ASU COMPLEX ADAPTIVE SYSTEMS INITIATIVE
ARIZONA STATE UNIVERSITY

The Convergence of Clinical Medicine, Engineering and Computing: New Horizons in Healthcare Delivery

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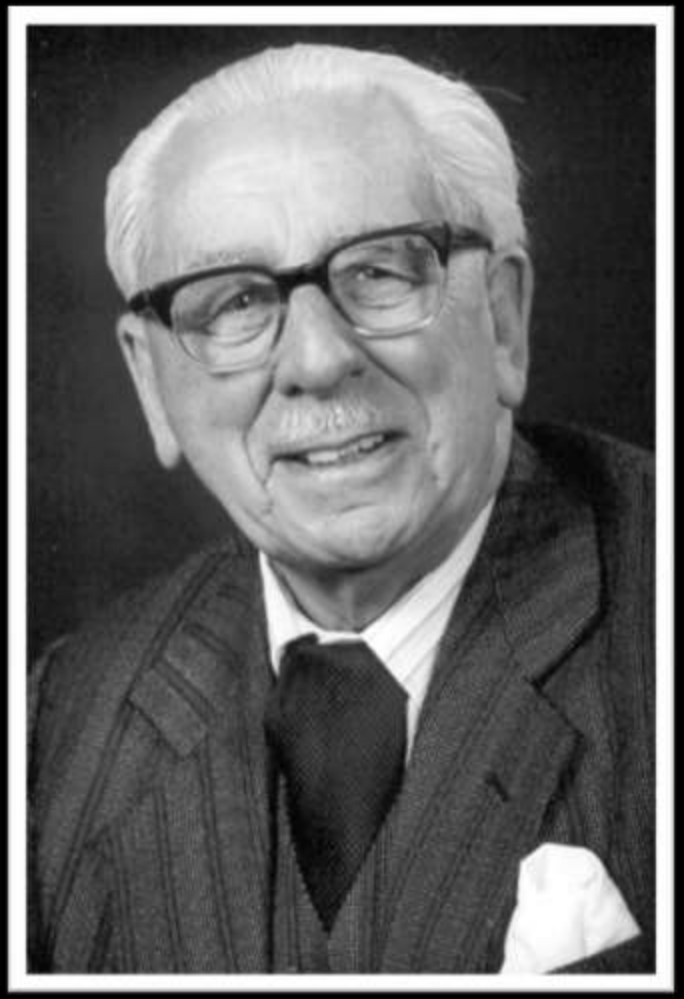
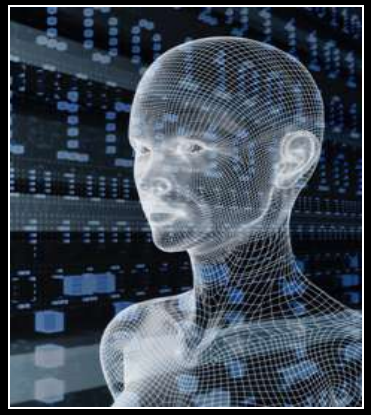
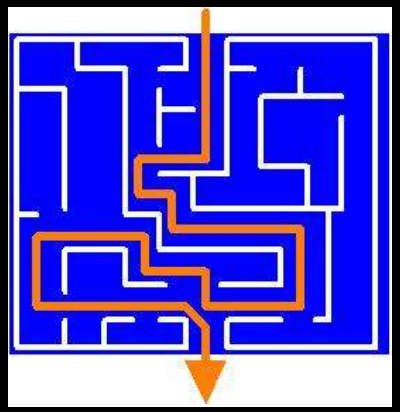
The John F. Wilkinson Memorial Lecture
Manchester Medical Society
5 May 2010

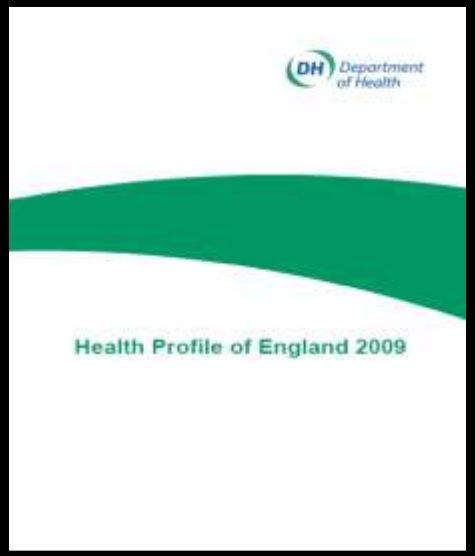
Dr. John F. Wilkinson (1897 - 1998)

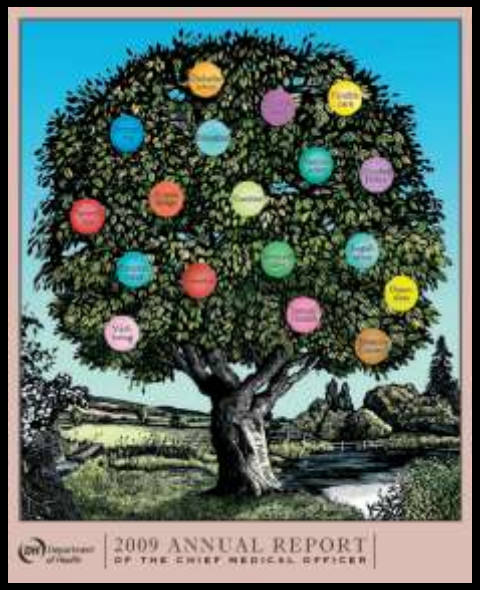


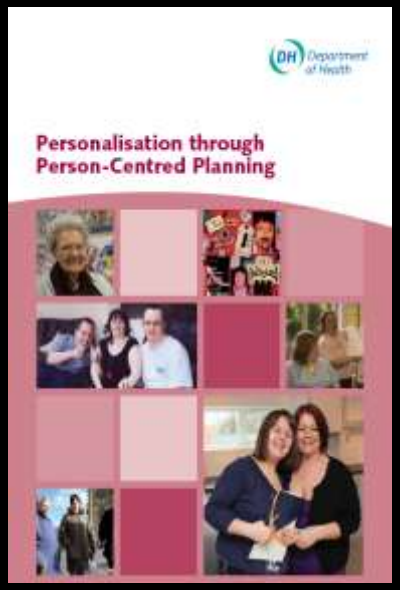
Challenges for Healthcare Delivery Systems

Cost	Demographics	Chronic Diseases	Life Style Disease
			
			
Inefficent use of Information	**Fragmented, Compartmentalized Services**	**Protracted Adoption of Best Practices**	**Complex Services**

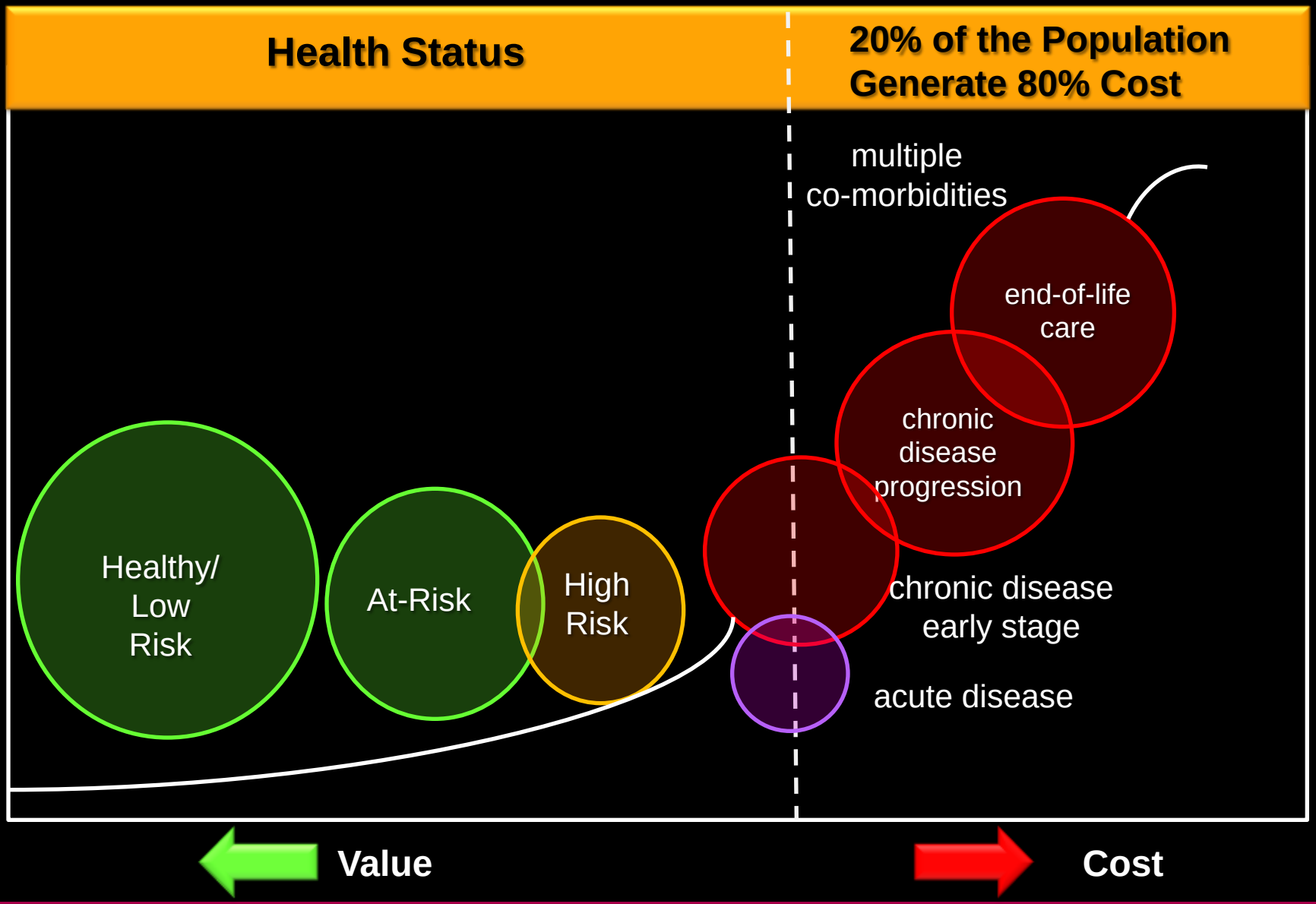
The Challenge of Delivery of Equitable and Effective Healthcare: Balancing Infinite Demand Versus Finite Resources







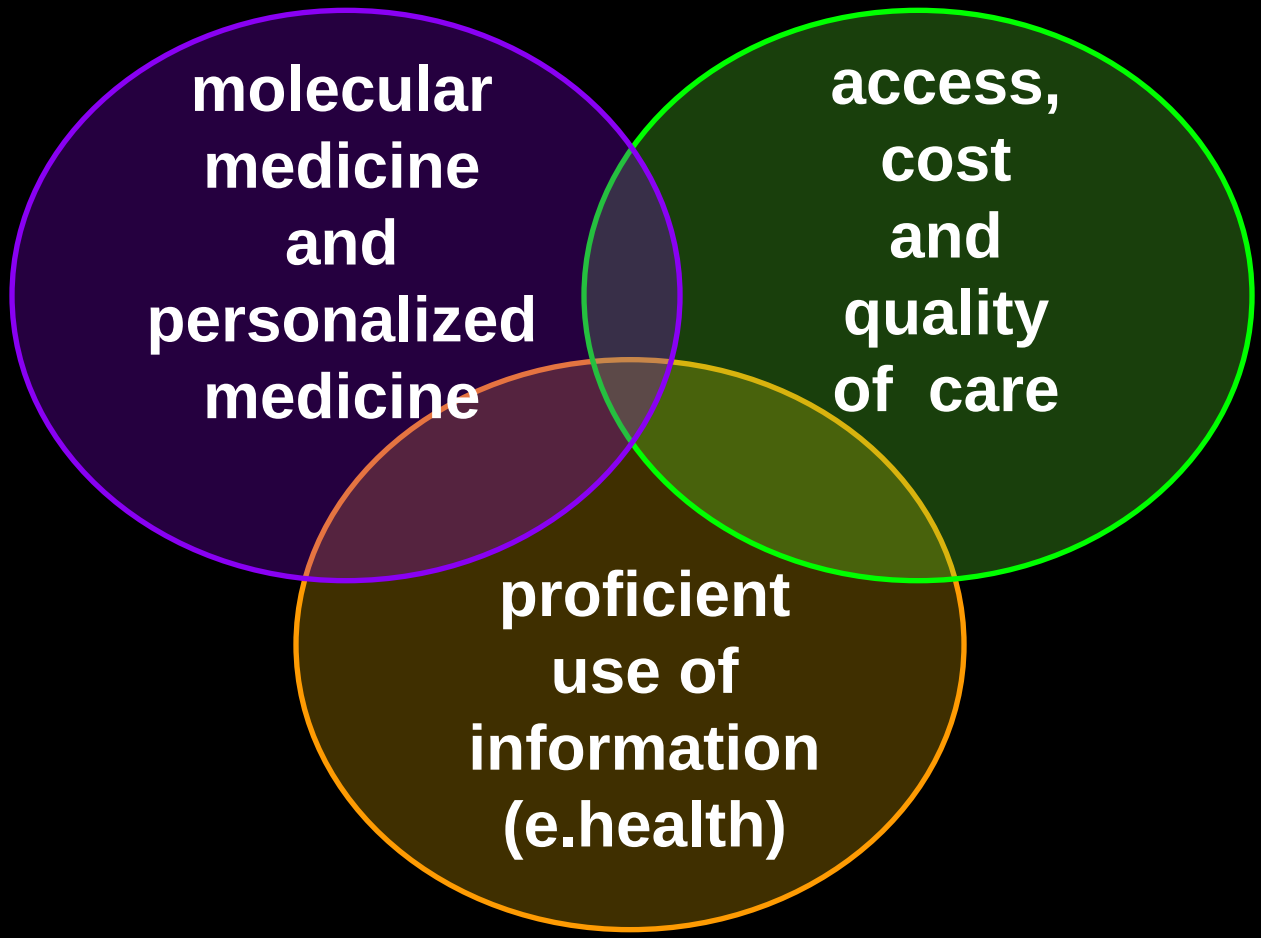
The Economic, Social and Clinical Benefits of Proactive Mitigation of Disease Risk and Chronic Disease Co-Morbidities



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

The Three Convergent Forces Shaping the Evolution of Healthcare

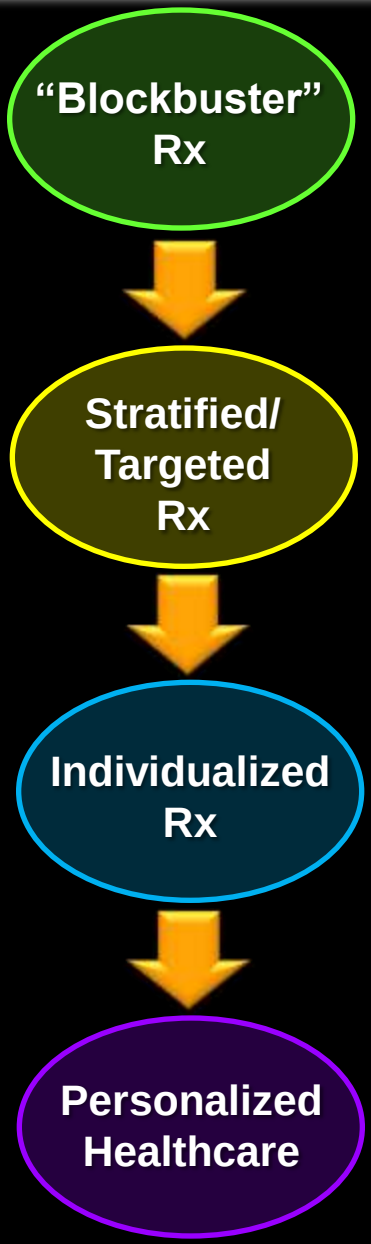


The Waste and Risk of Empirical Rx: Ignoring The Obvious in Clinical Practice

- diseases are not uniform
- patients are not uniform
- a “one-size fits all” Rx approach cannot continue

- inefficiency and waste of empirical Rx
- cost of futile therapy
- medical error and AEs

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

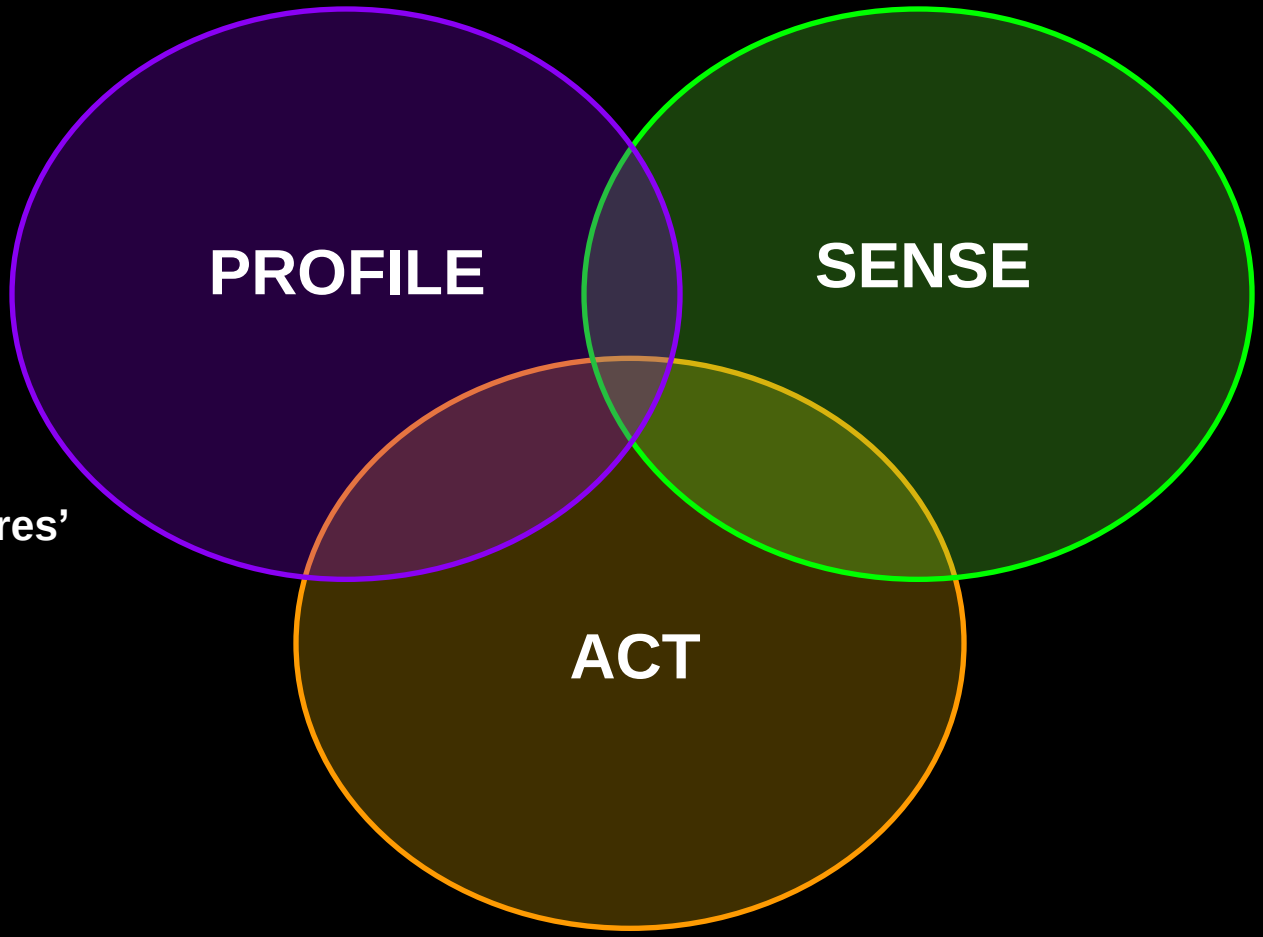
Molecular Diagnostics and Individual Patient Profiling: The Key Driver in Molecular Medicine and Rational Therapeutics

- mapping the causal pathology of disease versus diagnosis based on symptoms/biochemistry/ histopathology classifications
- identification of molecular subtypes of disease arising in same cell/organ and common symptoms
- disease subtypes and Rx selection
  - right Rx for right disease subtype
- profiling individual genetic variation in response to drugs
  - right Rx for right patient
- eventual mapping of individual disease predisposition risk profiles based on genetic uniqueness
  - new approaches to disease prevention

Mapping the Molecular Signatures of Disease

ID patterns of pathway and network dyregulation in disease

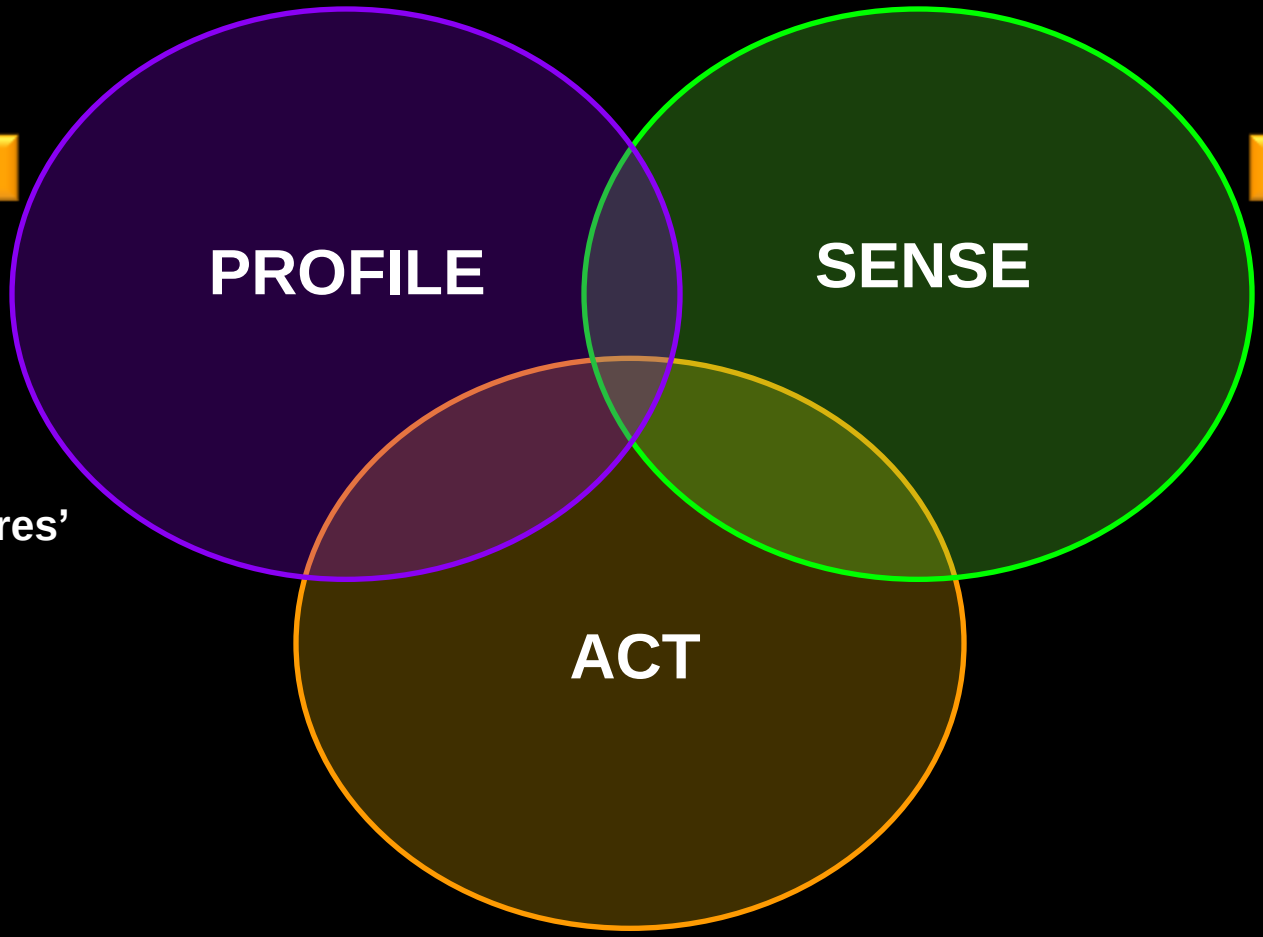
– “biosignatures’



automated platforms for rapid detection of multiplex analytes

rapid analytics and customized data formats/visualization to guide optimum decisions by clinicians, patients and payors

Mapping the Molecular Signatures of Disease



Life Sciences

ID patterns of pathway and network dyregulation in disease

– "biosignatures'

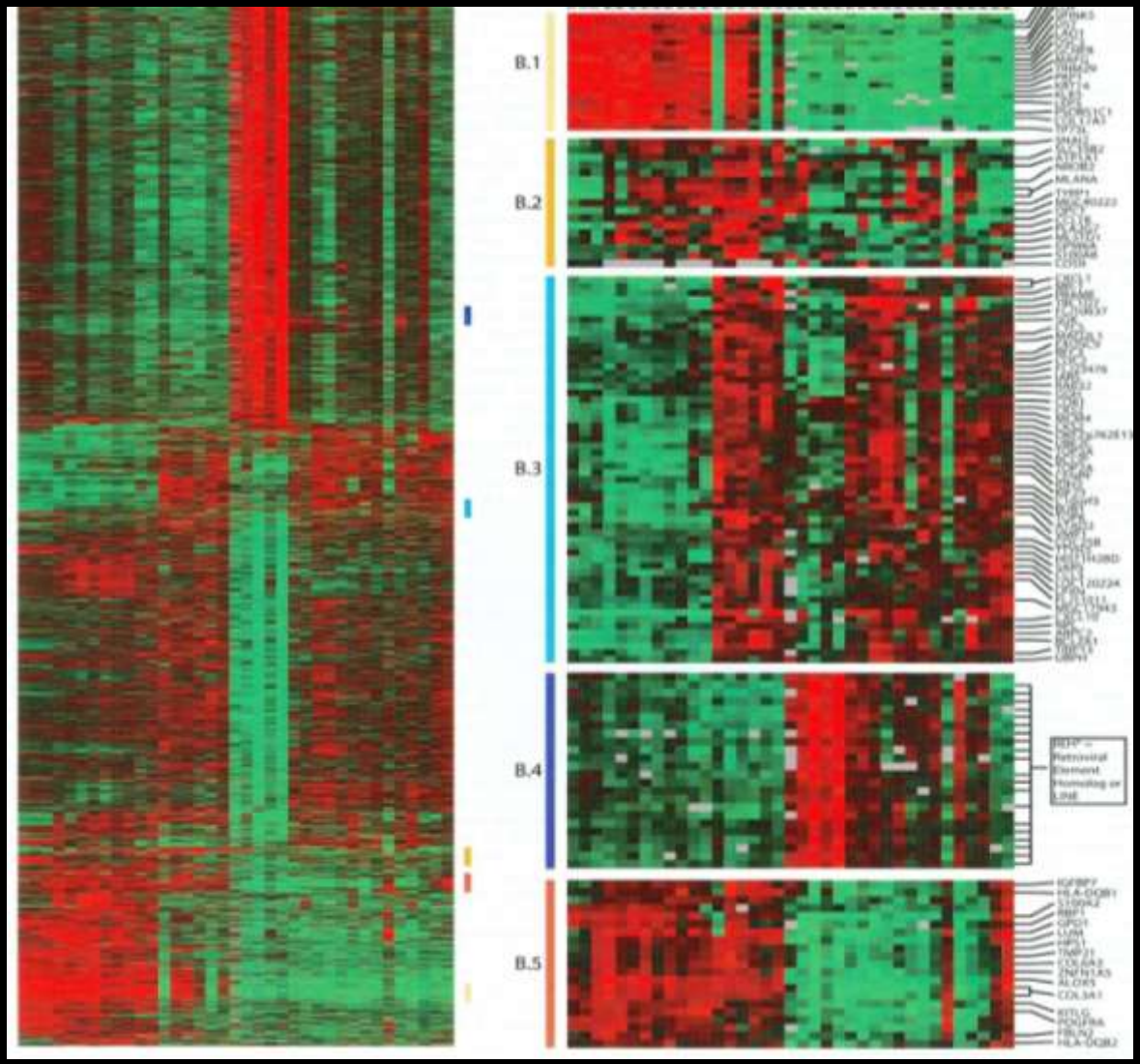
Engineering

automated platforms for rapid detection of multiplex analytes

rapid analytics and customized data formats/visualization to guide optimum decisions by clinicians, patients and payors

Computing

Disease Subtyping: Next-Generation Molecular Diagnostics (MDx) and a New Molecular Taxonomy of Disease



MDx Platforms

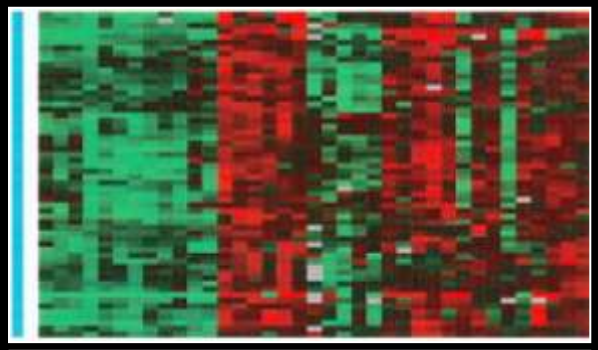
- massive parallelism
- miniaturization
- automation
- rapid
- POC

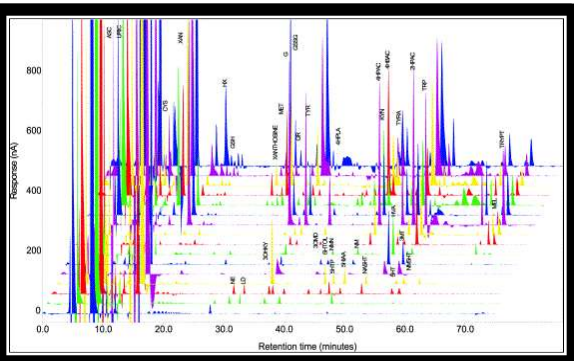
RIGHT Rx for RIGHT DISEASE SUBTYPE

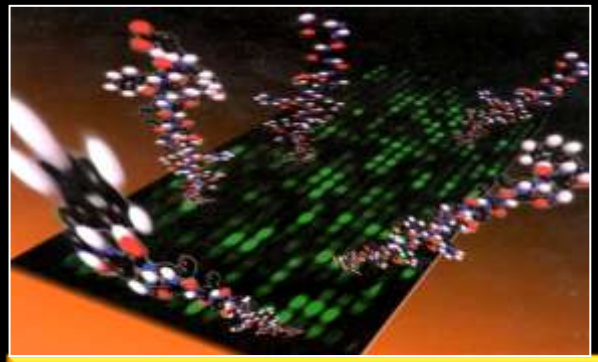
Molecular Diagnostics and Miniaturized Devices: A Key Future Driver in the Healthcare Value Chain

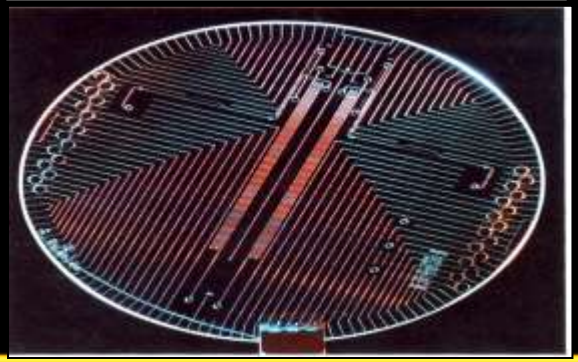
Complex Biosignature Profiling

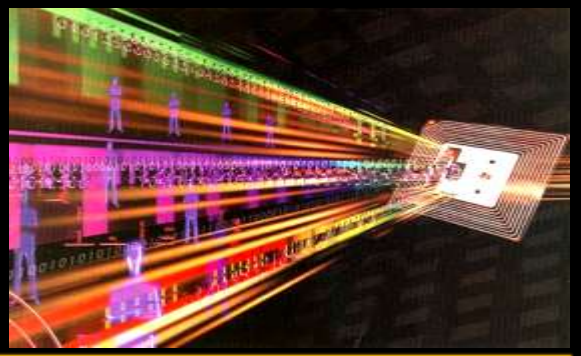
genomics	proteomics	immunosignatures











Signature Detection, Deconvolution and Multivariate Analysis

automated, high throughput multiplex assays	novel test formats and devices (POC)	new algorithms for complex signal/deconvolution

K-RAS Profiling and Anti-EGFR Monoclonal Antibody Therapy

clinical guidelines

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

- regulatory endorsement in product labeling

- payor adoption

Molecular Medicine and Rational Therapeutics: Targeted Rx and Rise of Molecular Diagnostics and Patient Profiling

- 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

Outcomes-Based Risk-Sharing Agreements (OBRAs)

NHS

- full or partial refund for non-responders

Johnson & Johnson

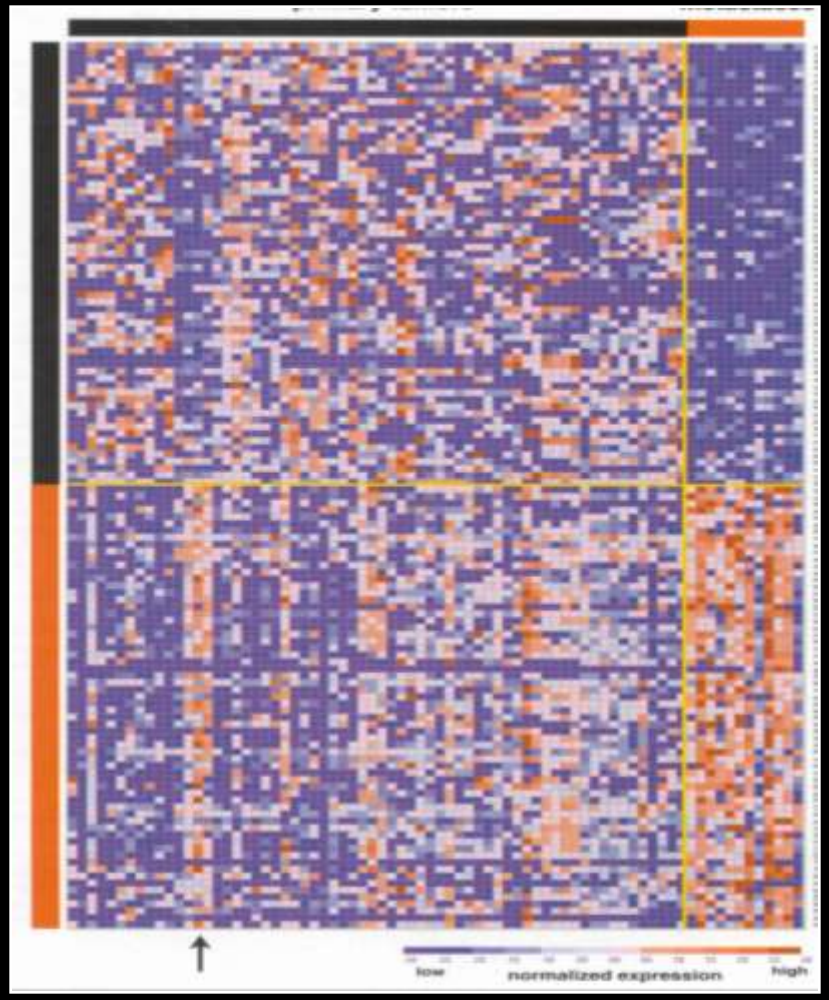
VELCADE® (bortezomib) FOR INJECTION

JANSSEN-CILAG
Your partner in integrated health care

- four Rx cycles
- 50% reduction in serum M protein
- NHS continues to fund
- <50% response company refunds cost of Rx

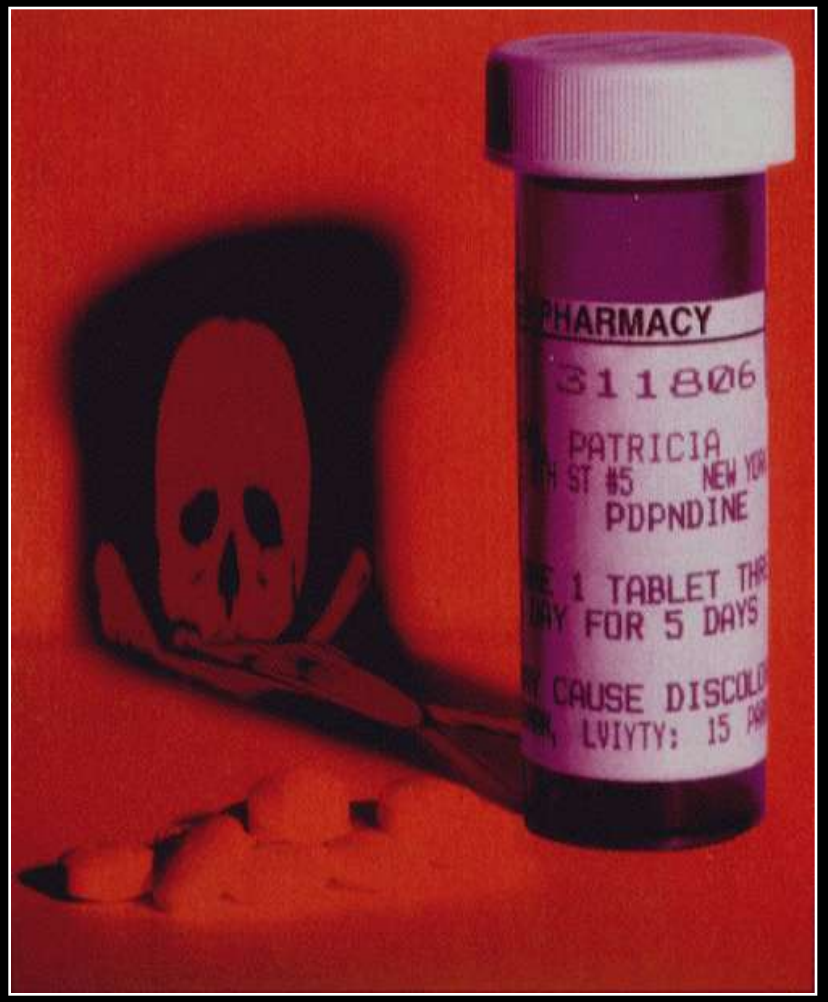
From Pharmaceuticals to Pharmasuitables

Disease Subtyping:



Right Rx for Right Disease

Individual Variation and AE risk

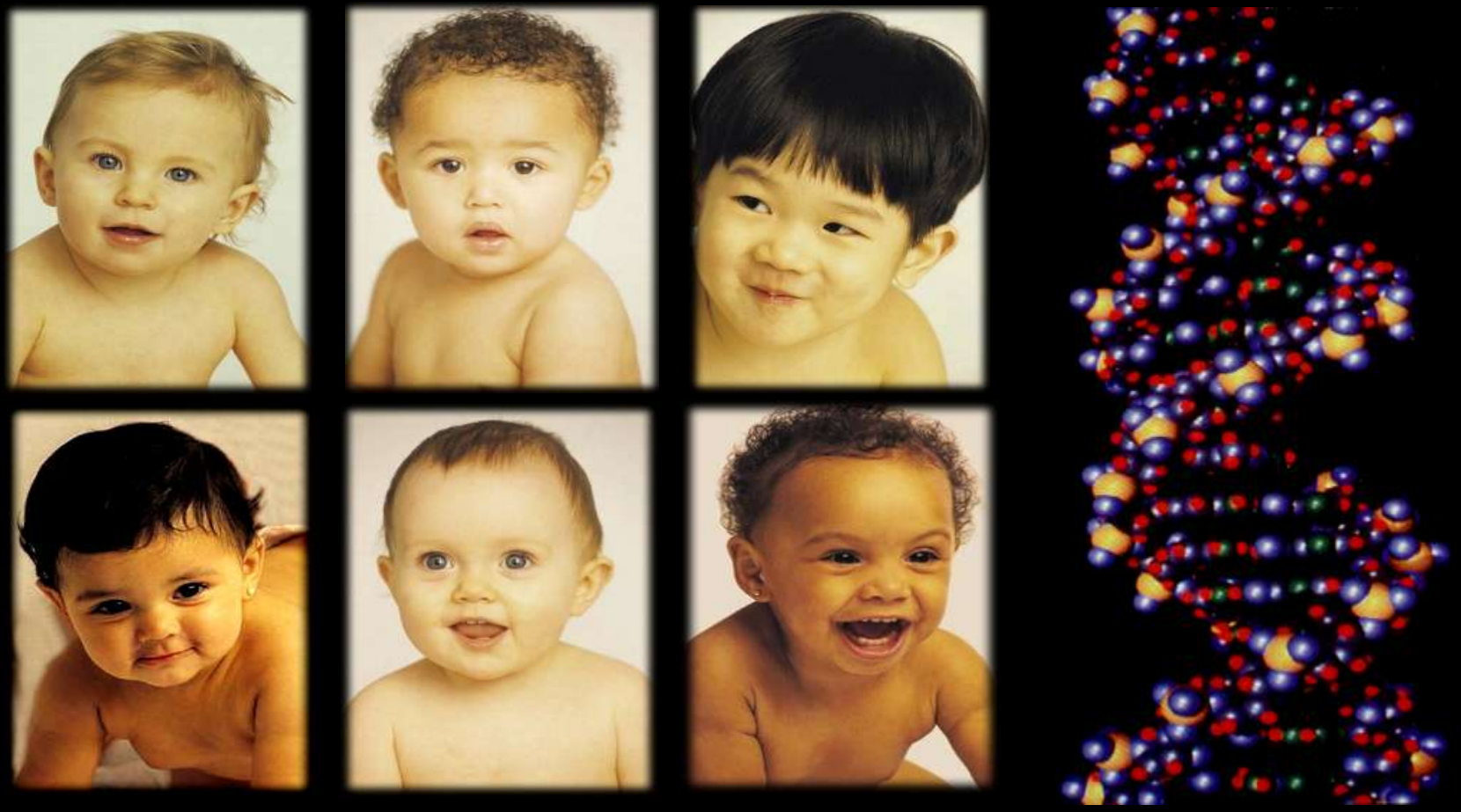


Right Rx for Right Patient

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 and immune response alleles as additional risk factor

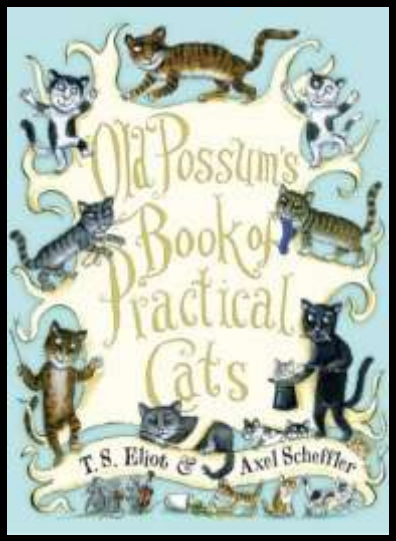
The Hunt for Gene Loci Associated with Complex Human Diseases



The “Missing Heritability in Complex Human Diseases”

“Human Genetics faces an unexpected problem.
It is plagued by what
might be called Macavity Genes.
Often the evidence for inheritance is clear,
but, like the mystery cat,
the agents responsible
are just not there.”

Dr. S. Jones
Lancet 3 April 2010 p. 1153



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

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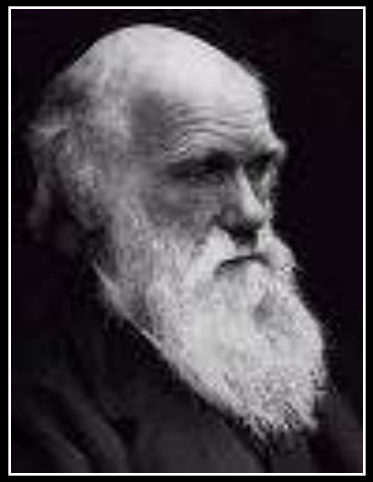
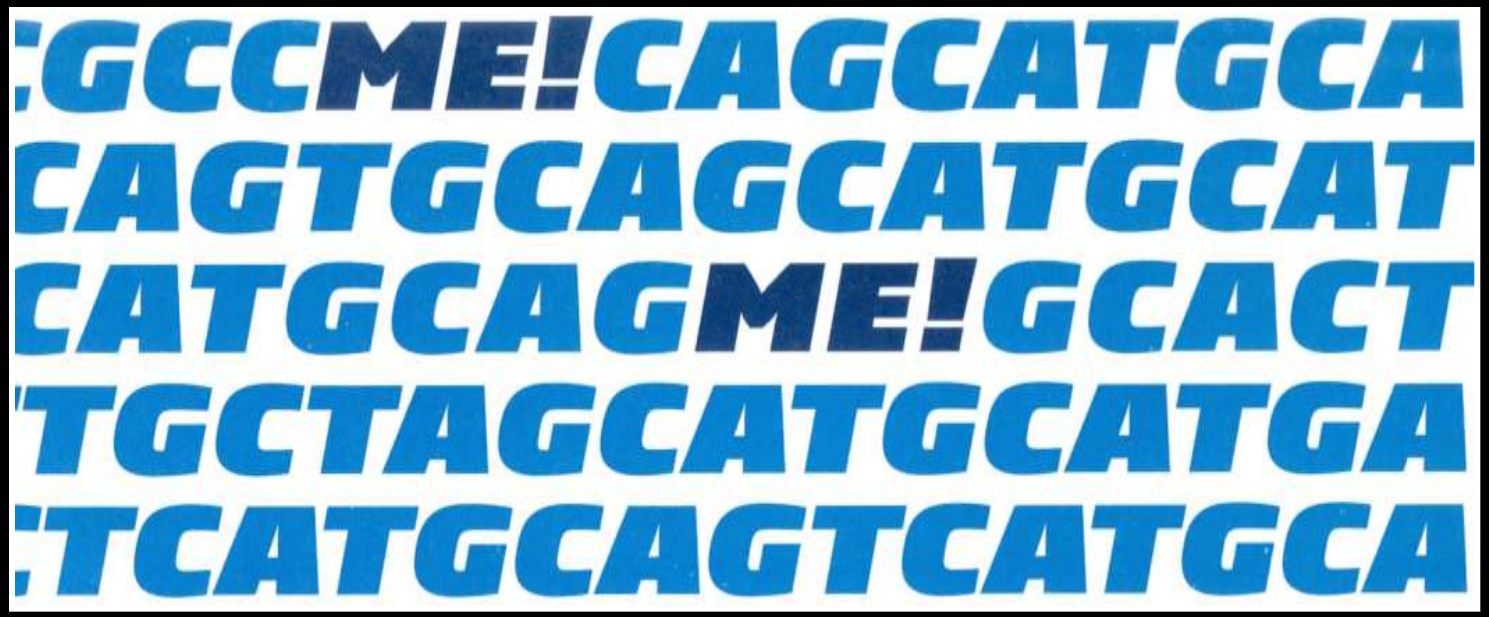
The premature quest to provide consumer genomic testing (CGx) for future risk of major diseases

Mapping Human Diversity

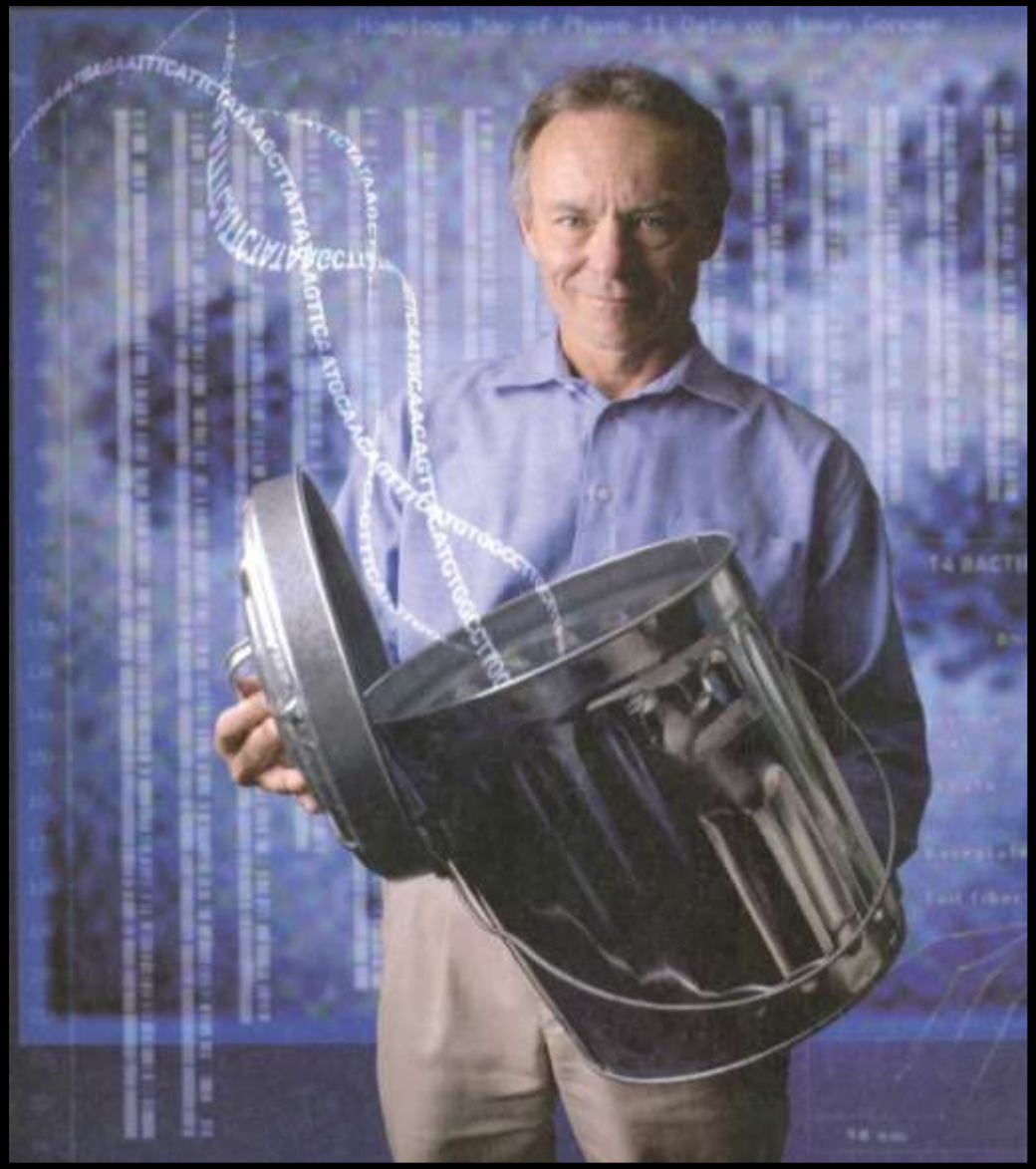


“Our ignorance of the laws of variation is profound”

Charles Darwin



Mapping the Complexity of Genome Organization



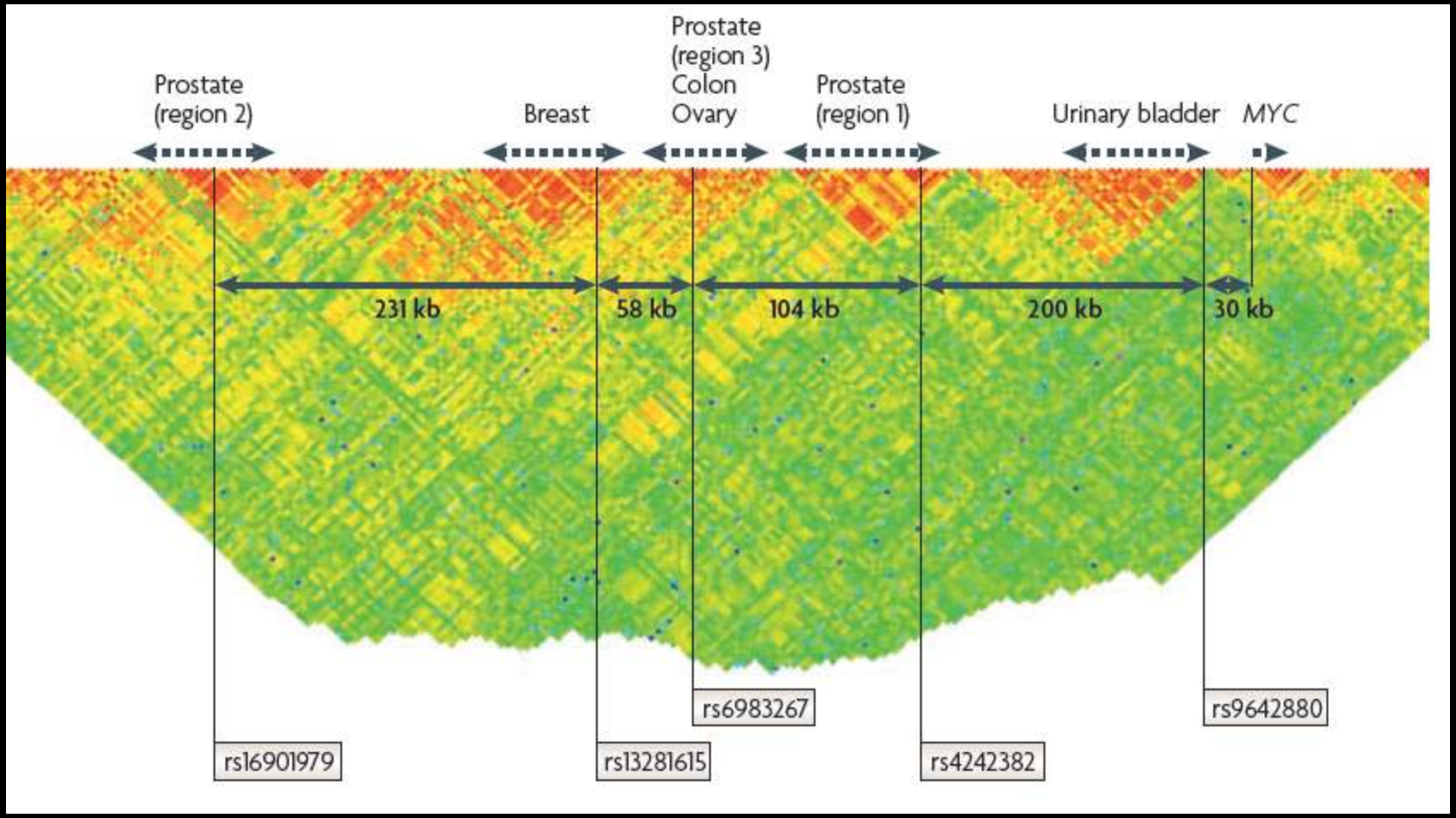
- recognition of increasing levels of organizational and regulatory complexity
  - haplotypes
  - CNV
  - indels
  - RNA universe
  - ‘dark’ elements
  - epistasis
  - epigenetics
  - nuclear compartmentalization and *trans*-expression

miRNAs Associated with Solid Cancers

Tumor	miRNA	Function
Breast cancer	miR-21, miR-125b	oncomiR
Breast cancer metastasis	miR-335, miR-206, miR-126	metastisis suppressor
Lung adenocarcinoma	let-7a, miR-143, miR-145	tumor suppressor
Lung adenocarcinoma	miR-17-92 cluster, miR-106b/93/25 cluster	oncomiR
Pancreatic ductal carcinoma	miR-196a, miR-196b	oncomiR
Ovarian carcinoma	miR-199a/b, miR-140, miR-145, miR-204, miR-125a/b	tumor suppressor
Ovarian carcinoma	miR-141, miR-200a/b/c	oncomiR
Hepatocellular carcinoma	miR-21, miR-224, miR-34a, miR-221/222, miR-106a, miR-203	oncomiR
Hepatocellular carcinoma	miR-122a, miR-422b, miR-145, miR-199a	tumor suppressor
Thyroid papillary cancer	miR-146b, miR-221, miR-222, miR-181b, miR-155, miR-224	oncomiR

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

Gene Deserts: The 8q24 Region and Cancer Susceptibility

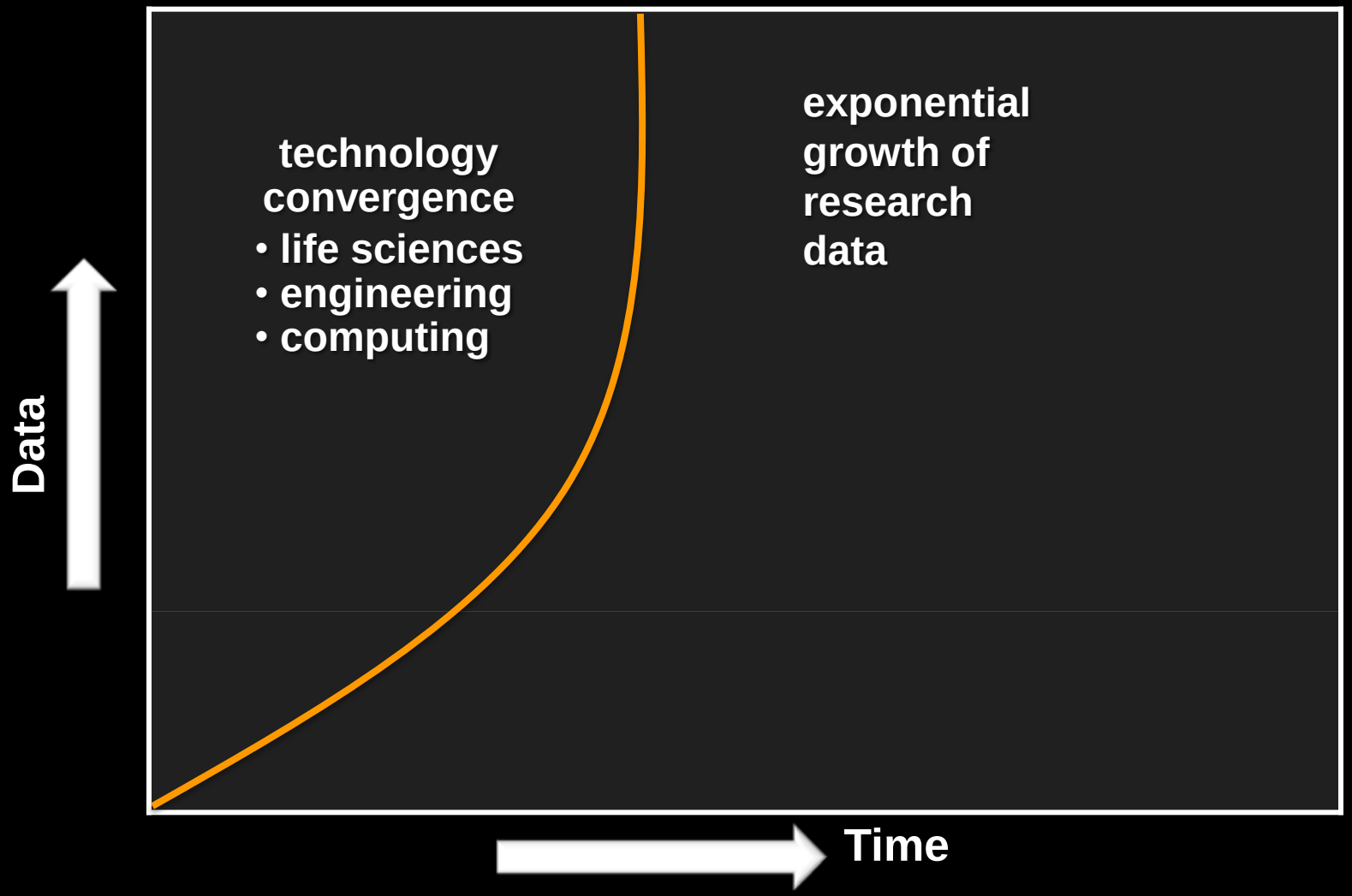


From: J. P. A. Ioannidis et al. (2009) Nature Rev. Genetics 10, 318

Translation of the Major Promise of Molecular Medicine into Routine Clinical Practice

A Complex, Multi-Dimensional Challenge

The Trajectories for Molecular Medicine



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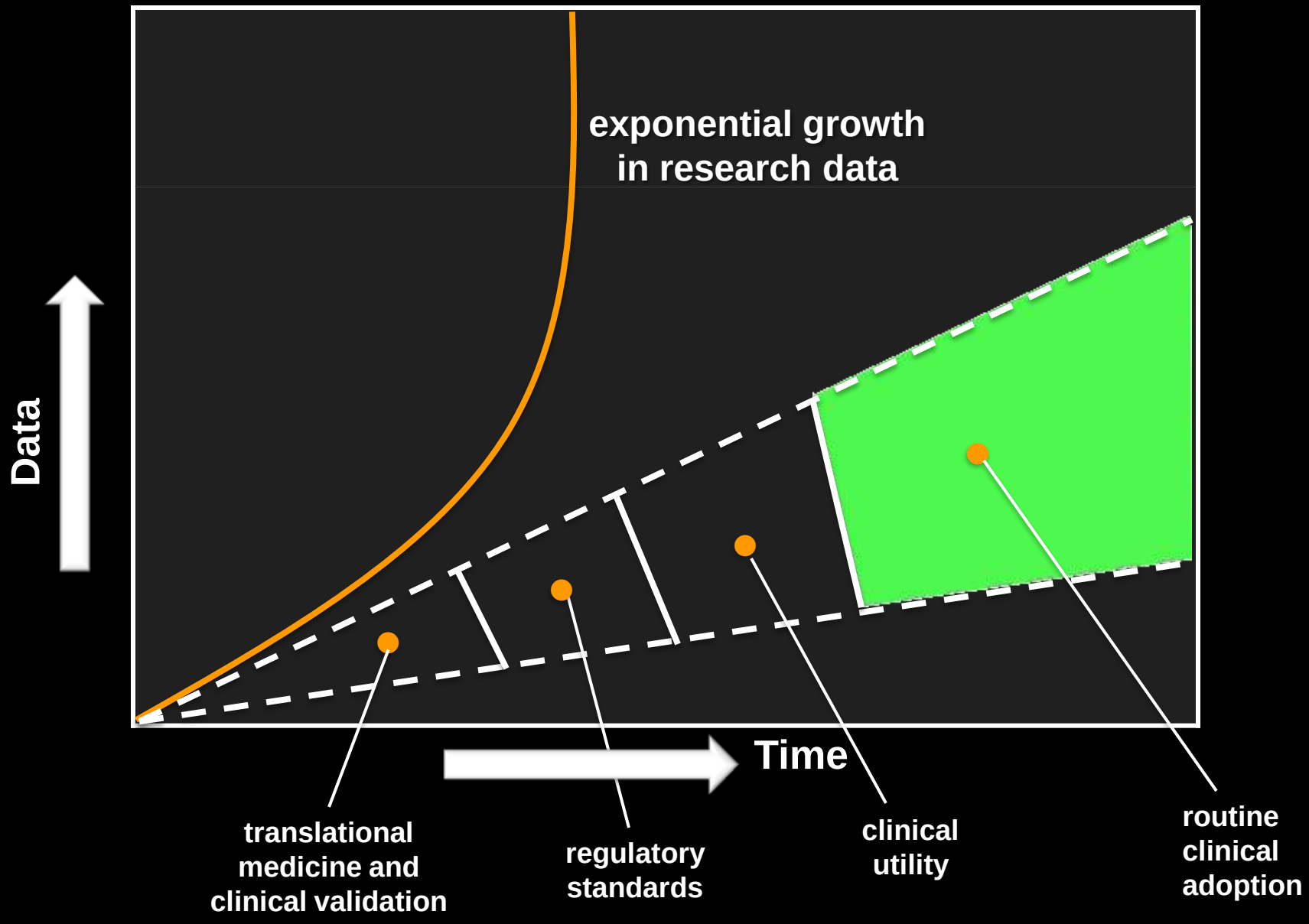


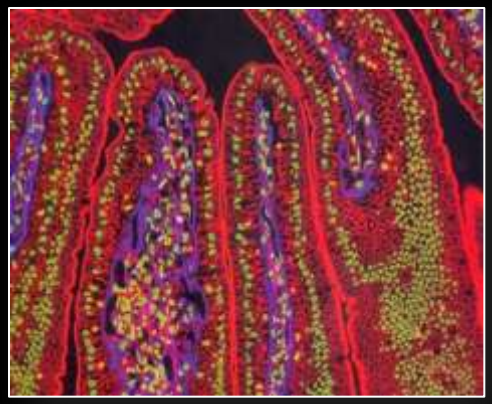
The Real World

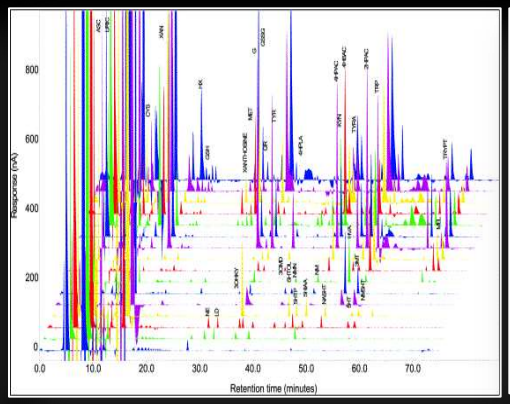
- innovation in science and technology alone is necessary but not sufficient
- adoption requires overcoming multiple barriers
  - existing standard of care
  - cultural conservatism
  - pricing, reimbursement and other obstacles
  - regulatory hurdles
  - intellectual property
- wide variation in adoption speed by different sectors
  - healthcare (10-30 years)
  - computing (1-2 years)
  - engineering (1-10 years)

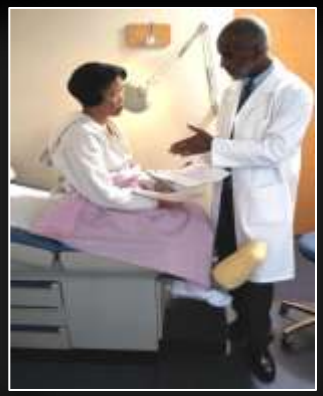
Deriving Value from “-Omics”

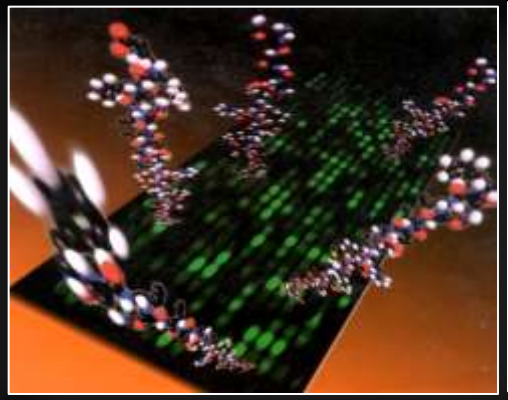
- useful only when correlated with additional parameters
  - clinical outcomes
  - clinical utility
  - actionable information
  - demonstrable economic value

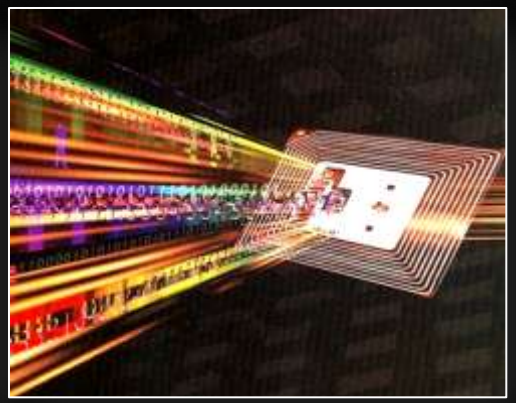
Identification and Validation of Disease-Associated Biomarkers: Obligate Need for a Systems-Based Approaches











Biospecimens and Molecular Pathway Analysis

Biomarker Validation and Multiplex Assays

Instrumentation and Informatics

Clinical Impact and Patient Monitoring

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)

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)

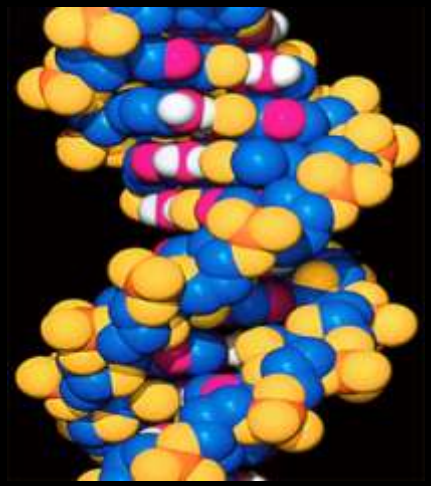
The Rise of Open-Source Networks and Consortia

Managing Mega-Data

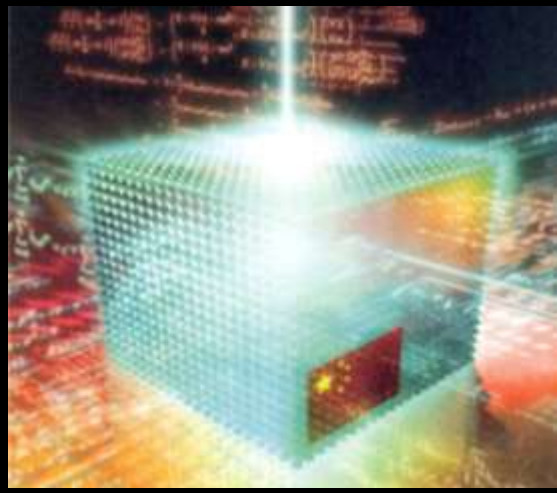
volume

scale

global networks

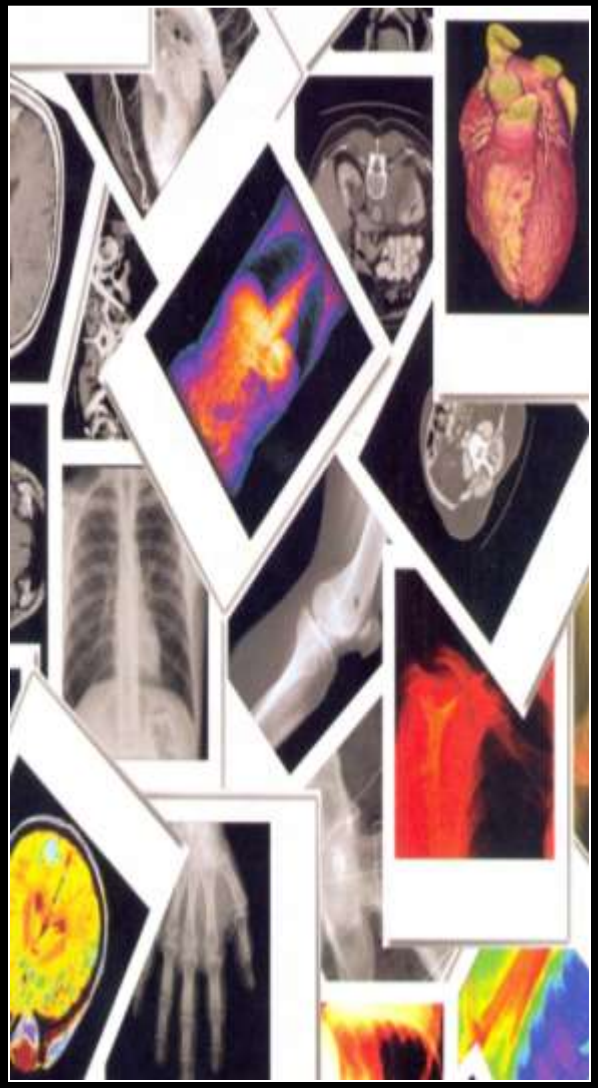


heterogeneity



integration

How Much New Technology Can We Afford?



UK National Institute for Health and Clinical Excellence (NICE)

Nice Gets Nasty (or Rational?)

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

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

- polypharmacy and AEs
- poor patient compliance
- multiple physician/venue encounters
- poor communication/ coordination between siloed healthcare services

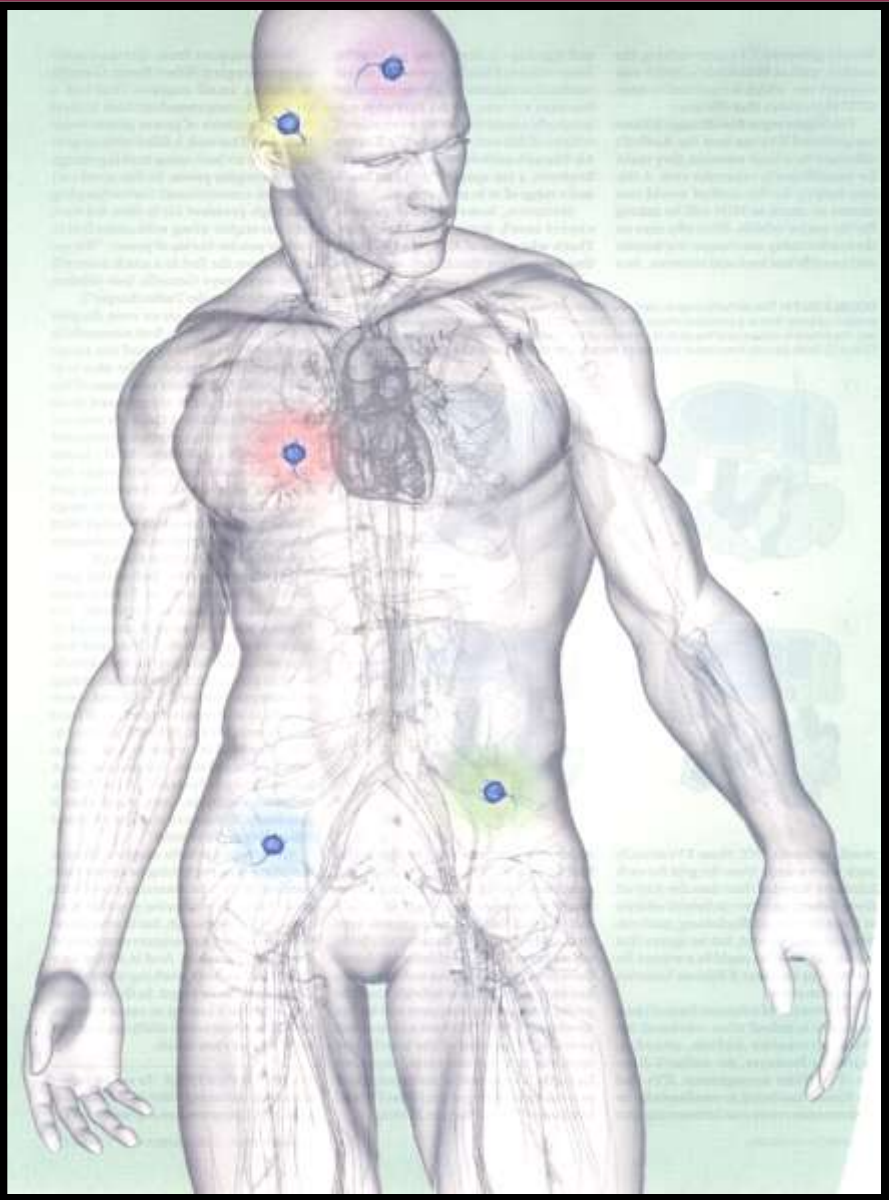
The Non-Compliance Problem

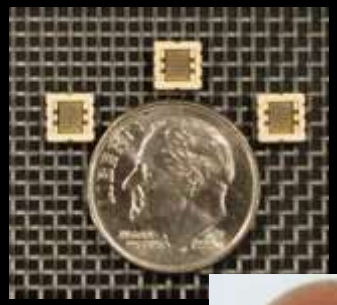
- non-compliance rates in both long-term and short-term treatments reach 50% of patients
- non-compliance “a worldwide problem of striking magnitude” (WHO, 2003)
- non-compliance is a major barrier for realizing the benefits evidence-based therapies
- lack of effective policies toward the problem of non-compliance at both national and European levels

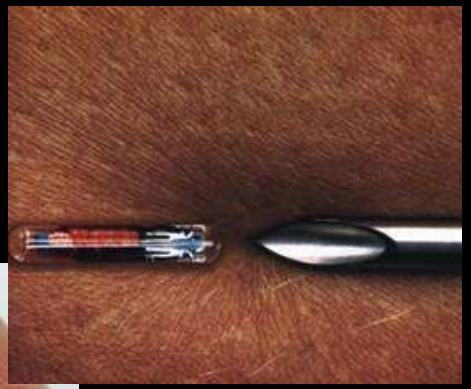
Health Status Monitoring and the Promotion of Wellness

On-Body: In-Body Sensors (OBIBs) and Remote Monitoring of Health Status

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







When Your Carpet Calls Your Doctor

The Economist 10 April 2010

Personal Health Systems:
On-Body: In-Body Sensors (OBIBs)

- wearable
- portable/mobile
- point-of-care
- implantable
- multi-parametric
- interoperability with electronic records

Mobile Health (mHealth)

Major Target Markets for Wireless Medicine

Disease	Parameter
Alzheimer's	vital signs, location, activity, balance
Asthma	respiratory rate, FEV, air quality, oximetry, pollen count
Breast CA	ultrasound self-exam
COPD	respiratory rate, FEV, air quality, oximetry
Depression	medication compliance, communication
Diabetes	glucose, hemoglobin ATC
Heart Failure	cardiac pressures, weight, blood pressure fluid status
Hypertension	continuous blood pressure monitoring, medication compliance
Obesity	smart scales, caloric in/out, activity
Sleep Disorders	sleep phases, quality, apnea, vital signs

Modified from: West Wireless Health Institute, Medtech Insight, August 2009

The Infocosm: Emerging Networks of Global Connectivity

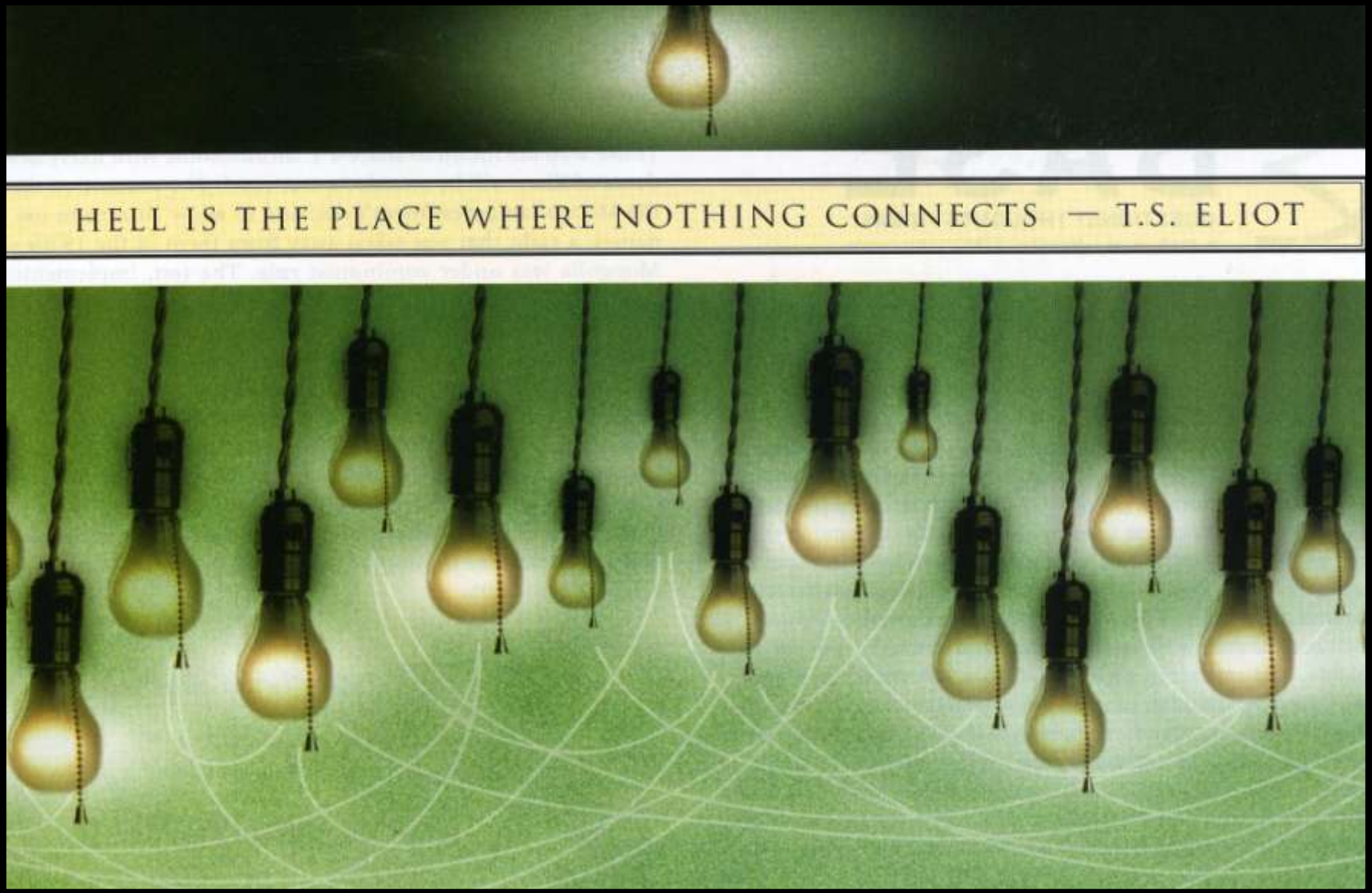
The Information Age: Proliferating Information as a Constant

"It is a shame that the telegraph
has been invented.
Now suddenly anyone can get the news"

"One already has too much to think about
when bathing,
which is not good"

James Rothschild (1852)

Information-Based Medicine



NHS Connecting for Health

NHS Connecting for Health supports the NHS in providing better, safer care, by delivering computer systems and services that improve how patient information is stored and accessed.

NHS staff, the media and patients can use this site to learn about our work and its benefits.

New & updated sections | New content, FAQs and cases | QuickLinks

Summary Care Records (SCR)

Faster, safer access to key health information.

NHS Pathways

For emergency or urgent care assessment.

Automatic identification and data capture

Bar codes and radio frequency technology.

Electronic Prescription Service Release 2

Four stages of PCT readiness for Release 2.

Picture Archiving and Communications System (PACS)

Digital x-rays and scans.

Clinical Dashboards Demonstrator

Selection of pilot stage demo dashboards.

NHS Number: adult social care

Supporting health and social care integration.

NHS Interoperability Toolkit

Framework & standards for local integration.

Source: http://www.connectingforhealth.nhs.uk/

"I look forward to the day when a physician *without* mathematics
will seem as incongruous an idea
as that of an educated man
without Latin or Greek"

Dr. Gilbert, Physician to Elizabeth I

"A physician without a computer
will soon be as rare a phenomenon
as one *with* knowledge of Latin and Greek"

Professor Ian Isherwood CBE
MANCHESTER MEDICAL SOCIETY
20 June 2003

Telecommunications and Media Industry Convergence: Implications for Healthcare

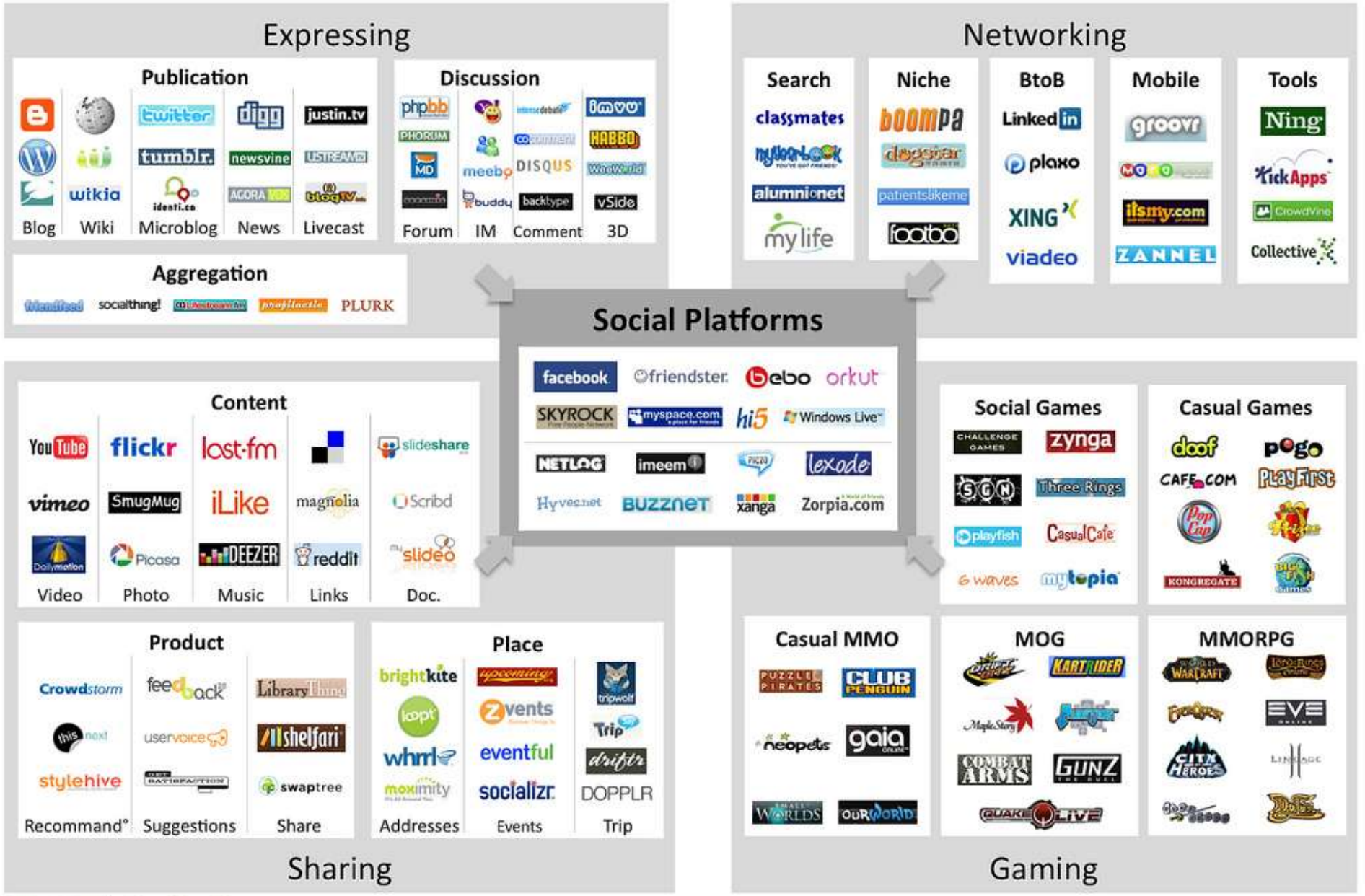
Wireless Technologies: Consumer and Clinical Markets Converge

e-Patient Revolution

Integrated Data Systems for Mobile Networks

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

Social Media Landscape



FredCavazza.net

Pharma and Healthcare Social Media Brand Sponsored Patient Communities

Pharma and Healthcare Social Media Brand Physician and Nurse Communities

ASKLEPIOS
THE CANADIAN PHYSICIAN'S COMMUNITY

HCPs' social network operated by the Canadian Medical Association

coliquio
medizin, einfach wissen

Social network serving the German speaking countries

dermRounds

social and professional networking site dedicated to connecting dermatologists, and others in the field of dermatology

DocCheck Faces

HCPs' Social network physicians, dentists, pharmacists, and veterinary surgeons

doc 2 doc beta
connecting doctors worldwide

online doctors community

Doctors.net.uk

UK-registered doctors in primary and secondary care

DooOX®
the healthcare community

medical and healthcare communities

DOCTORNETWORKING.COM

Network for physicians

Network for physicians

DoctorsHangout.com

Personal& Professional Networking for Doctors& Medical Students Worldwide

doctrs

exclusive social net for Physicians

iMedX

connects physicians with information, opportunities, and each other.

MedicSpeak

network of doctors and medical students communication, collaborations, exchange of ideas and sharing of knowledge.

Medscape Physician Connect

Engage your peers through our FREE global physician community

MedicalExchange
MEDTING

interactive platform on web for the medical professionals

New Media | Medicine

medical students', and pre-medical students' social network

nurse connect

online nursing community and networking site

QBGYN.net
The Universe of Women's Health

research and support community

ozmosis
The Trusted Physician's Network

Trusted Physician's Network

present diabetes

multi-disciplinary diabetes Learn, share, collaborate

present PODIATRY

Podiatric Residency Education Online community

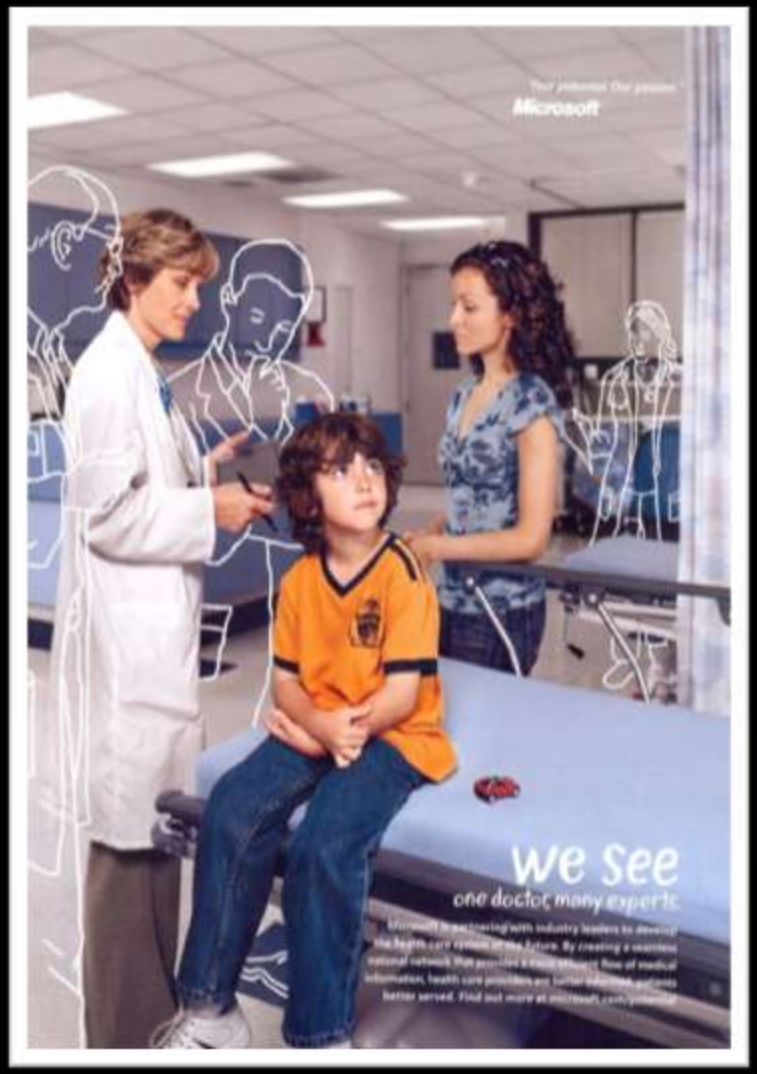
In-Home Health Connection: Engaging the Elderly

Wii Fit Plus

“We’ll have an entire generation of people
who never truly have a private moment”

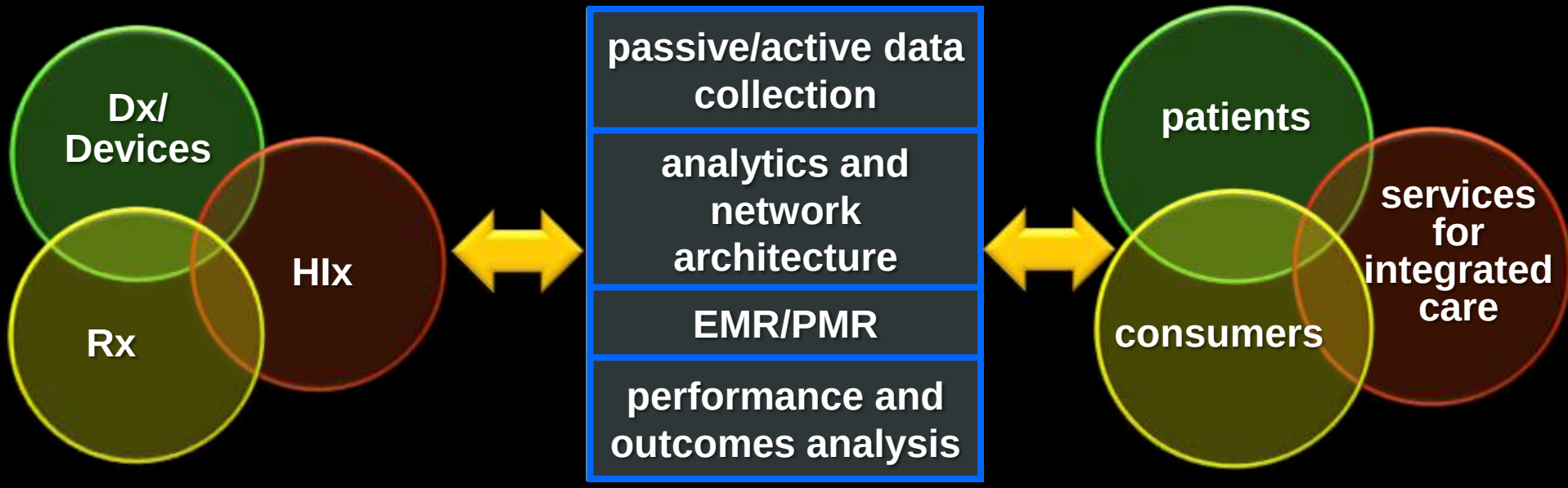
Patrick Tucker
Director of Communications
World Future Society
www.laptopmag.com/2008/sept.

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

A New Healthcare Ecosystem Arising From Technology and Market Convergence



Integrated Technology Platforms

Data Mining and Integration Services

Increasingly Targeted Care and Efficient Use of Finite Resources

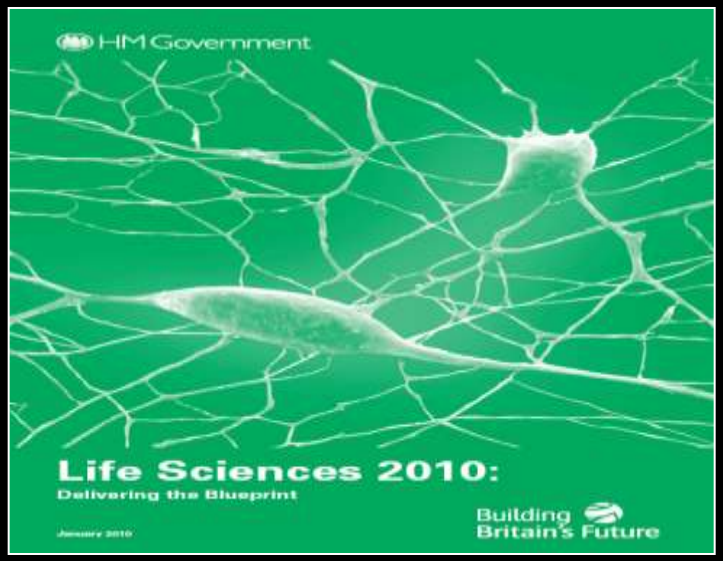
Global Health:
Understanding the Implications of Major Economic and Environmental Dislocations

The Academy of Medical Sciences (2010)

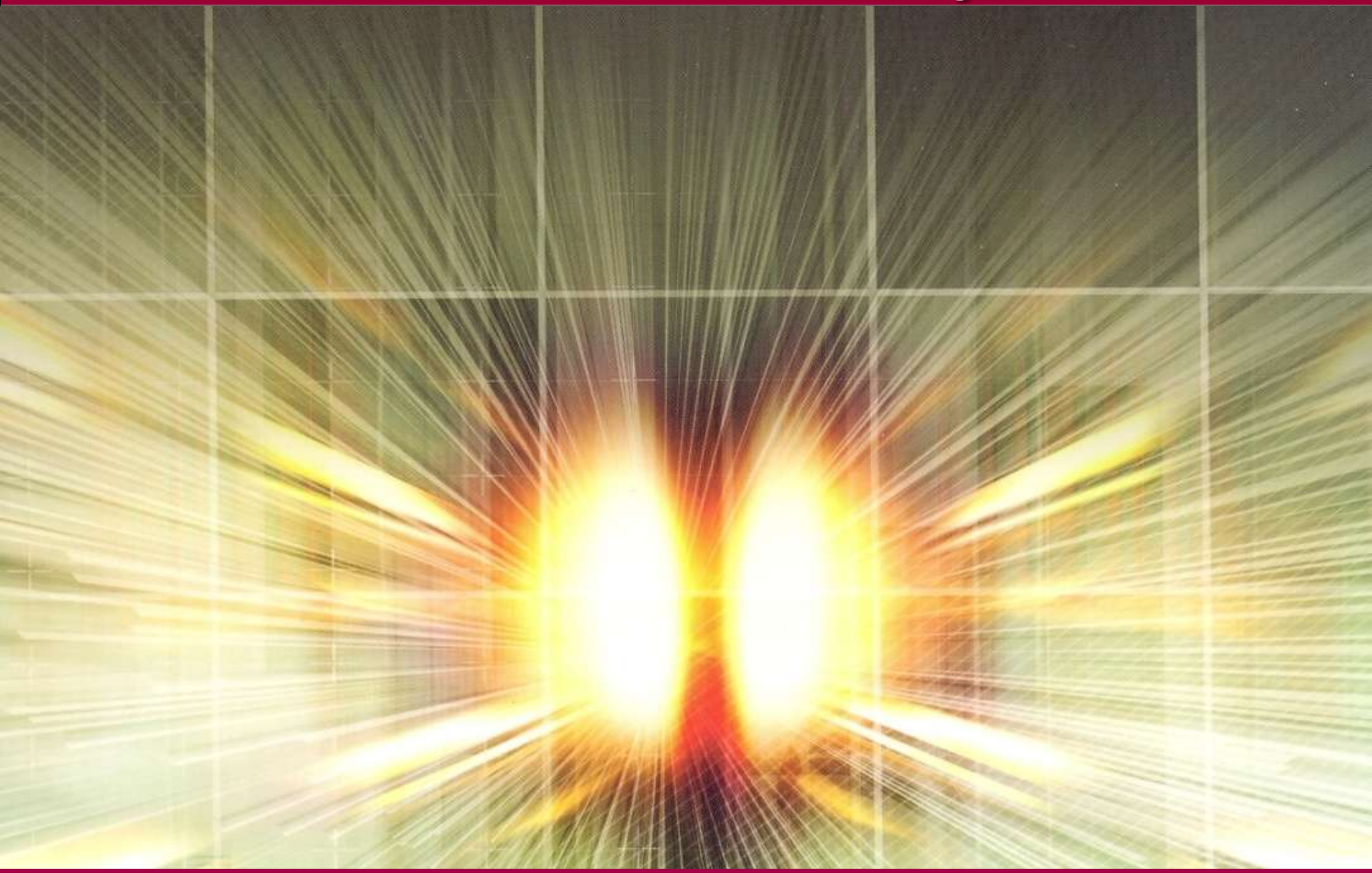
Reaping the rewards: a vision for UK medical science

Groundbreaking advances in medical science over the last 30 years offer the next UK Government an unprecedented opportunity to reinvigorate the economy, to enhance the productivity of the NHS and to make public services more cost-effective. Bold leadership will ensure that the UK can continue to generate world-class medical science that is translated into health and wealth benefits, and can become the best location in the world for medical research in both the public and private sectors.

Sustaining UK Research Innovation



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

“to encourage harmony”