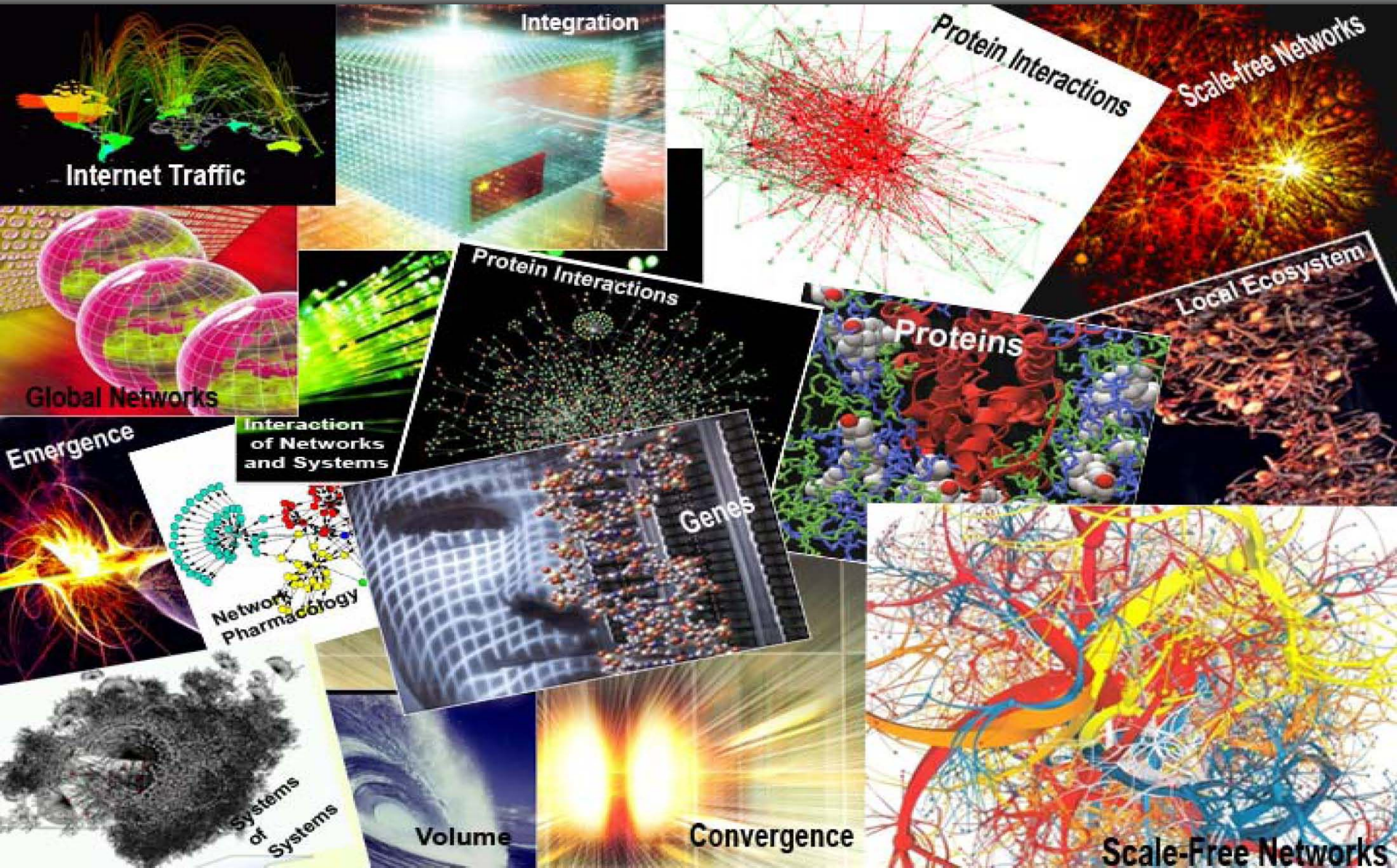
**Biomarker  
Validation  
and  
Multiplex Assays**

**Instrumentation  
and  
Informatics**

**Clinical  
Impact  
and  
Patient  
Monitoring**



# Data: The Fastest Growing Resource on Earth





# **Standards for 'Omics' Data Cross-Domain Integration, Open-Source Data Sharing and Computational Analysis**



# OBO Foundry Ontologies

## *Nature Biotechnology* 25, 1251 - 1255 (2009)



The Open Biomedical Ontologies

**Cell Ontology (CL)**

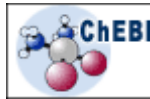


**Gene Ontology (GO)**

Foundational Model of Anatomy

**ZFIN**

**Zebrafish Anatomical Ontology**



**Chemical Entities  
of Biological Interest (ChEBI)**

**Disease Ontology (DO)**



**Plant Ontology (PO)**

**SO**  
The Sequence Ontology Project

**Sequence Ontology (SO)**

**Ontology for Clinical  
Investigations (OCI)**



The Open Biomedical Ontologies

**Common Anatomy  
Reference Ontology**



The Open Biomedical Ontologies

**Environment Ontology**



**Ontology for Biomedical Investigations**

**Phenotypic Quality  
Ontology (PATO)**



**Protein Ontology (PRO)**



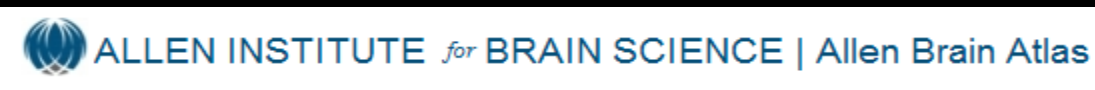
**OBO Relation  
Ontology**



**RNA Ontology  
(RnaO)**



# The Rise of Open-Source Networks and Consortia

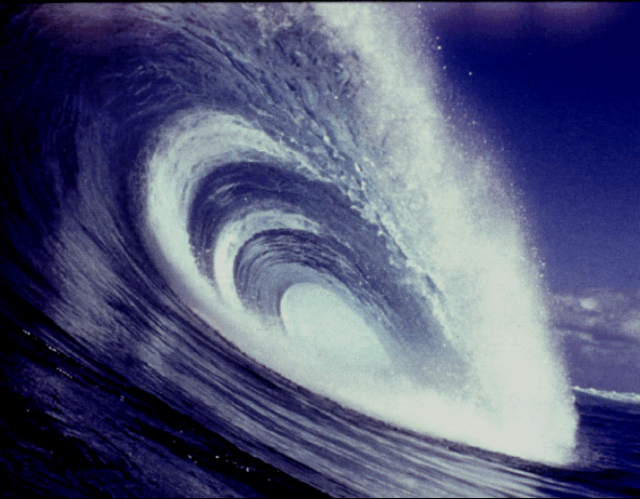


FDA/Severe Adverse Events (SAE) Consortium



# Managing “Mega-Data” (Who Knows Wins)

volume



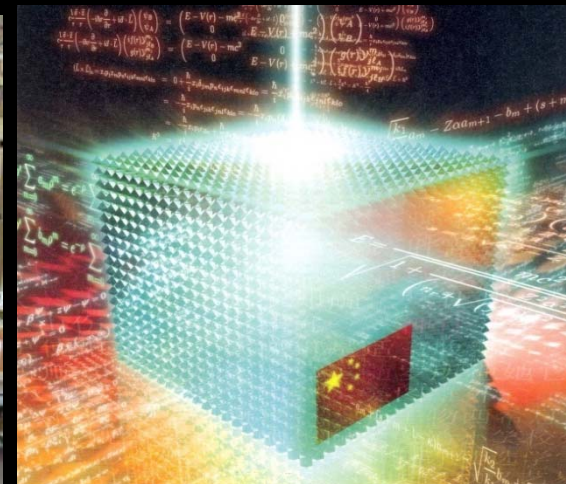
scale



global networks



heterogeneity

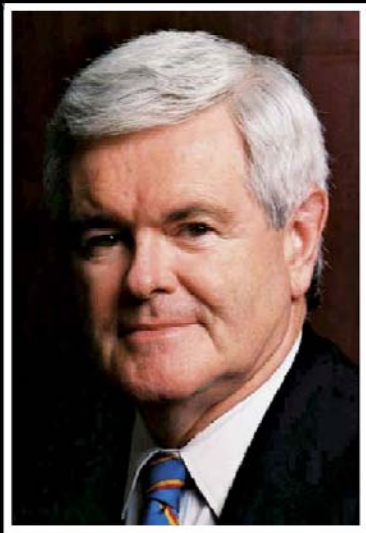


integration



# Misaligned Reimbursement Incentives: Rewarding Process Versus Results

**“If it isn’t billable – it isn’t going to happen!”**



**“You have a (healthcare) system that traps us  
into bad performance  
because it’s the only way you can bill”**

**Hon. Newt Gingrich  
Medical Device Daily (2009) 27 Jan. p8**

# Genes and Intellectual Property



**14 March 2000**



**SACGHS**

**5 February 2010 Report**



**29 March 2010 SDNY Court Decision**



**16 April 2010 WSJ Editorial**



# How Much New Technology Can We Afford?





# UK National Institute for Health and Clinical Excellence (NICE)



# Nice Gets Nasty (or Rational?)



**ERBITUX**<sup>™</sup>  
CETUXIMAB INJECTION



**SUTENT**<sup>®</sup> capsules  
sunitinib malate

**Wyeth**

**TORISEL**<sup>®</sup>  
(temsirolimus) injection



**ARICEPT**<sup>®</sup>  
(donepezil HCl)  
5-MG AND 10-MG TABLETS



**Nexavar**<sup>®</sup>  
(sorafenib) tablets  
More Time for Living

**Genentech**  
IN BUSINESS FOR LIFE

**LUCENTIS**<sup>®</sup>  
RANIBIZUMAB INJECTION

**TEVA**  
TEVA PHARMACEUTICALS

**COPAXONE**<sup>®</sup>  
(glatiramer acetate injection)

**gsk** GlaxoSmithKline

**Tykerb**<sup>®</sup>  
(lapatinib)

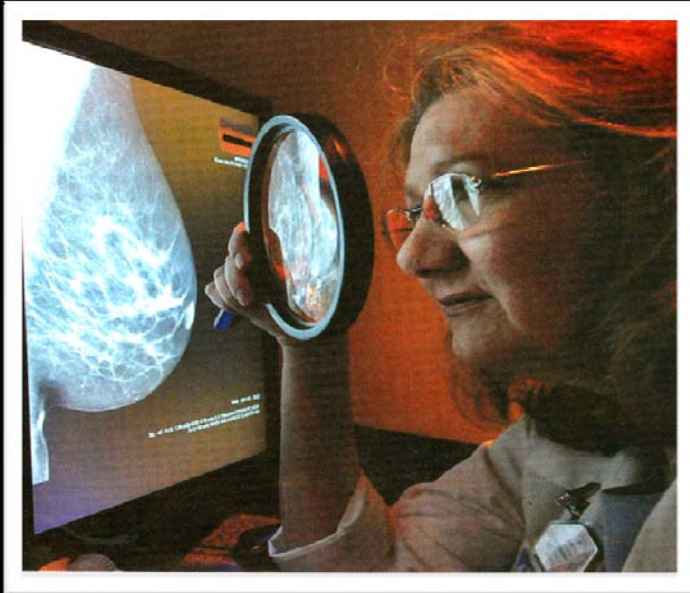
**Rebif**<sup>®</sup>  
(interferon beta-1a)  
sc injection

**MERCK**  
SERONO

**eyetech Inc.**

**MACUGEN**<sup>®</sup>  
PEGAPTANIB SODIUM INJECTION

# Who Defines Best Practices?



- controversy over US Preventive Task Force (USPTF) recommendations on mammograms for women age 40-49
- endorsed by ACP
- opposed by ASCO and NCCN
- USPTF did not address cost but it dominated public debate
- “should policy makers set a price on saving a life?”



# Wellness:

**The Most Broad and Most Valuable  
Definition of Successful Healthcare**

**Consumers at the Center**

# After a Short Stay in America, Michelangelo's David Returned to Europe





# Consumer Behavior and Healthcare Costs



**“diabetesity” \$200 billion**



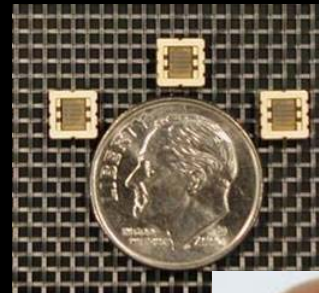
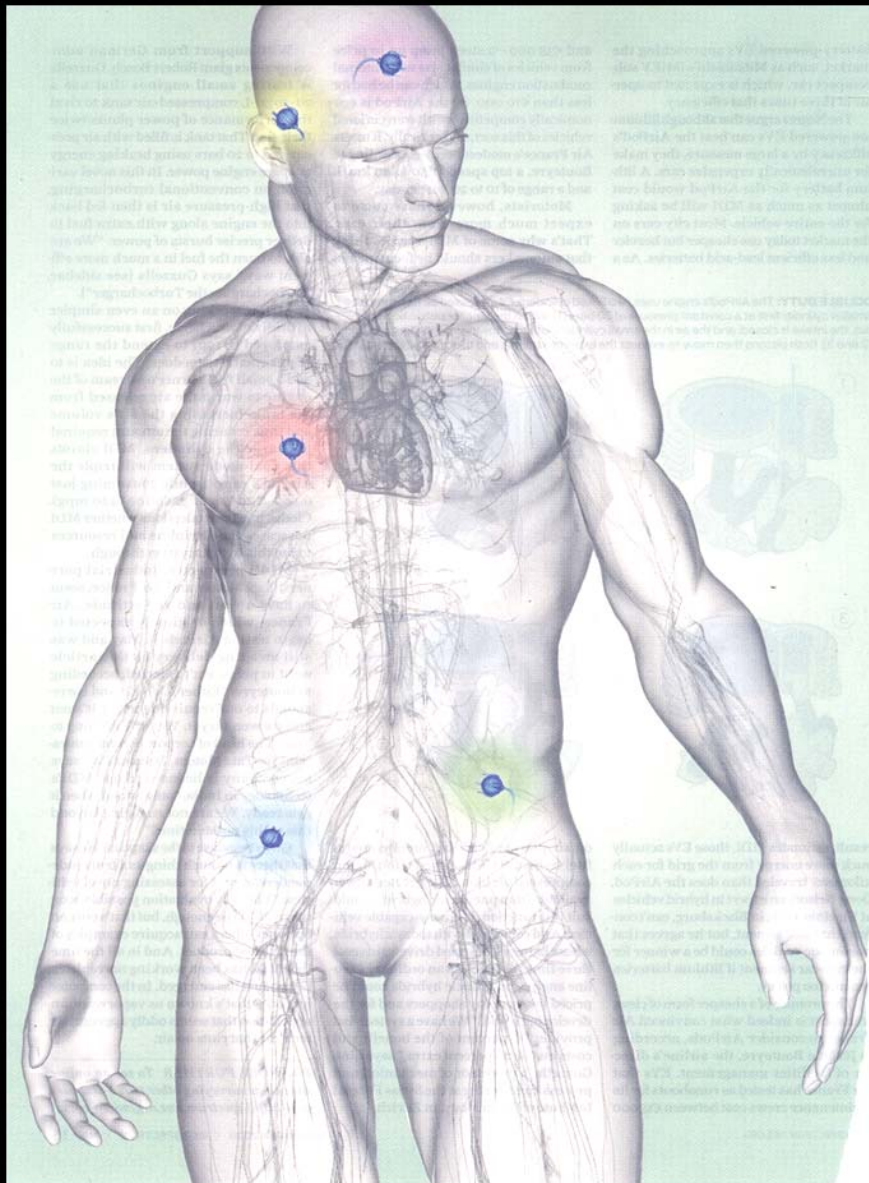
**smoking \$190 billion  
alcohol \$20 billion**

# **Engaging Consumers and Patients for Wellness and Greater Responsibility for Mitigation of Health Risk(s)**

- **entitlement mentality**
- **lack of accountability**
- **lack of transparency in pricing and evidence-based performance to guide choice**
- **cost-shifting**
  - **a negative but blunt economic driver**
- **economic incentives**
  - **positive drivers for wellness**
  - **employers, payors, taxation policies**
- **providing tools and information to support informed choices and improved outcomes tracking**



# On Body: In Body Sensors/Devices For Real Time and Remote Monitoring of Individual Health Status



# When Your Carpet Calls Your Doctor

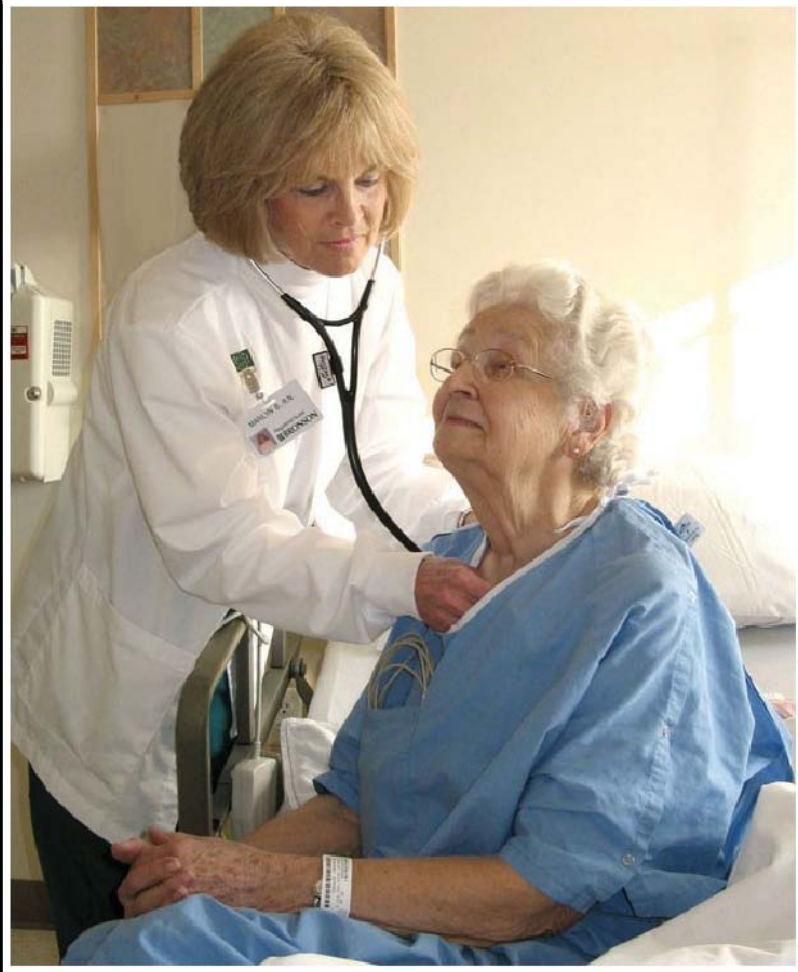


Wireless health care

The Economist 10 April 2010



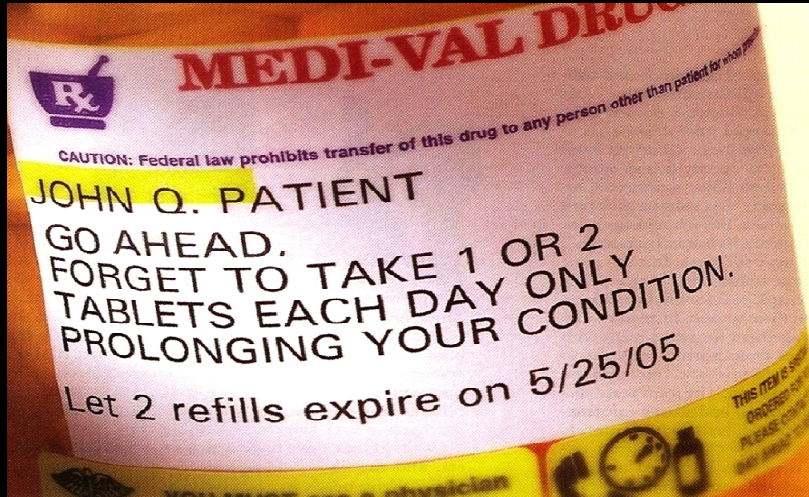
# Demographic Trends and the Clinical and Economic Burden of Complex, Chronic Conditions/Co-Morbidities



- **23% Medicare beneficiaries have 5 or more conditions**
- **polypharmacy and AEs**
- **poor patient compliance**
- **multiple physician/venue encounters**
- **poor communication/coordination between siloed healthcare services**
- **procedure-based reimbursement versus care continuum integrated**



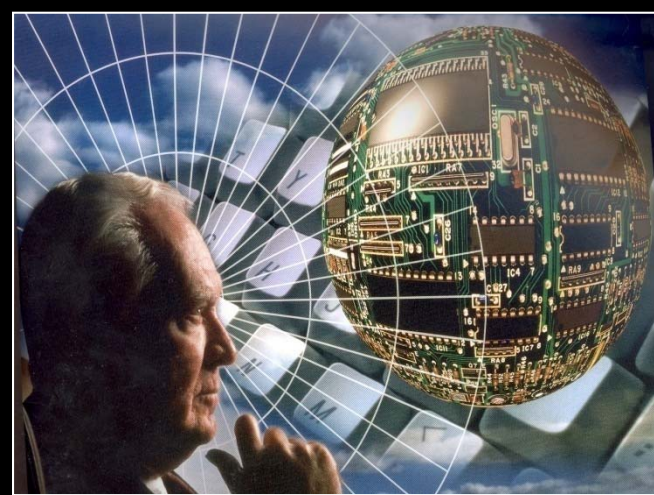
# The Costs of Non-Compliance with Rx Regimens



- **\$177 billion projected cost**
- **20 million workdays/year lost (IHPM)**
- **40% of nursing home admissions**
- **projected 45-75% non-compliance (WHO)**
- **50-60% depressed patients (IHPM)**
- **50% chronic care Rx (WHO)**

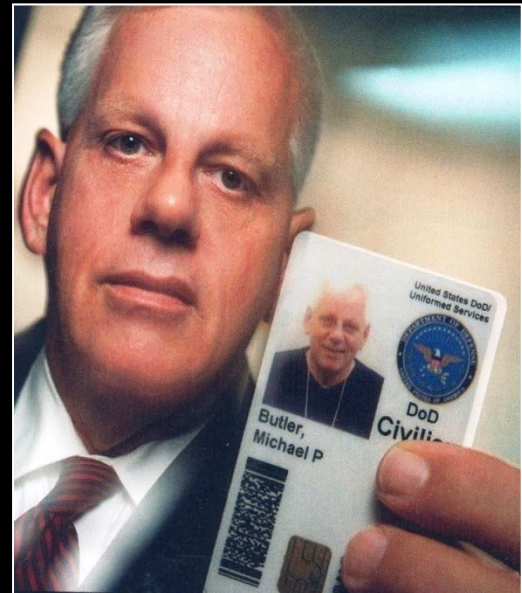


# The Infocosm: Emerging Networks of Global Connectivity



## Life's a game

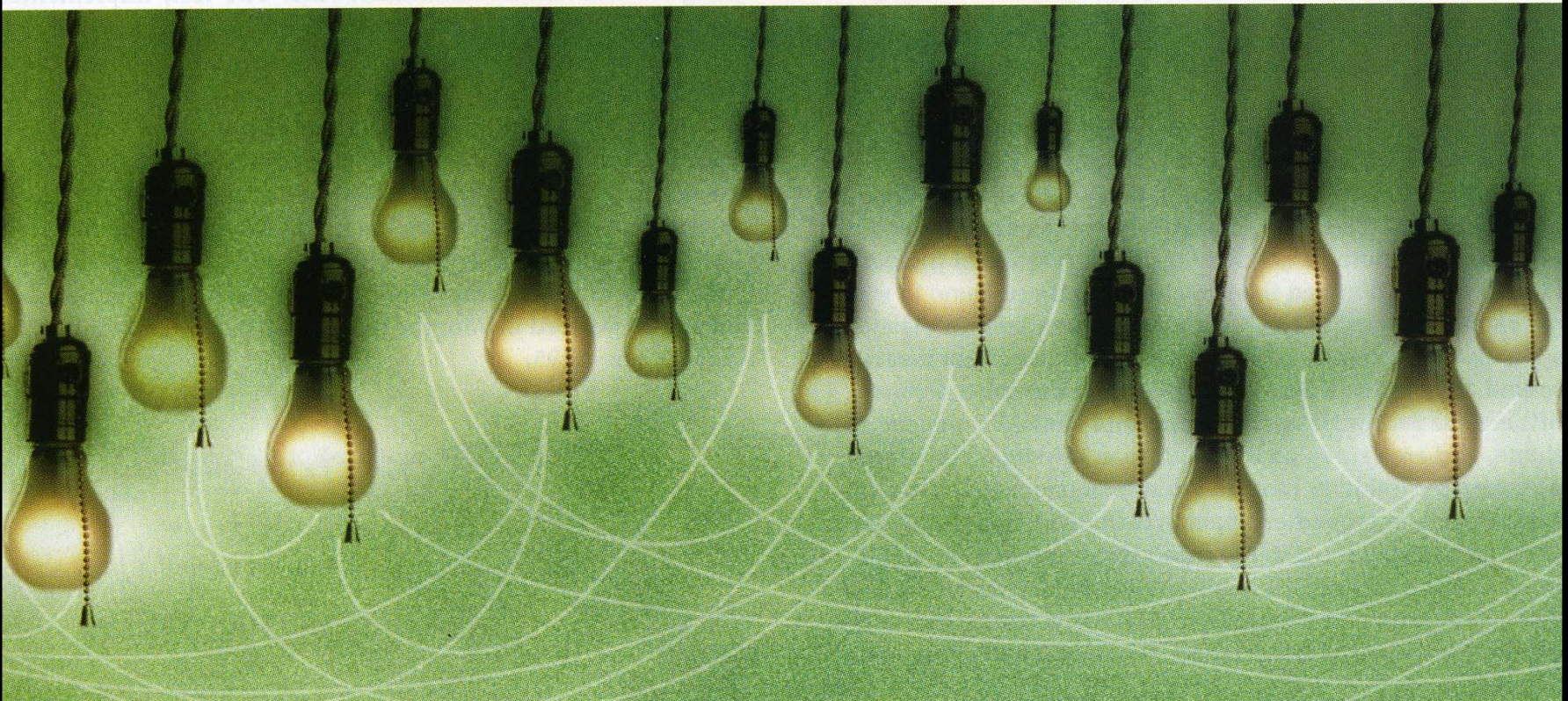
Manipulating society has traditionally been the preserve of politicians and the gods. Does the current boom in virtual worlds give social scientists and economists an opportunity to join them? **Jim Giles** investigates.





# Information-Based Medicine

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





# EHR Incentive Programs Funded by ARRA 2009

## “Meaningful Use”



- proposed rule and fact sheet comment deadline 2/28/10
- [www.cms.hhs.gov/recovery/11-healthit.asp](http://www.cms.hhs.gov/recovery/11-healthit.asp)

Health Information Technology *and*  
For the Future of Health ^ Care



- interim final rule: comment deadline 2/28/10
- <http://healthit.hhs.gov/standardsandcertification>

# Wireless Technologies: Consumer and Clinical Markets Converge



# Wireless Integrated Data Systems

- geolocation data (where)
- temporal information (when)
- contextual information (what)





# Virtual Medicine Networks: Increasingly Integrated Care and Continuity of Care



- rapid, real time access
- clinical specialties
- health records
- lab data
- drug interactions
- electronic Rx prescribing

# The Dominant Future Element in Primary Healthcare Delivery???



# The Expanding Universe of Health Information Resources

- **diversified information sources**
- **dramatic expansion of social-media networks**
- **new brokers for validation of information authenticity**
- **shift in trust from traditional medical establishment to other institutions**



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# THE DECISION TREE

TAKING CONTROL OF YOUR HEALTH  
IN THE NEW ERA OF PERSONALIZED MEDICINE



THOMAS GOETZ

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**“Real personalized medicine should begin long before we’re faced with pharmacology”**

**“Our health information is too important to leave to an archaic, insular system.**

**If there’s no longer a need to rely solely on a doctors advice for treatment and care, why should we be expected to artificially limit our options.”**

**Thomas Goetz  
Deputy Editor of Wired**

The Decision Tree: Taking Control of Your Health in the New Era of Personalized Medicine (Hardcover)  
Thomas Goetz (Author) . Image Source: [Amazon.com](https://www.amazon.com)

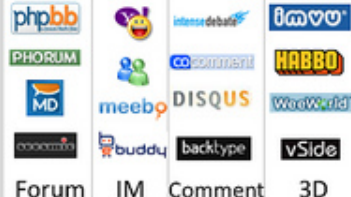
# Social Media Landscape

## Expressing

### Publication



### Discussion



### Aggregation

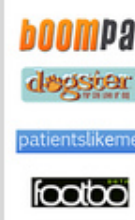


## Networking

### Search



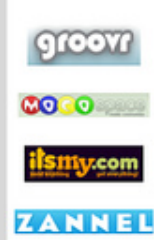
### Niche



### BtoB



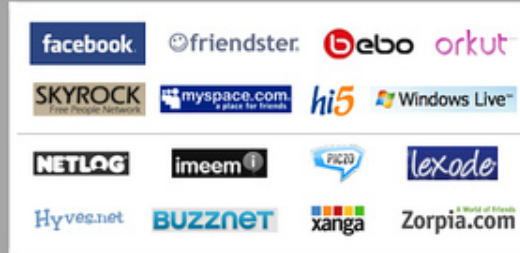
### Mobile



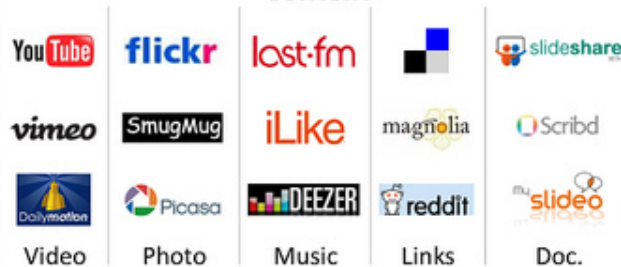
### Tools



## Social Platforms



### Content



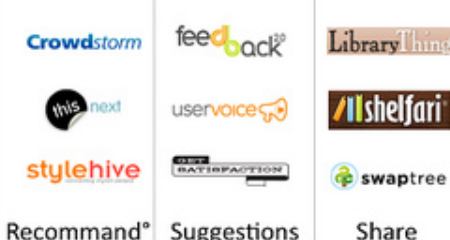
### Social Games



### Casual Games



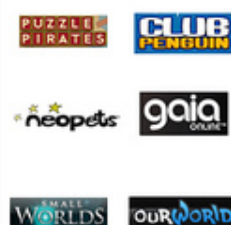
### Product



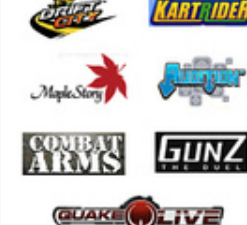
### Place



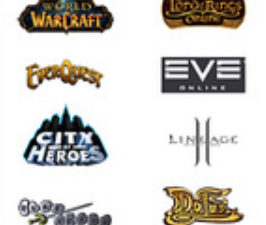
### Casual MMO



### MOG



### MMORPG



## Sharing

## Gaming

# Pharma and Healthcare Social Media Brand Sponsored Patient Communities





# In-Home Health Connection: Engaging the Elderly



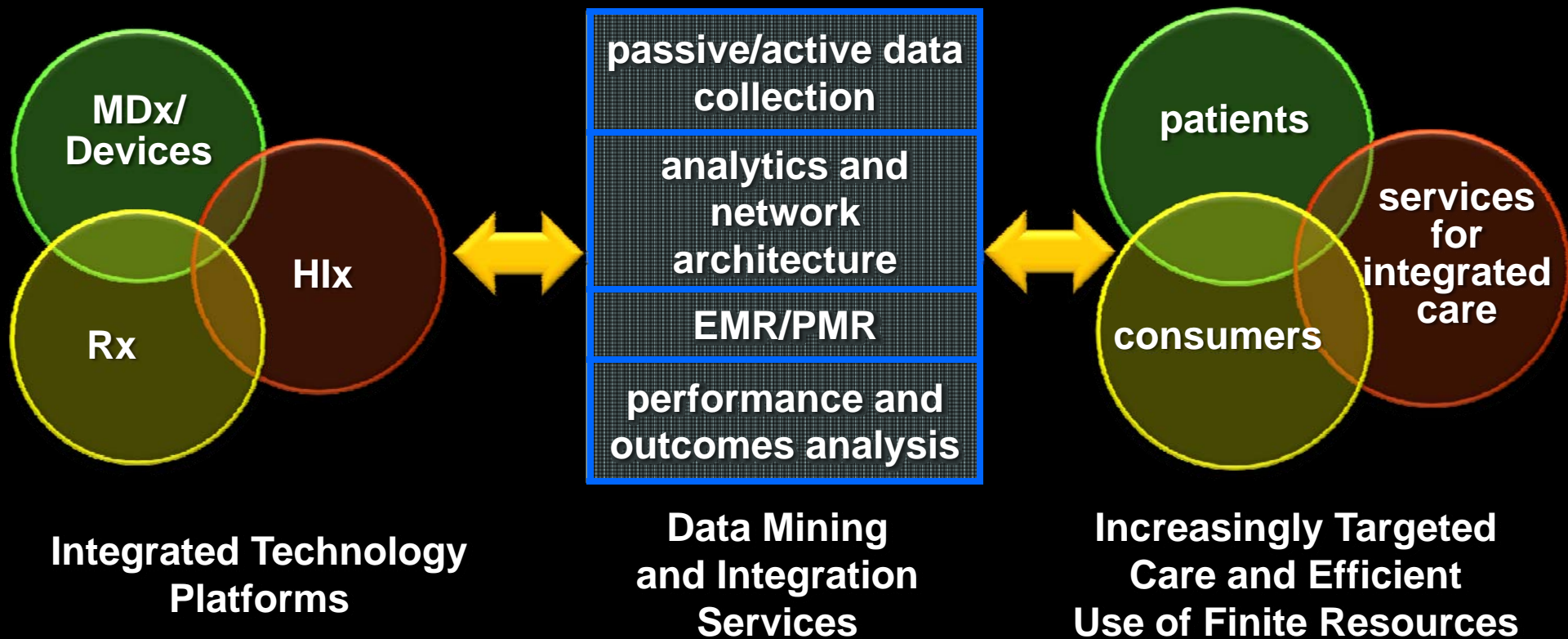


Wii **Fit** Plus





# A New Healthcare Ecosystem Arising From Technology and Market Convergence





# Technology Acceleration and Convergence in Healthcare Delivery



# The Coming Convergence in Healthcare Delivery

## Technologies

- biotechnology, medicine, engineering, computing, telecommunications and social media

## Clinical Practice

- molecular medicine and increasingly customized care
- diagnostic, drug and device combinations
- POC testing and remote monitoring
- reduced error and improved compliance
- improved outcomes

## Realigned Incentives

- integrated care for complex chronic diseases
- earlier disease detection and risk reduction
- wellness versus illness
- remote health status monitoring

# The Coming Convergence in Healthcare Delivery

## Consumers

- increased personal responsibility for health
- new incentives for wellness/compliance
- remote health status monitoring

## Connectivity

- integrated care networks for chronic disease
- social media networks and informed consumers
- new supplier networks of specialized turnkey expertise
- value added 'content' services for clinical data mining
- clinical decision-support systems