ASU COMPLEX ADAPTIVE SYSTEMS INITIATIVE
ARIZONA STATE UNIVERSITY

Promise, Peril, Productivity and Politics: The Strategic Environment for Healthcare R&D

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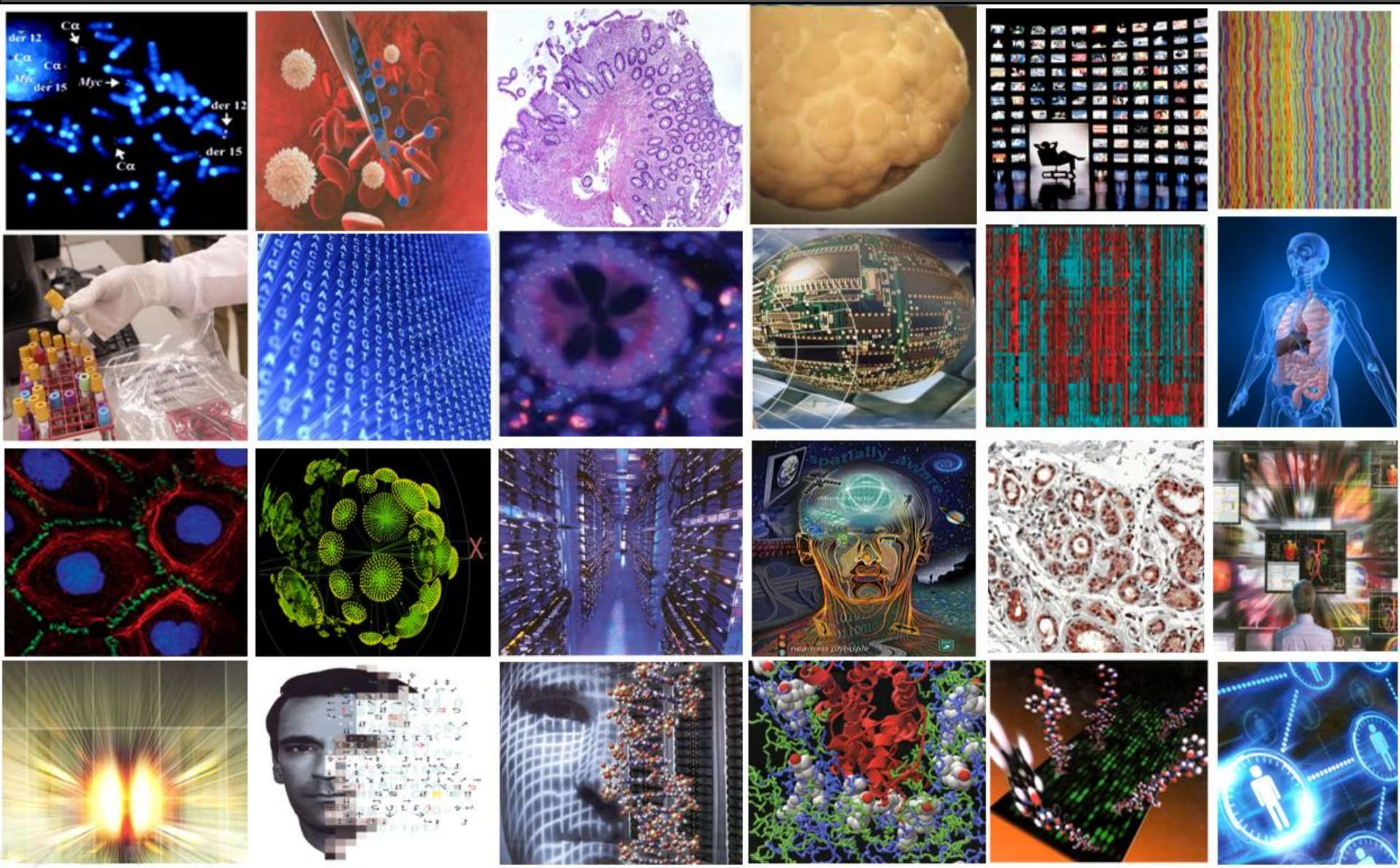
Keynote Presentation at the Burrill & Company 2011
Annual Limited Partners and Advisory Board Meeting
Park City, UT • April 6, 2011

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



Sustaining Healthcare Innovation in an Era of Constraint

The Challenge of Translation of Discovery Advances to Tangible Benefits for Patients and Society

Prospect of Continuing Productivity Decline in Rx Pipelines

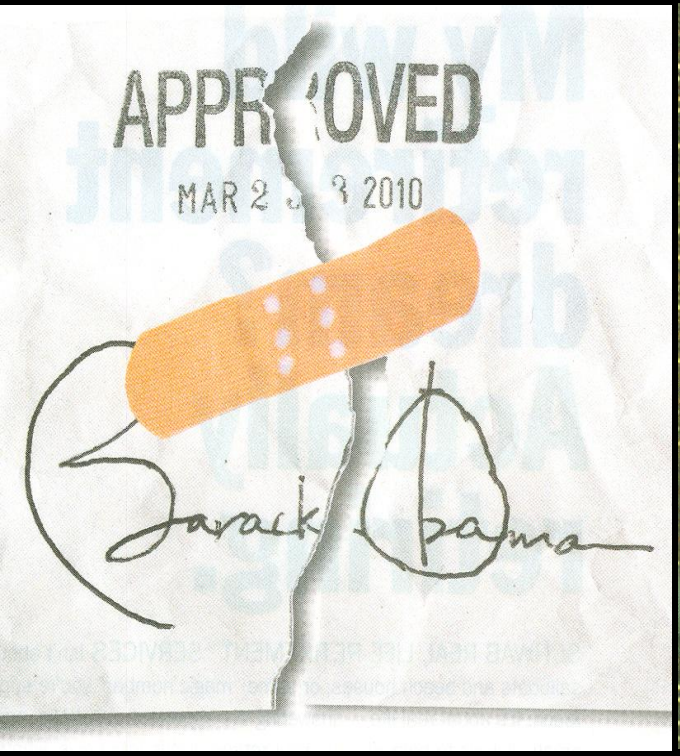
Molecular Diagnostics (MDx) and Data-Information Services (Ix) as Emerging Value Drivers in Improving Disease Detection and Treatment Outcome

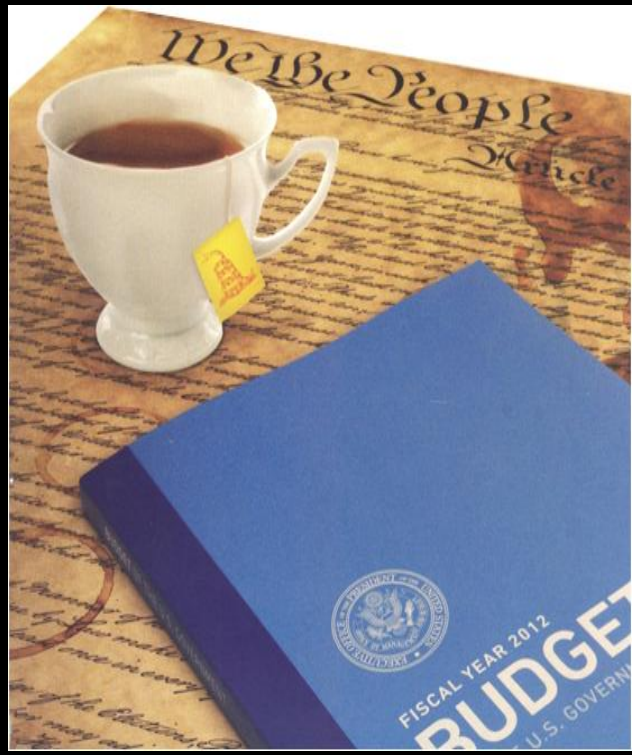
Sustained Productivity in Healthcare R&D Will Require Systems-Based Approaches That Integrate Diagnostics, Therapeutics and Information Systems for Optimum Outcomes

Disruptive R&D Innovations Are Needed Urgently to Transcend Current Linear Incremental Strategies That Are Insufficient to Meet Future Healthcare Delivery Needs

Progress in Achieving Major Productivity Gains and Disruptive Innovations Will Require Radical Reform of the Organization and Funding of Approaches to Discovery and Proficient Translation to Products/Services

Real Healthcare Reform or Reducing Costs Without Addressing the Fundamental Problems?

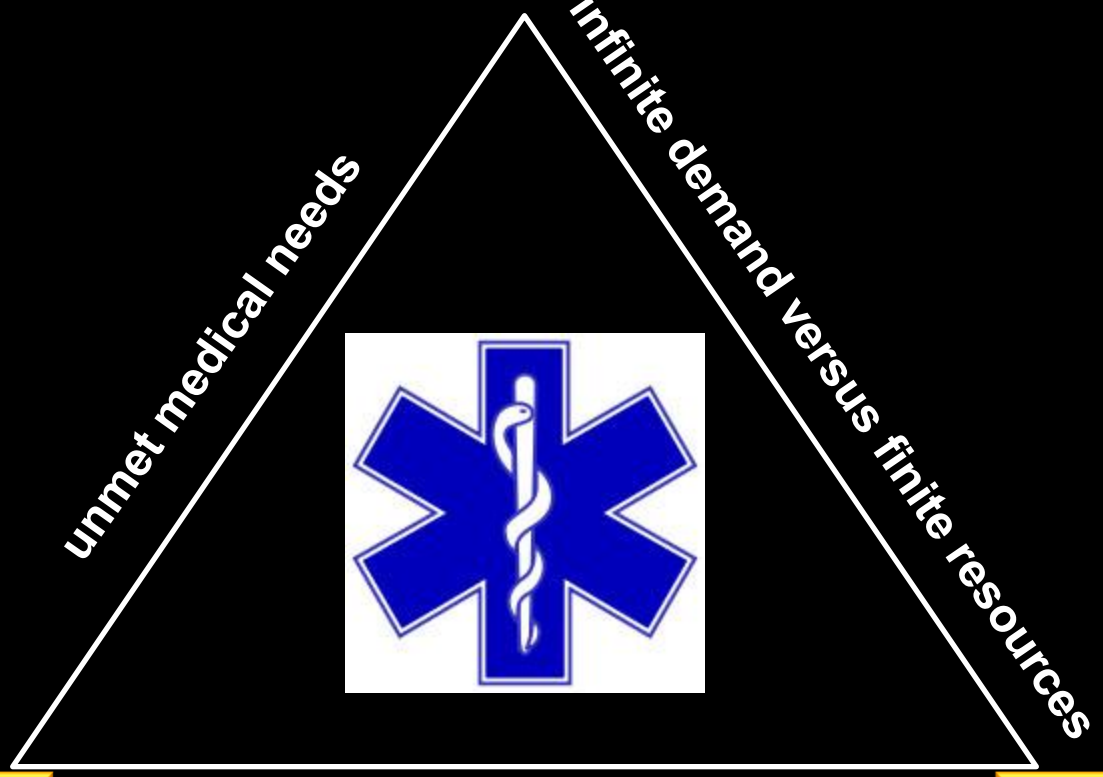




The Healthcare Challenge

Outcomes

clinical, economic, quality-of-life

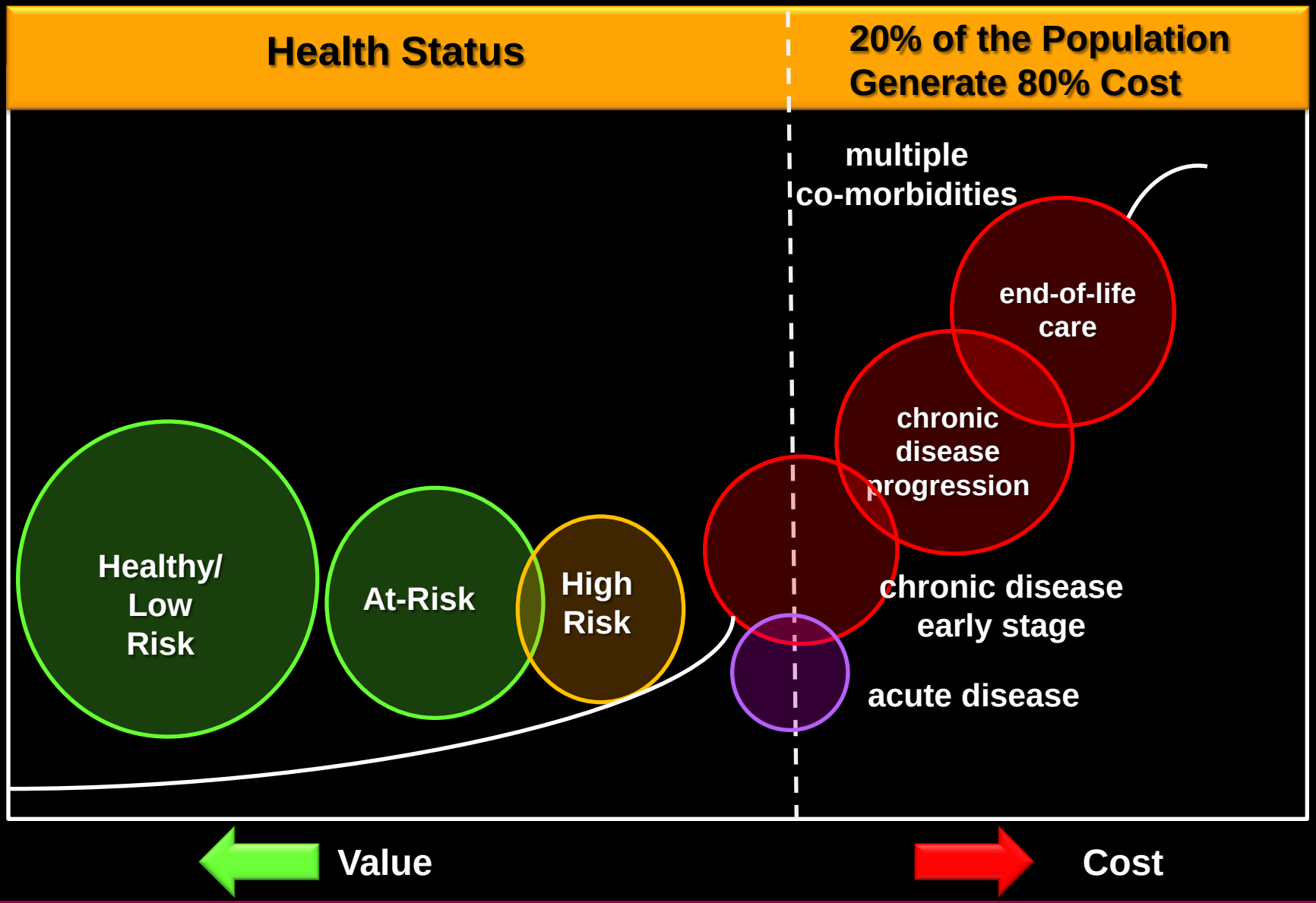


Innovation and Cost of Care

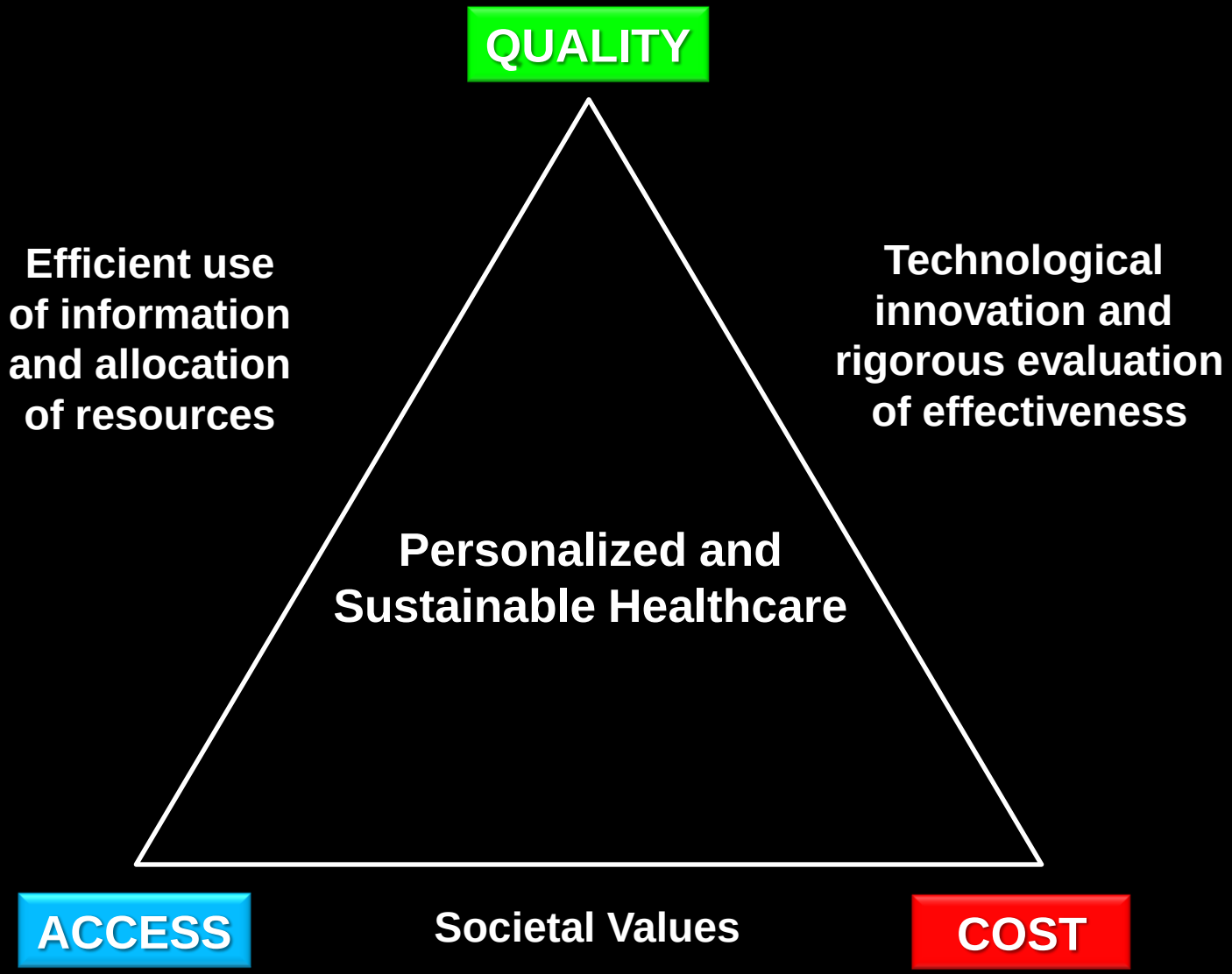
increasing cost of care
and acceleration of new technologies

Access to Care

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



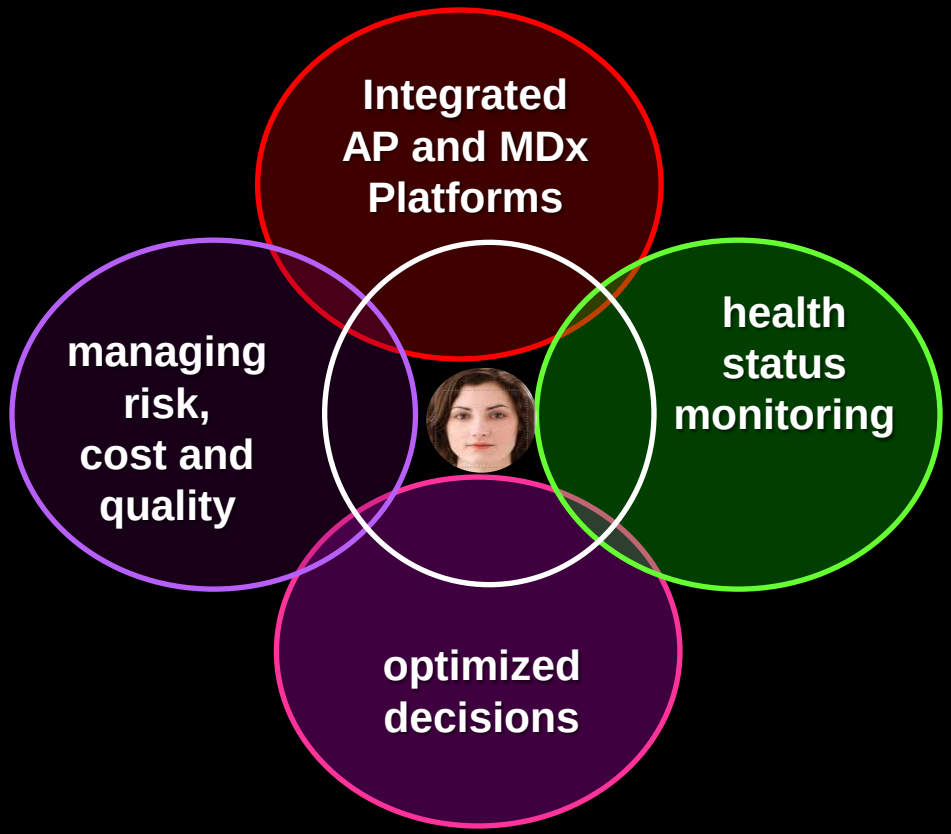
Optimizing Healthcare Delivery



Disruptive Innovation in Healthcare: Redefining the Value Equation in Healthcare

PRECISION DIAGNOSIS

BETTER CARE AT LOWER COST

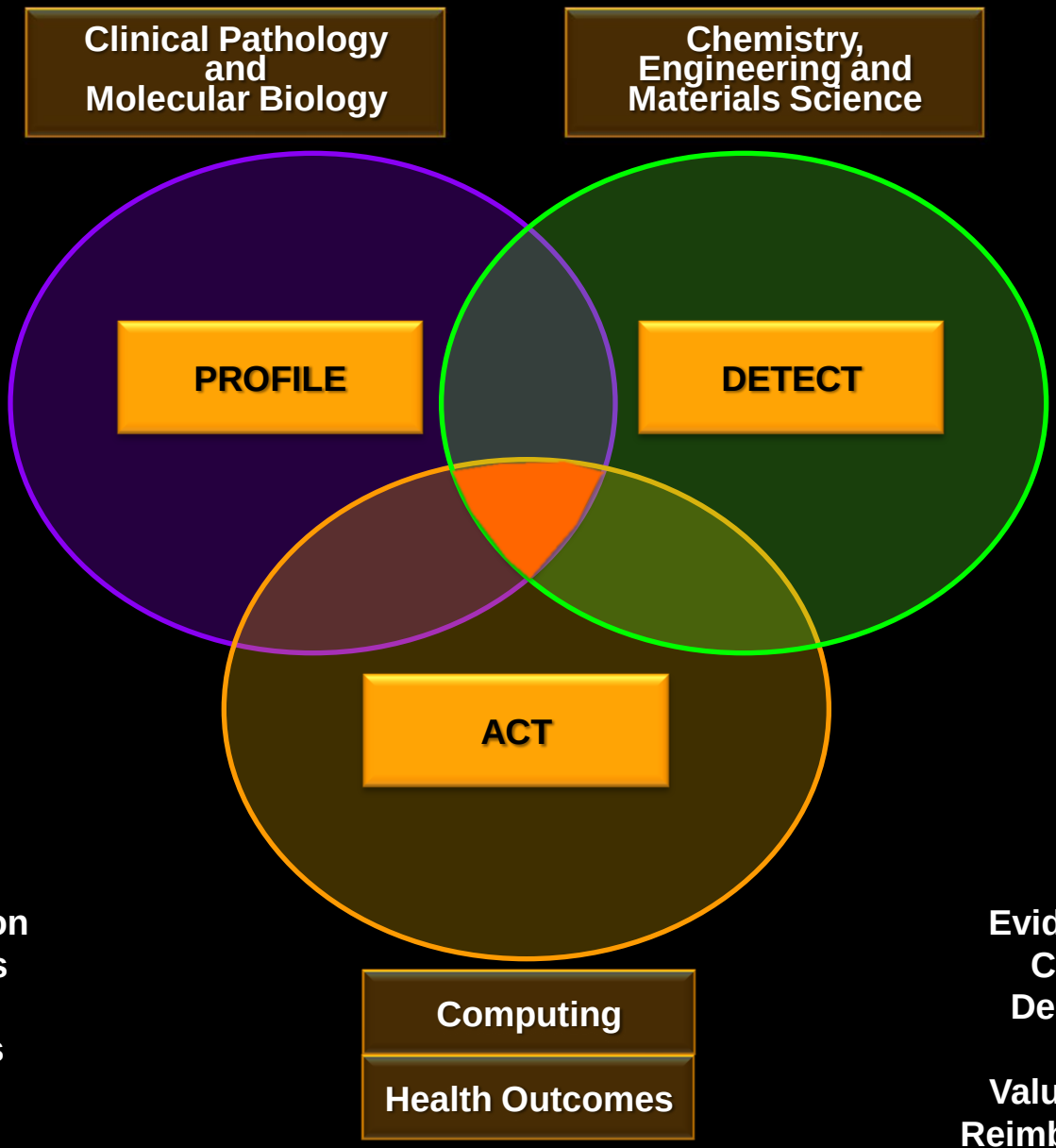


EARLIER DISEASE DETECTION AND RESPONSE TO RX

TREATMENT PERSONALIZED TO THE PATIENT

Promise

Patterns of Technology Convergence: Mapping Disease Mechanisms at the Molecular Level



Disease Markers and Rx Targets

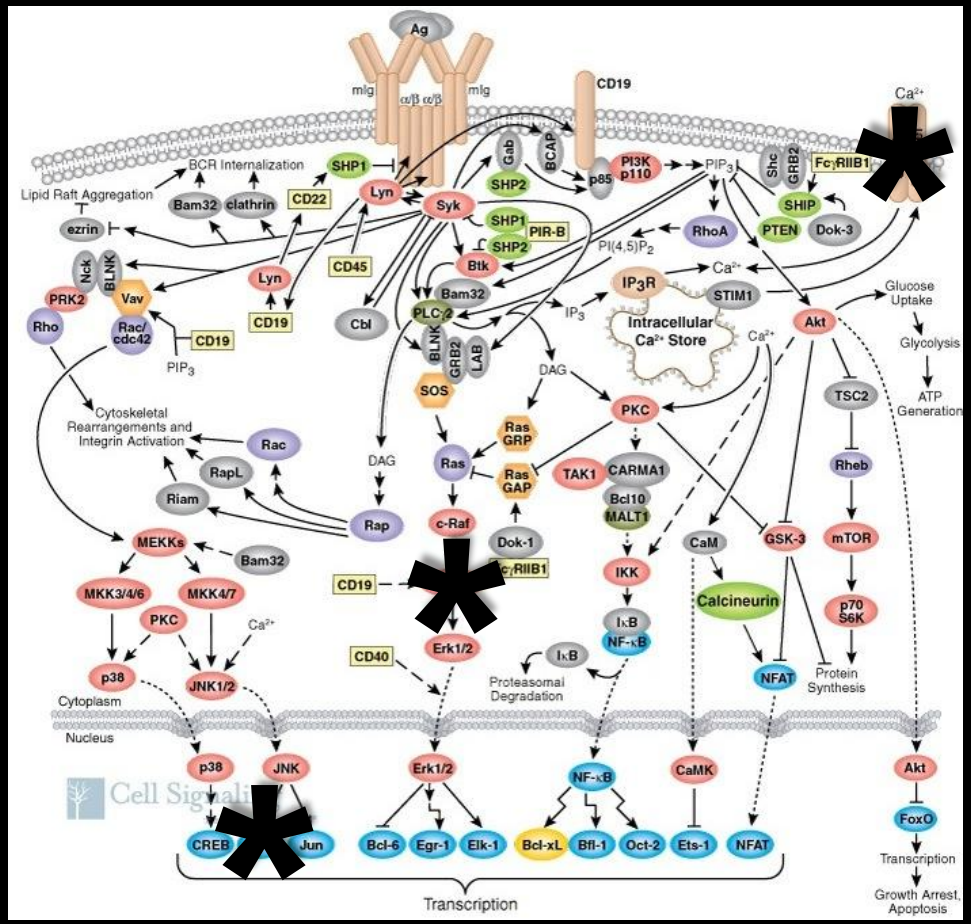
Automated Miniaturized High Throughput Assay Systems

Information Products and Services

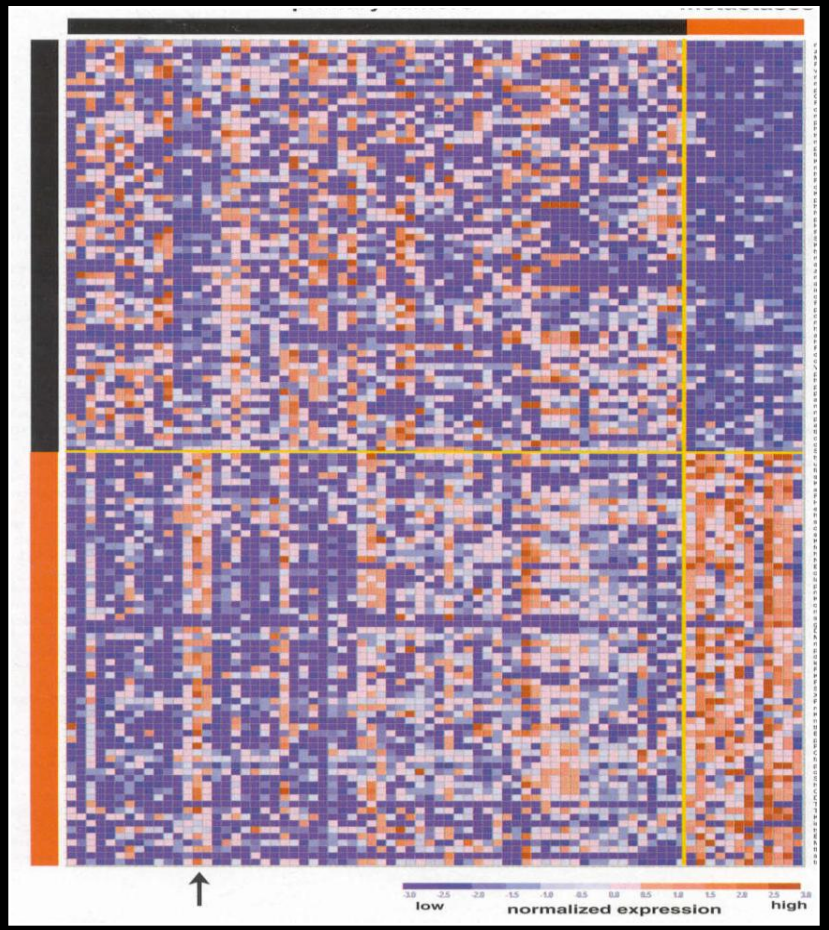
Evidence for Clinical Decisions and Value-Based Reimbursement

From Pharmaceuticals to Pharmasuitables: Right Rx for the Right Disease (Subtype)

ID Molecular Targets for Rx Action



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



K-RAS Profiling and Anti-EGFR Monoclonal Antibody Therapy

Vectibix® (panitumumab)

ERBITUX® CETUXIMAB

NCCN

ASCO®

clinical guidelines

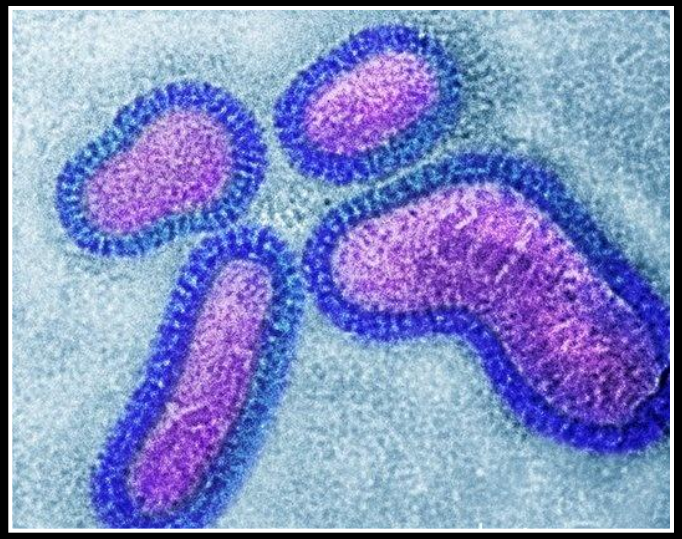
- higher response in patients with K-RAS versus mutant-K-RAS
- estimated $604 million/year savings (ASCO)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

FDA

- regulatory endorsement in product labeling

The Challenge Posed by Two Very Different Disease Categories



Infectious Diseases

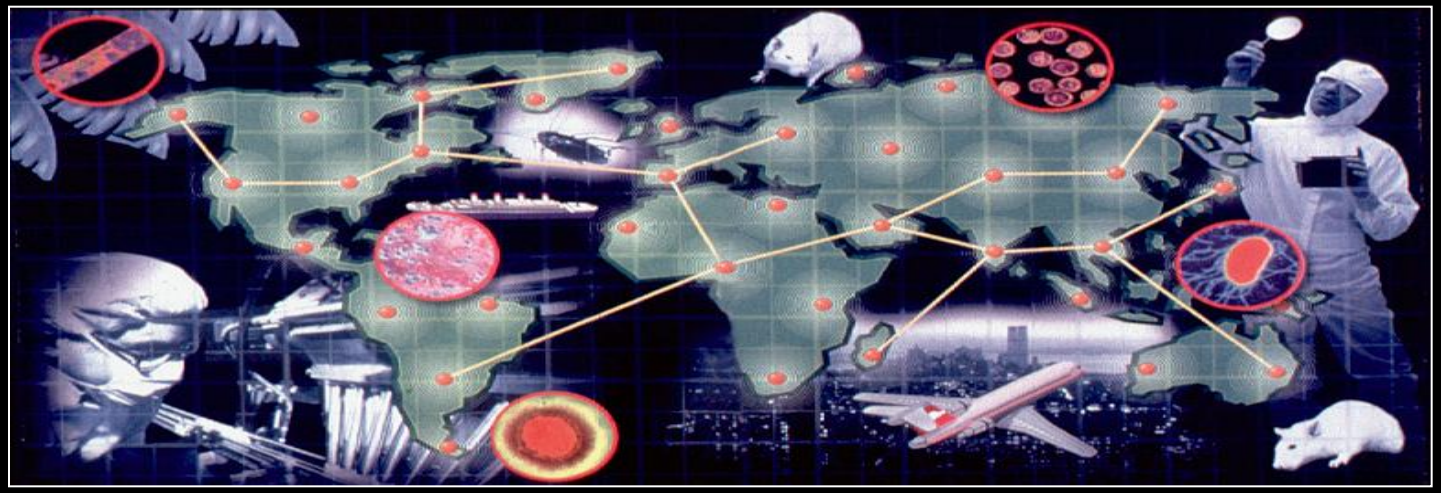
- acute
- populations (public health)
- drug resistance
- tractable Rx target space
- problematic market incentives

Cancer

- chronic
- individuals (albeit global)
- drug resistance
- disease heterogeneity and uncertain Rx target space
- high margin markets (but sustainable?)

A Shared Global Risk:

The Omnipresent Threat Posed By Microorganisms and Parasites



Infectious Diseases: A Shared Global Risk

#1

- cause of neonatal and maternal death worldwide
- economic impact of disease via premature death, disability and reduced productivity
- growing drug-resistance as most important clinical threat in both industrialized nations and DCs

#2

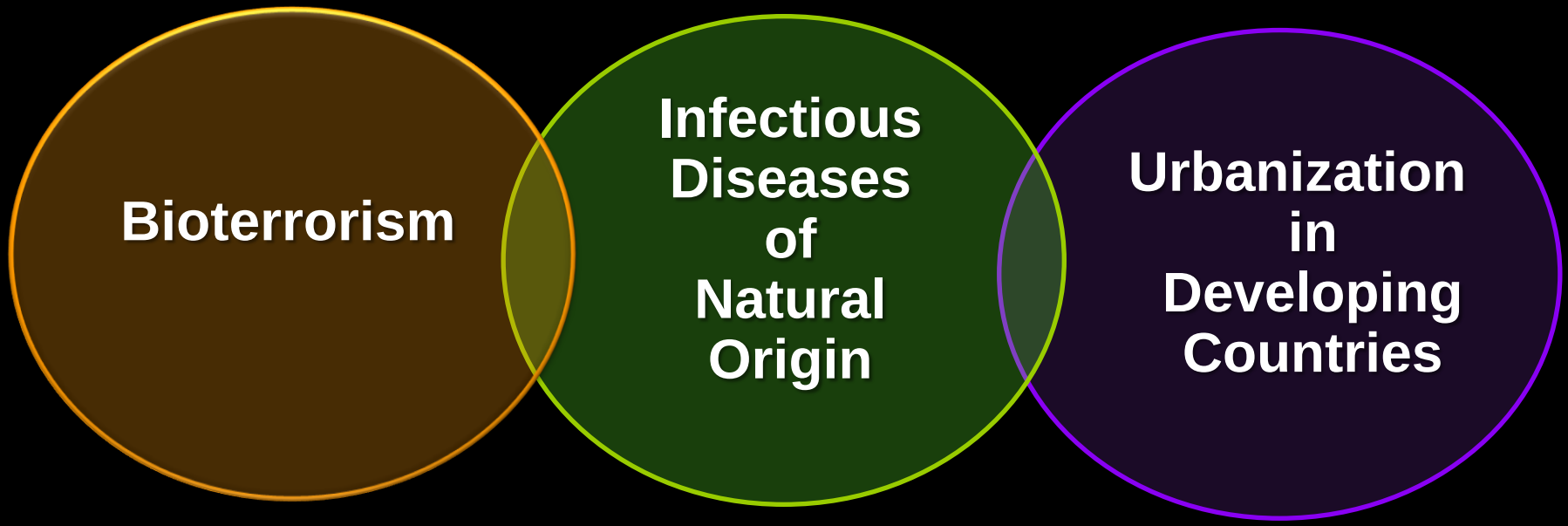
- cause of death worldwide

#3

- cause of death in US and Europe

The Imperative for new R&D Strategies and Investments in Diagnostics, Drugs and Vaccines

Biosecurity: Outpacing Infectious Diseases

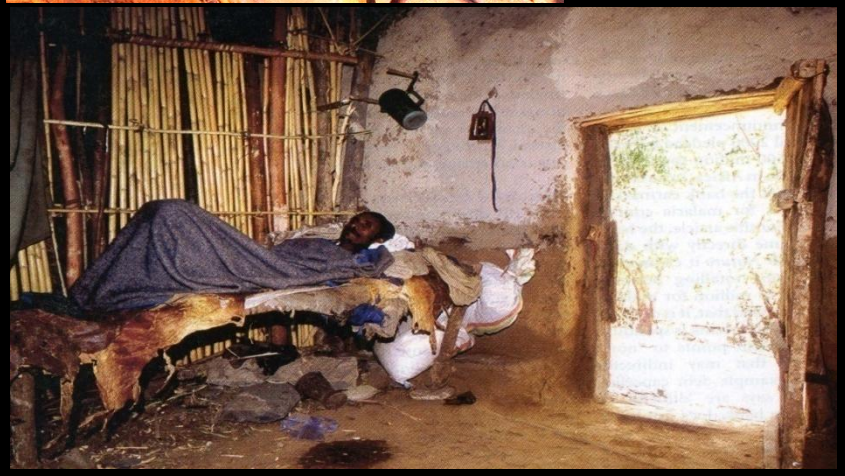


The Global Public Health Challenge Posed by Rapid Urbanization in Developing Countries

High Disease Transmission

Lack of Safe Water

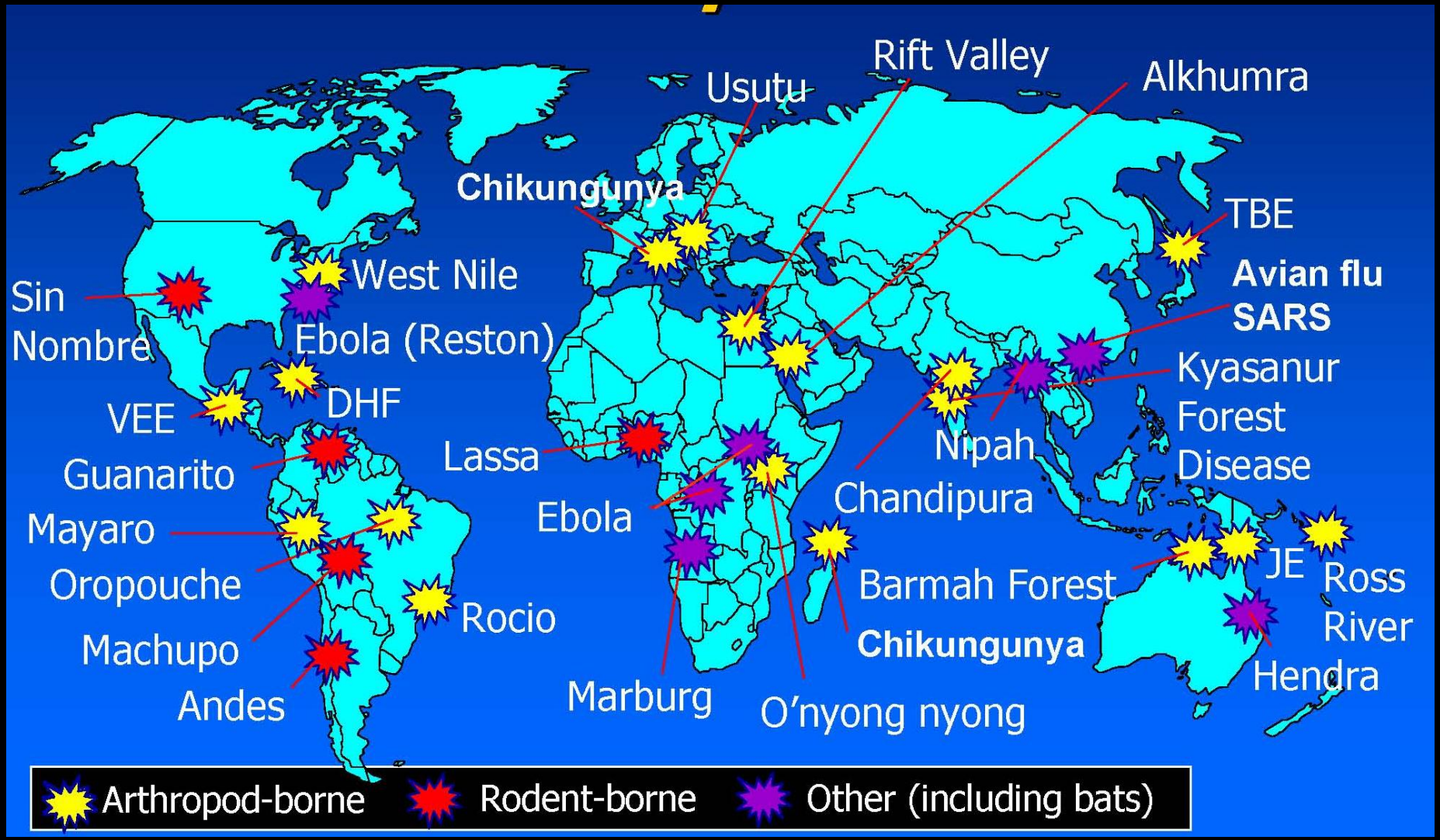
Toxic Waste



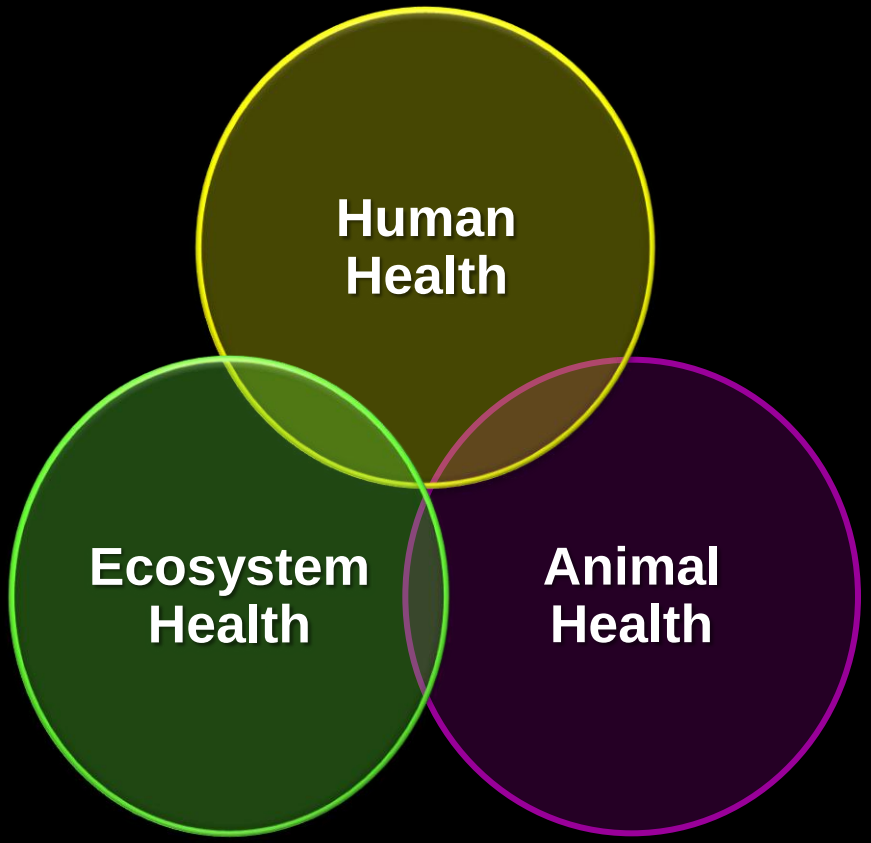
Major Deficits in Health Infrastructure

Expanded Eco-niches and Increased Zoonotic Risks

Emerging Infections:

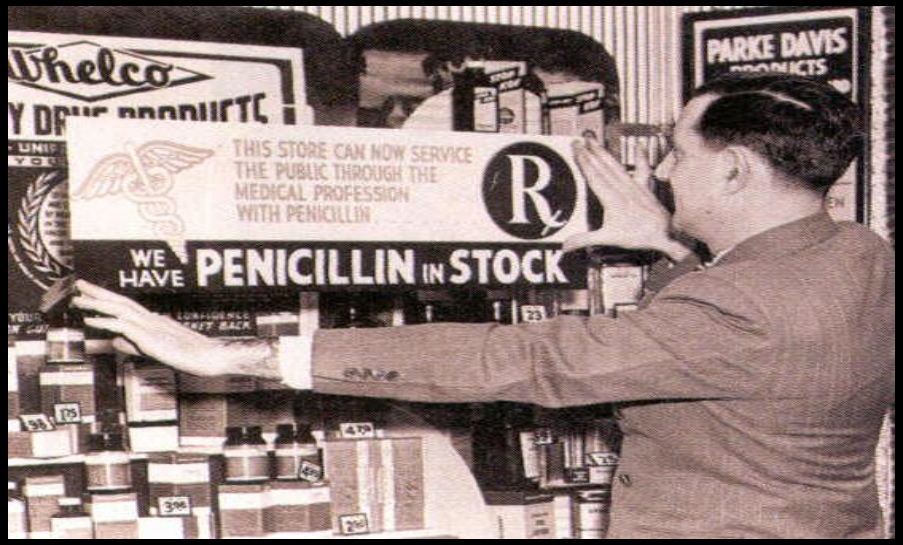


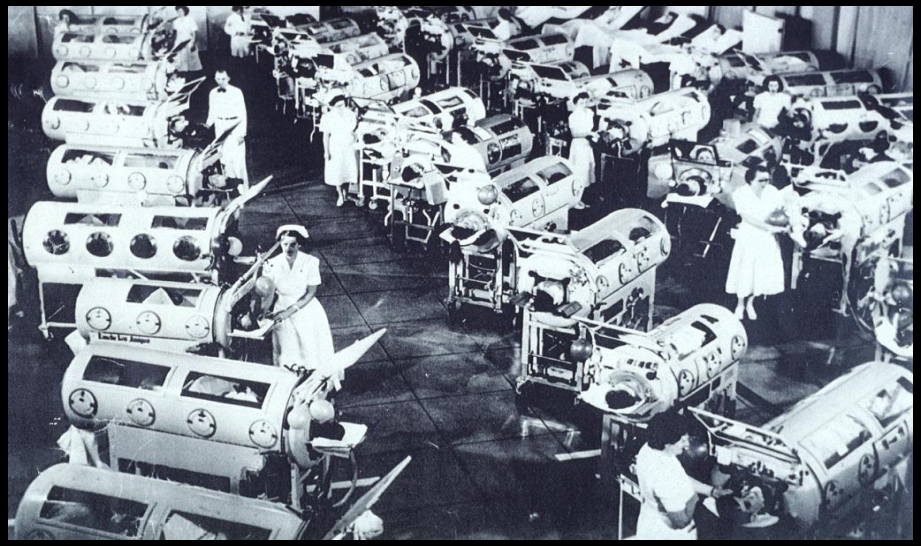
"One Health": The Rationale for Integration of Historically Separate Domains and Responsibilities



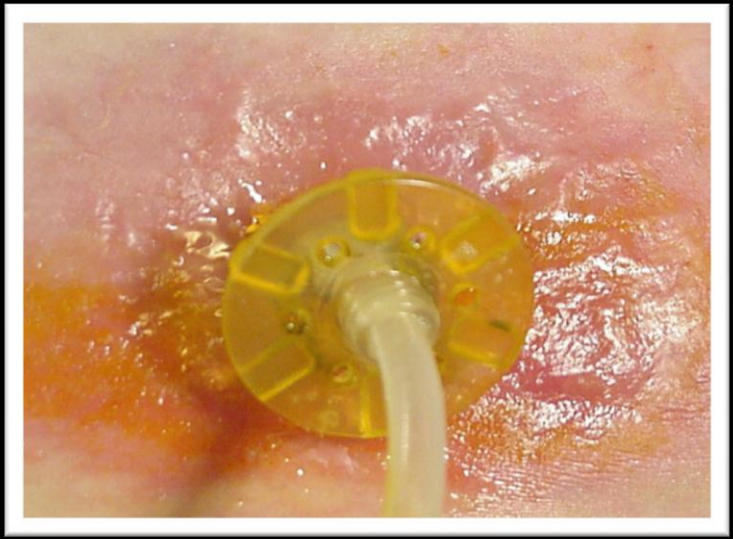
- urbanization of DCs and emergence of new zoonotic threats
- food chain as increasing source of disease risks
- enhanced agricultural productivity to support global population growth
- economic impact of agricultural disease on trade, development and resources/production footprints

Comfort and Complacency: The Enemies of Vigilance and Preparedness





NO ESKAPE!: Resistant Bugs and Few New Drugs



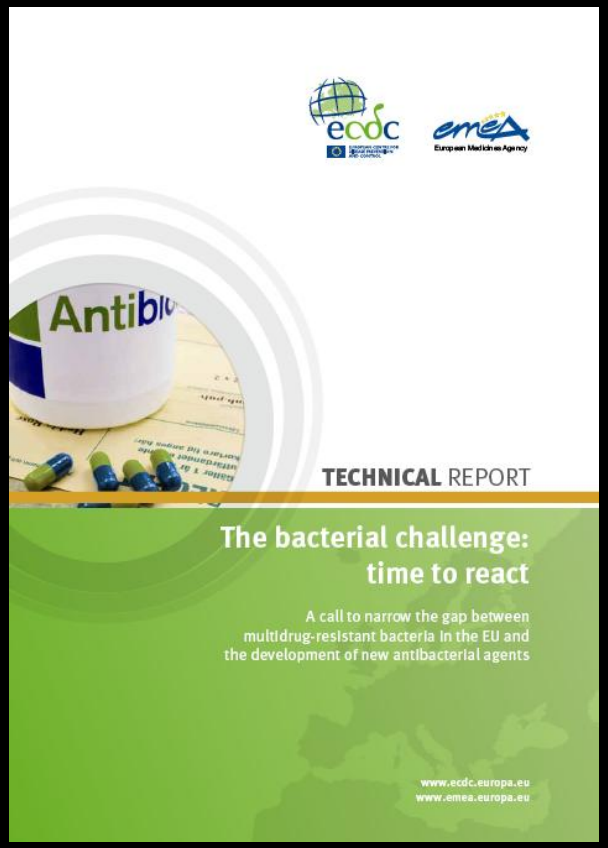
- increasing resistance in G^+ and G^- pathogens in hospital and community settings
- the **ESKAPE** pathogens
  - ***E**nterococcus faecium*
  - ***S**taphylococcus aureus*
  - ***K**lebsiella pneumoniae*
  - ***A**cinetobacter baumanii*
  - ***P**seudomonas aeruginosa*
  - ***E**nterobacter species*

The Valley of Dearth:
The Consequence of Declining R&D Investment in Antibiotic Discovery*

- 75% decrease in antibacterials approved from 1983 to 2009
- only 16 agents currently in Phase II / III clinical trials
  - only 3 as new ‘classes’ with novel mechanisms of action
  - absence of agents for therapy of AMR in G^-bacilli
  - lack of systemic agents in advanced development for organisms resistant to all current antibacterials

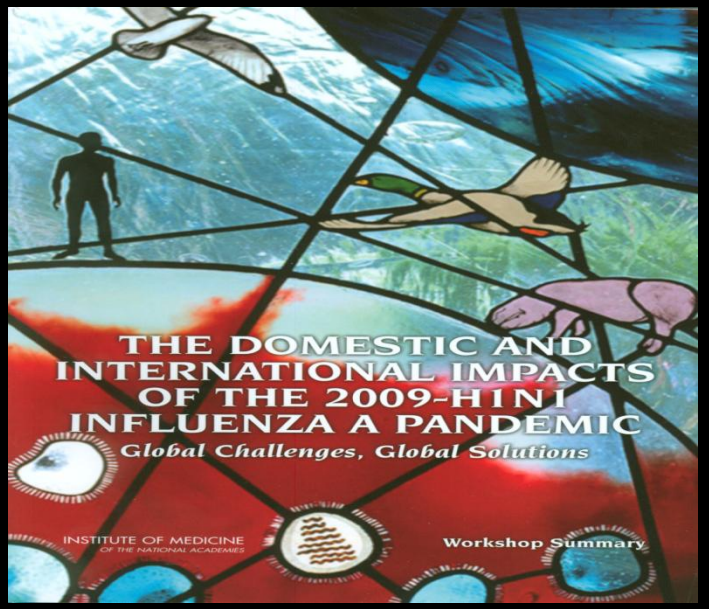
* source: H.W. Boucher et. al. (2009) Clin. Inf. Dis. 48, 1

Incentives for R&D Investment in Antibiotics



Equal Relevance to Stimulating R&D Innovation In Diagnostics, Anti-virals and Vaccines

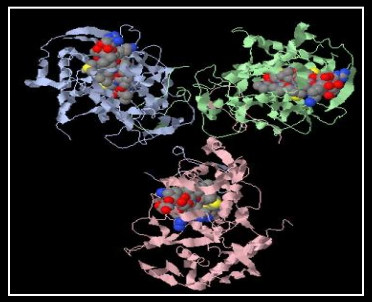
The Imperative for Innovation in Vaccine Production Technologies



"If this virus was killing more of its victims, there'd be lots of questions about whether this vaccine was produced soon enough"

Dr. Michael Osterholm
Director, CIDRAP, Univ. Minnesota
USA Today 8 Oct. 2009

Combating ‘Agent-X’
The Imperative for Innovation in Vaccine Production Technologies

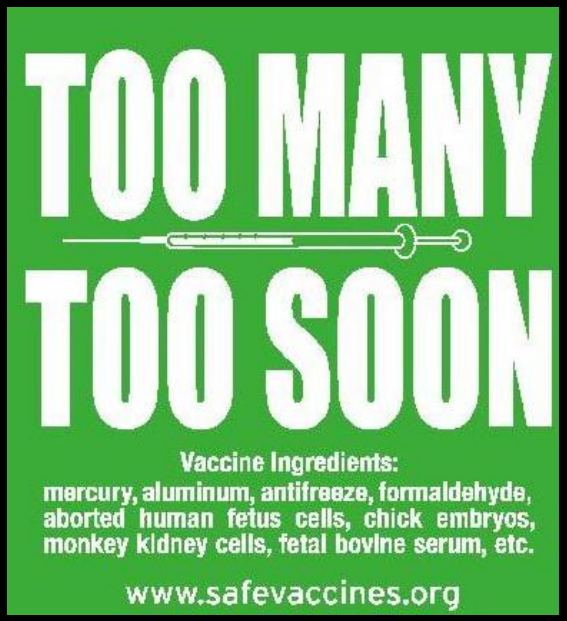


- production of the relevant epitopes by chemical synthesis versus traditional ‘biological’ production methods
- dramatic reduction in vaccine production time
- rapid scaleability and production plant flexibility versus ‘biological’ methods
- compositional uniformity of chemically synthesized antigens eliminates need for regulatory approval of individual lots (unlike biological products)

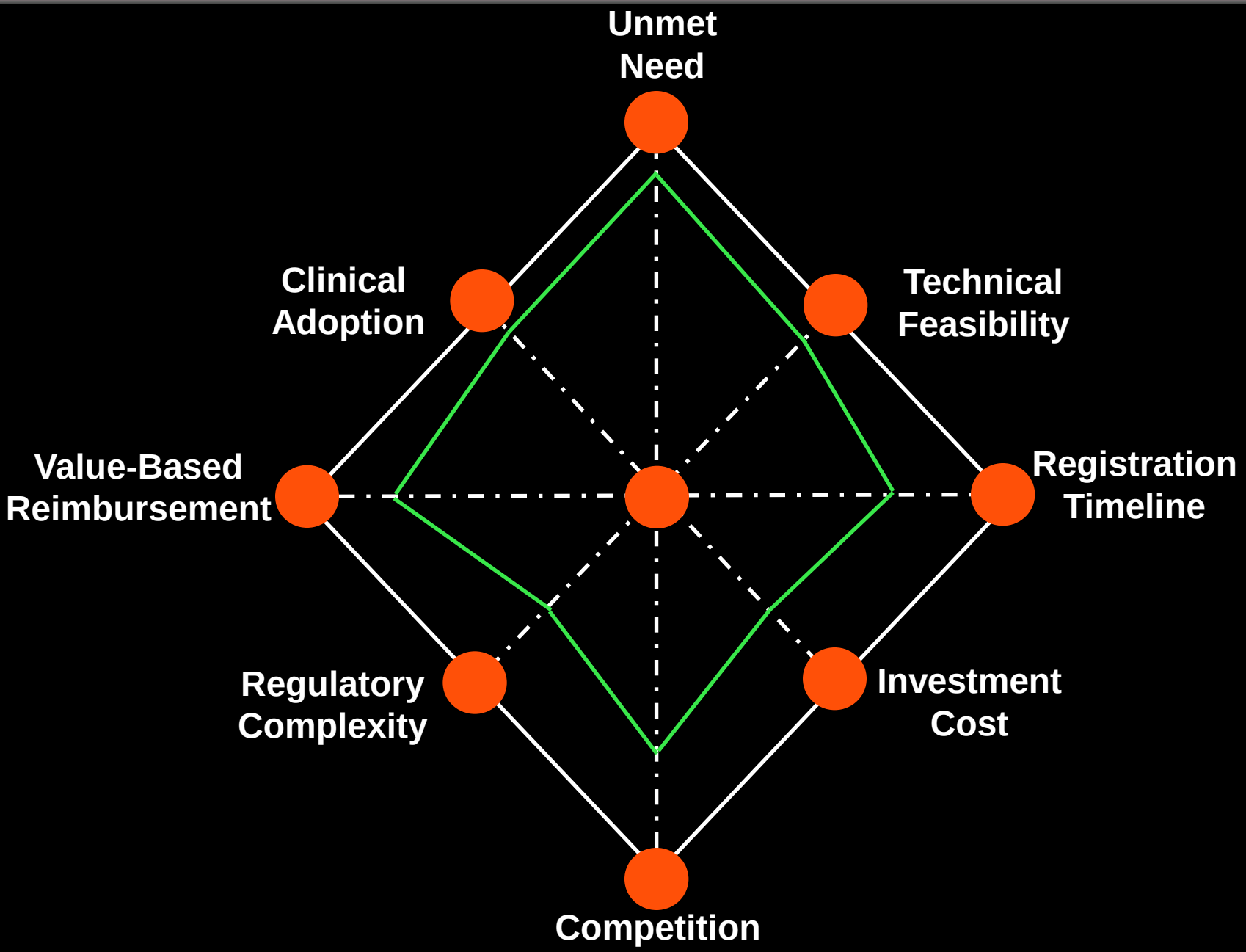
FDA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Vaccine Safety:
Media Sensationalism and Celebrity Quackery



The Strategic Environment for Antimicrobials and Vaccines



We Are Not Alone

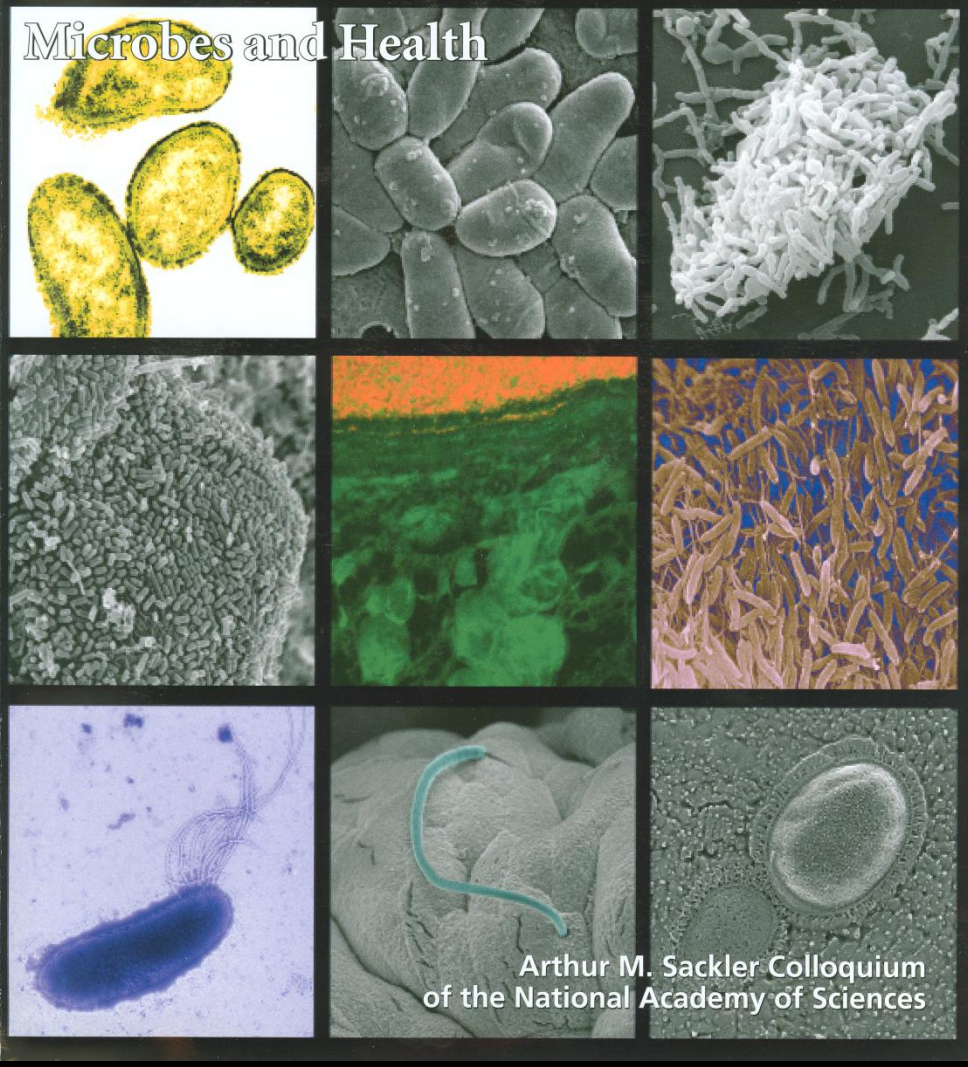
Supplement to PNAS

March 15, 2011 | vol. 108 | suppl. 1 | pp. 4513–4696

Proceedings of the National Academy of Sciences of the United States of America

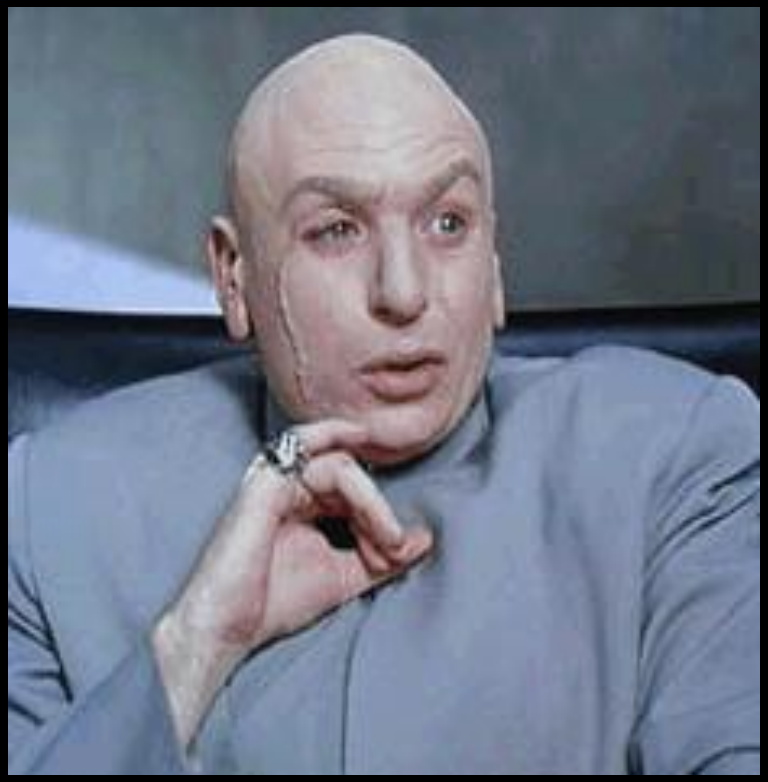
www.pnas.org

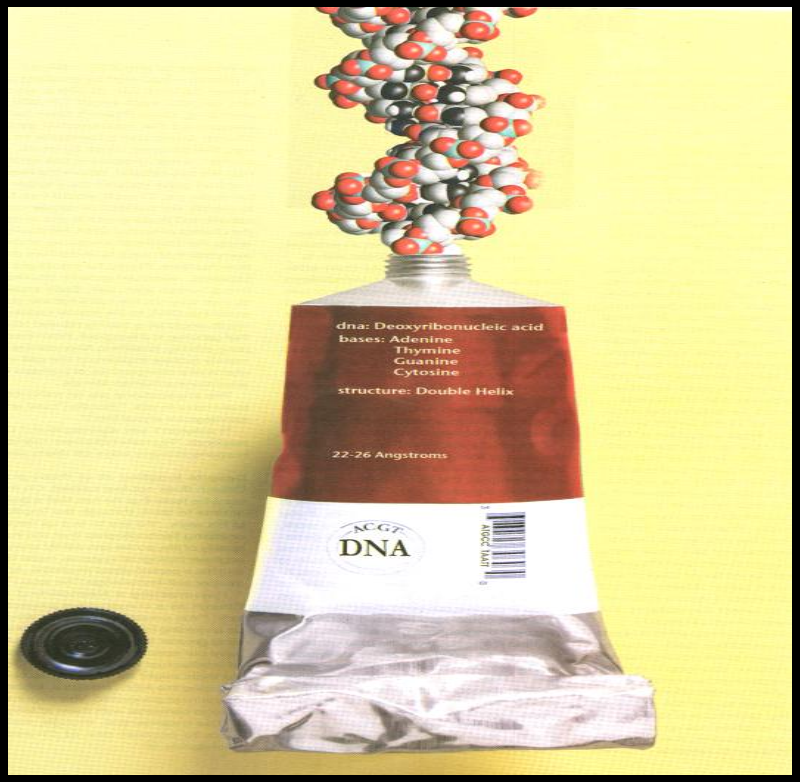
Microbes and Health



Arthur M. Sackler Colloquium of the National Academy of Sciences

New Perils?





New 'Dual-Use' Technologies

INSTITUTE OF MEDICINE AND NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

GLOBALIZATION, BIOSECURITY, AND THE FUTURE OF THE LIFE SCIENCES

THE ROYAL SOCIETY
CELEBRATING 350 YEARS

New approaches to biological risk assessment

Science Policy Centre
INTERNATIONAL WORKSHOP

web royalsociety.org/policy

twenty ten and beyond | 350 years of excellence in science

NATIONAL SCIENCE ADVISORY BOARD FOR BIOSECURITY

Strategic Plan for Outreach and Education On Dual Use Research Issues

Report of the National Science Advisory Board for Biosecurity (NSABB)

December 10, 2008

THE ROYAL SOCIETY
CELEBRATING 350 YEARS

Synthetic biology

2 and 3 June 2008

scientific
DISCUSSION MEETING SUMMARY

web royalsociety.org

twenty ten and beyond | 350 years of excellence in science

EUROPEAN COMMISSION
Community research

SYNTHETIC BIOLOGY

A NEST PATHFINDER INITIATIVE

Parliamentary Office of Science and Technology

postnote

July 2009 Number 340

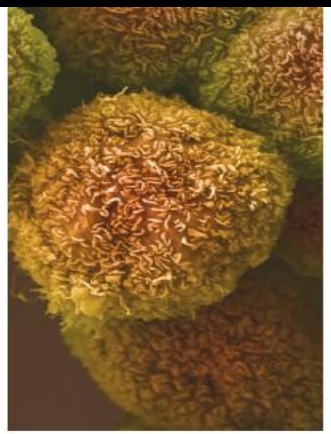
THE DUAL-USE DILEMMA

Promise or Peril?

“The War on Cancer”

National Cancer Act of 1971

December 23, 1971



Science (2011) 331, 1539

SPECIAL SECTION

INTRODUCTION

Celebrating an Anniversary

In this issue of *Science*, we commemorate the 40th anniversary of the U.S. National Cancer Act, which provided a massive stimulus for cancer research. At the start of this “Cancer Crusade,” researchers were already tackling some tough questions, as reflected in papers published by *Science* in 1971. Among them: How do abnormalities in chromosome number arise in tumor cells? Can tissue-specific markers be used to determine the epithelial versus mesenchymal origin of a solid tumor? Can the immune system be manipulated so that it recog-

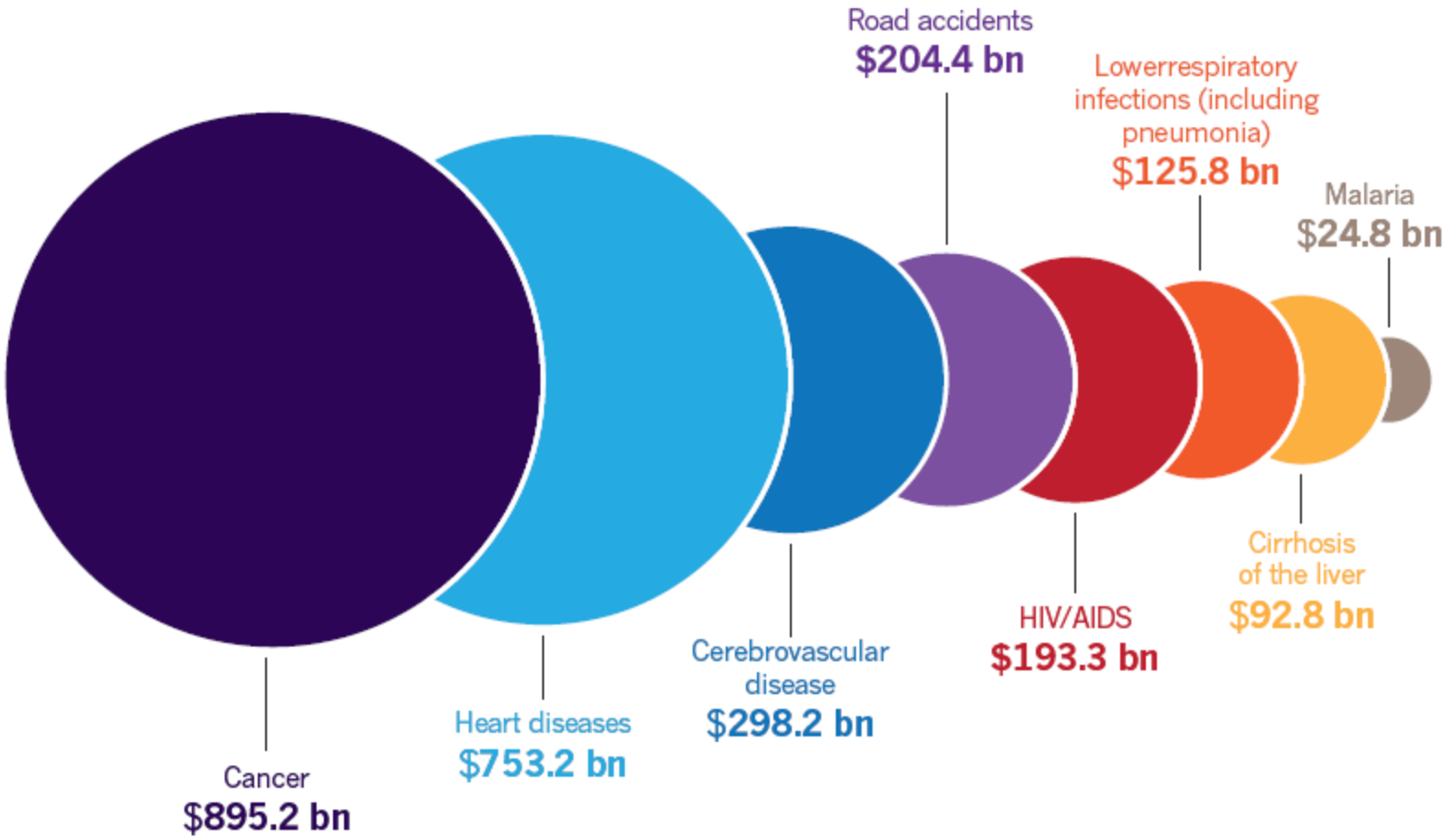
Cancer Crusade at 40

How Many Americans Will Die of Cancer Today?

- 100?
- 500?
- 1000?
- 1500?
- 2000?
- 5000?

COUNTING THE COST OF CANCER

The burden of cancer, calculated as the cost of years lost from ill-health, disability or early death, outweighs all other health concerns.



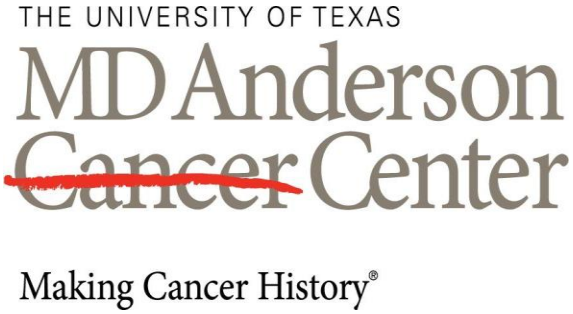
From: T. O'Callaghan (2011) Nature 471, S4

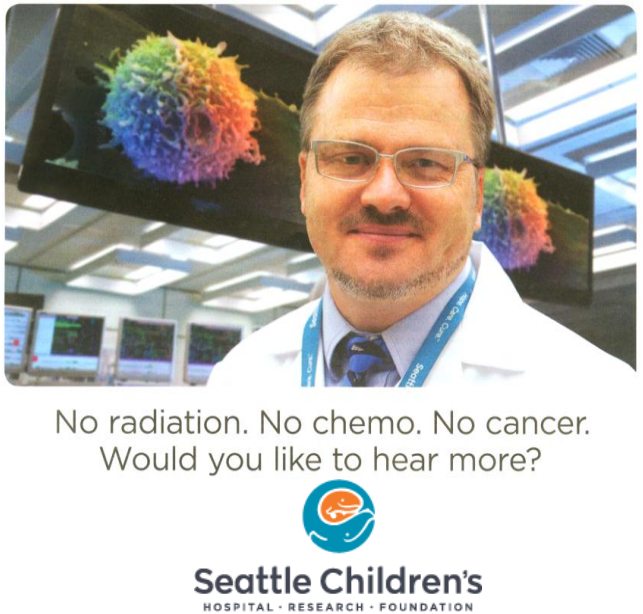
US Cancer Prevalence Estimates 2010 and 2020

Site	# People (thousands) 2010	2020	% change
Breast	3461	4538	31
Prostate	2311	3265	41
Colorectal	1216	1517	25
Melanoma	1225	1714	40
Lymphoma	639	812	27
Uterus	588	672	15
Bladder	514	629	22
Lung	374	457	22
Kidney	308	426	38
Leukemia	263	240	29
All Sites	13,772	18,071	32

From: A.B. Mariotto et al. (2011) J. Nat. Cancer Inst. 103, 117

The Ethics of Hope, Hyperbole and Hubris





The Distressing State of Investigational Cancer Drug Trials in the USA

- Armitage (1997) and IOM Reports (2010)
- less than 5% cancer patients enrolled
- unacceptable inefficiencies
  - 54% of 2685 industry/NCCN trials at 14 major centers failed to accrue single patient
  - 296 to 481 steps to activate trials by NCI-STEP and/or cooperative groups
- impact of regulatory creep
  - initiation of EC/Asia trials x2 faster than in USA
- offshore migration of clinical trials

Surging Investments in Oncology R&D*

- **861 oncology/cancer drugs in clinical trials**
- **147 equity offerings**
- **30 debt offerings**
- **117 partnerships**
- **81 licensing agreements**
- **4 PE deals**
- **158 VC deals**

*2010 data: http://edbgroup.com-globaldatareport
*PhRMA: website accessed Feb.2011

Hurdles for Regulatory Approval and Clinical Adoption of Cancer Treatments

“The bar for what we call ‘significant’ has fallen so low we risk tripping over it.”

Dr. Antonio Tito Fojo
Head, Experimental Therapeutics Section, NCI
2010 AACR Meeting cited in Oncology Times 25June 2010

Pivotal Phase III Studies Used for FDA Approval of Targeted Anti-Cancer Drugs

Tarceva (erlotinib): Genentech

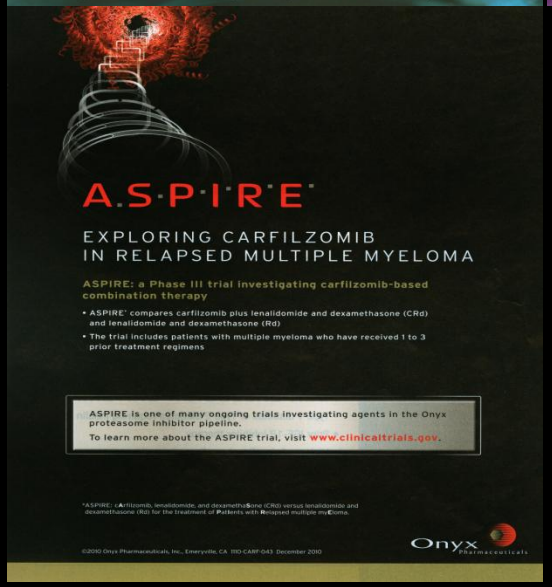
- 2005 approval for use with gemcitabine for pancreatic cancer
- increased median survival by 10 days
- J. Clin. Oncol (2007) 25, 1960

Vectibix (panitumumab): Amgen

- 2006 approval for advanced CRC
- tumor progression slowed by 5 days
- J. Clin. Oncol (2007) 25, 1658

Cancer Therapeutics:
Some Perplexing Questions

How Should the Value of Oncology Drugs Be Assessed?



UK National Institute for Health and Clinical Excellence (NICE)

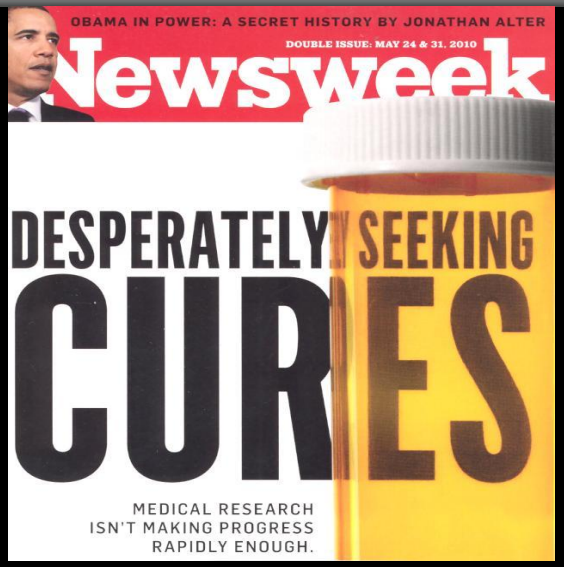
Nice Gets Nasty (or Rational?)

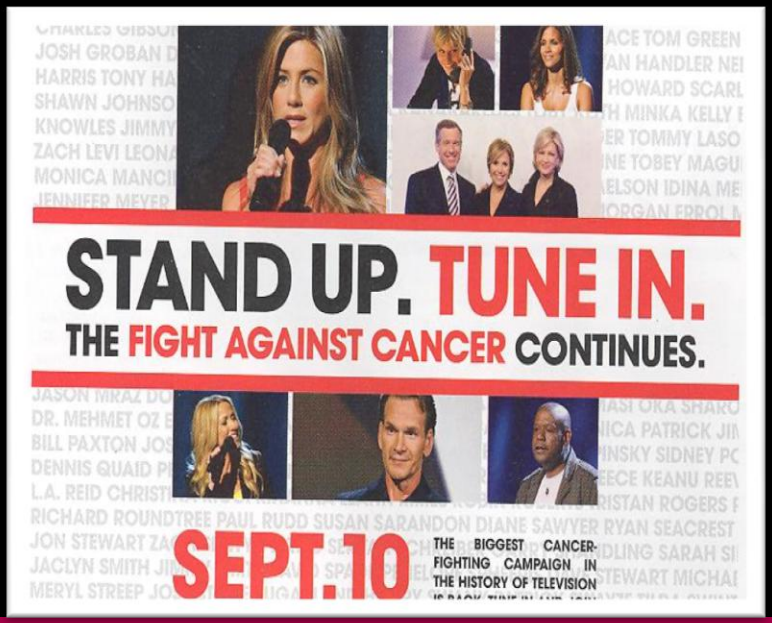
What Are We Willing to Pay for Added Months of Survival in Cancer?

Lifetime cost above standard care	If cancer is on par with other diseases ($150,000 per life year gained), months of added overall survival benefit needed	Treating cancer as worthy of much higher reimbursement ($250,000 per life year gained), months of added overall survival benefit needed
$50,000	4 months	2.4 months
$100,000	8 months	4.8 months
$150,000	12 months	7.2 months
$200,000	16 months	9.6 months
$250,000	20 months	12 months
$300,000	24 months	14.4 months
$350,000	28 months	16.8 months
$400,000	32 months	19.2 months
$450,000	36 months	21.6 months
$500,000	40 months	24 months

Source: Pink Sheet 13 Sept. 2010. Adapted from S. Ramsey FHCRC, ASCO 2010

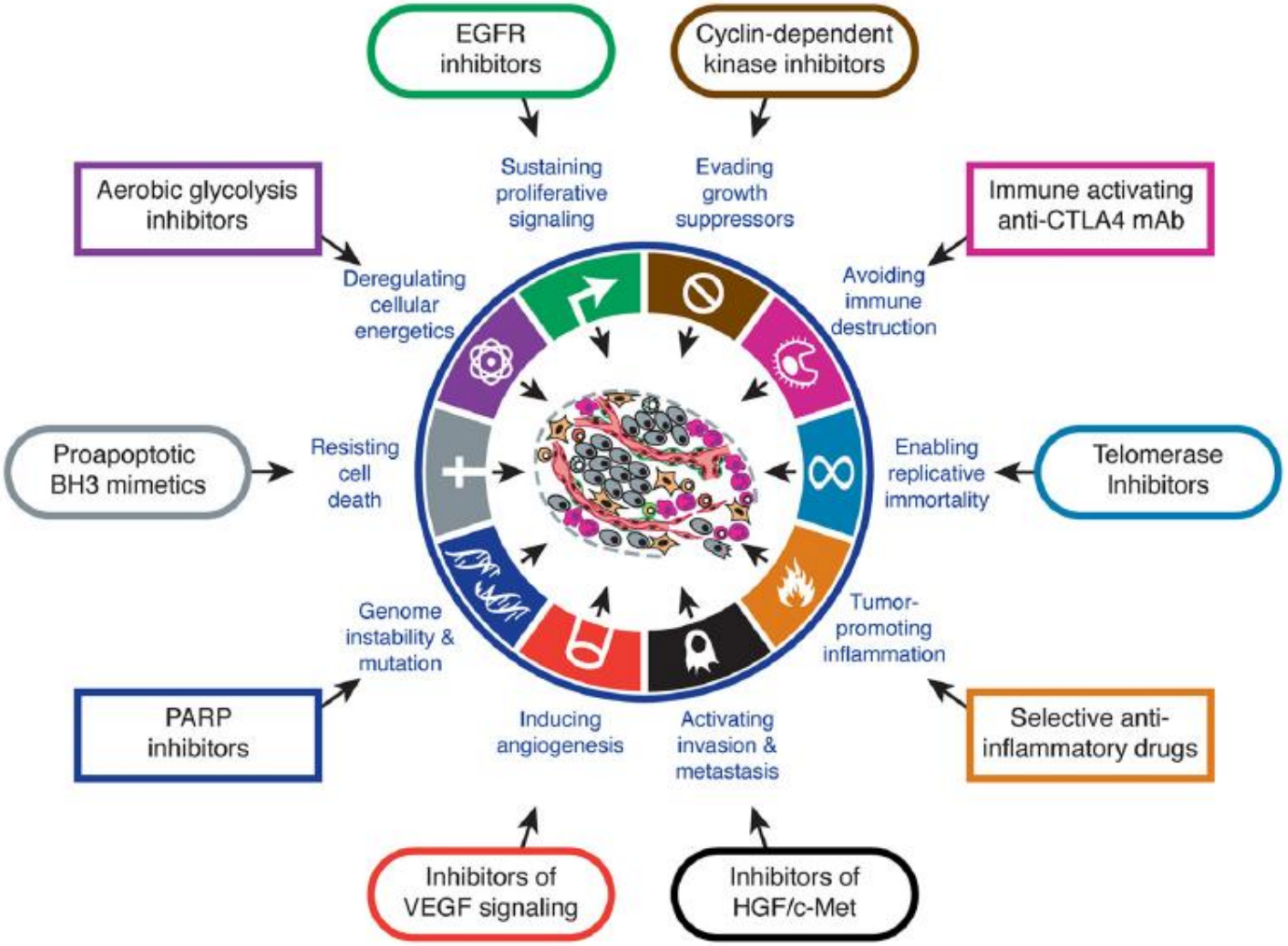

YOU'RE NOT JUST
STRENGTHENING MUSCLES.
YOU'RE STRENGTHENING
A MOVEMENT.


OBAMA IN POWER: A SECRET HISTORY BY JONATHAN ALTER
DOUBLE ISSUE: MAY 24 & 31, 2010
Newsweek
DESPERATELY SEEKING
CURES
MEDICAL RESEARCH
ISN'T MAKING PROGRESS
RAPIDLY ENOUGH.


STAND UP. TUNE IN.
THE FIGHT AGAINST CANCER CONTINUES.
SEPT.10
THE BIGGEST CANCER-FIGHTING CAMPAIGN IN THE HISTORY OF TELEVISION

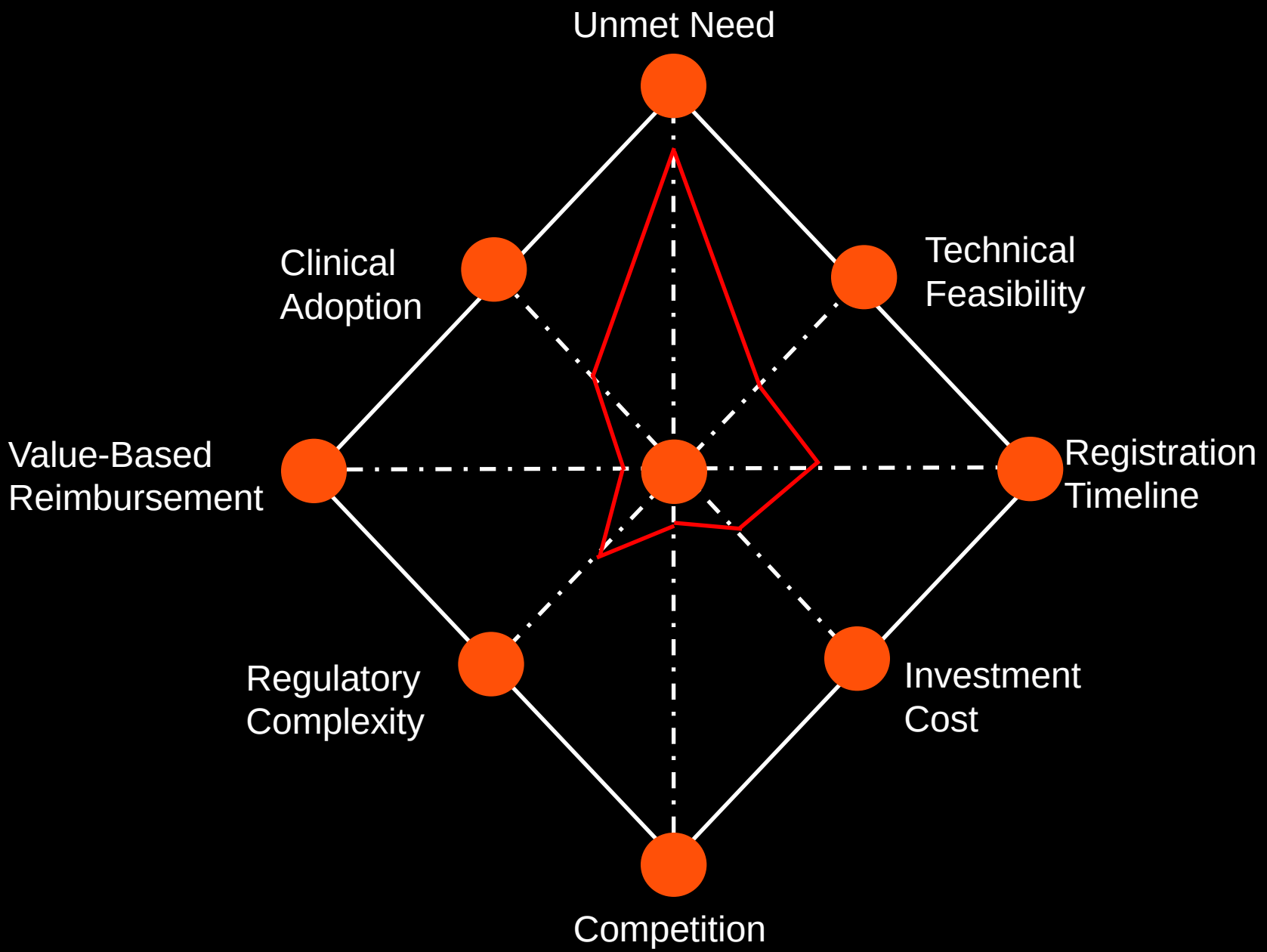

National Breast Cancer Coalition
The
Breast
Cancer
Deadline
2020
Breast Cancer Deadline
Why Now?
September 20, 2010
BreastCancerDeadline2020.org

Therapeutic Targeting of the Principal Phenotypic Hallmarks of Cancer



From: D. Hanahan and R. A. Weinberg (2011) Cell 144, 646

The Strategic Environment for New Oncology Therapeutics



Rethinking Approaches to Cancer

Is There a Fundamental Imbalance in Investment in Diagnostics Versus Therapeutics?

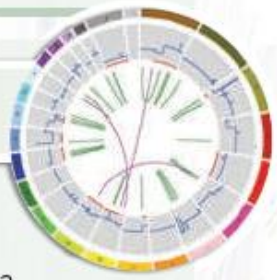
The Complexity of Cancer Genomes

LUNG CANCER
Cancer: small-cell lung carcinoma

- Sequenced: full genome
- Source: NCI-H209 cell line
- Point mutations: 22,910
- Point mutations in gene regions: 134
- Genomic rearrangements: 58
- Copy-number changes: 334

Highlights:
Duplication of the *CHD7* gene confirmed in two other small-cell lung carcinoma cell lines.

Source: E. D. Pleasance *et al. Nature* **463,** 184–190 (2010).



SKIN CANCER
Cancer: metastatic melanoma

- Sequenced: full genome
- Source: COLO-829 cell line
- Point mutations: 33,345
- Point mutations in gene regions: 292
- Genomic rearrangements: 51
- Copy-number changes: 41

Highlights:
Patterns of mutation reflect damage by ultraviolet light.

Source: E. D. Pleasance *et al. Nature* **463,** 191–196 (2010).

BREAST CANCER
Cancer: basal-like breast cancer

- Sequenced: full genome
- Source: primary tumour, brain metastasis, and tumours transplanted into mice
- Point mutations: 27,173 in primary, 51,710 in metastasis and 109,078 in transplant
- Point mutations in gene regions: 200 in primary, 225 in metastasis, 328 in transplant
- Genomic rearrangements: 34
- Copy-number changes: 155 in primary, 101 in metastasis, 97 in transplant

Highlights:
The *CTNNA1* gene encodes a putative suppressor of metastasis that is deleted in all tumour samples.

Source: L. Ding *et al. Nature* **464,** 999–1005 (2010).

BRAIN CANCER
Cancer: glioblastoma multiforme

- Sequenced: exome (no complete Circos plot)
- Source: 7 patient tumours, 15 tumours transplanted into mice (follow-up sequencing on 21 genes for 83 additional samples)
- Genes containing at least one protein-altering mutation: 685
- Genes containing at least one protein-altering point mutation: 644
- Copy-number changes: 281

Highlights:
Mutations in the active site of *IDH1* have been found in 12% of patients.

Source: E. R. Mardis *et al. N. Engl. J. Med.* **361,** 1058–1066 (2009).

http://www.nature.com/news/2010/100414/pdf/464972a.pdf

Cancer Therapeutics: Some Perplexing Emerging Questions

- is the multiplicity of pathways dysregulated in metastatic advanced disease an insurmountable technical barrier to design of poly-target (promiscuous) agent/combinations?
  - highest failure rate of new Rx in any therapeutic category (8% success)
- is the only viable strategy for mitigating the clinical, economic and emotional toll of cancer to focus on early diagnosis and removal of pre-metastatic lesions?

Successful use of MDx for Early (Pre-Metastatic) Detection in Major Cancers Will Not Eliminate Need for New Rx and Rational Rx Selection Tools

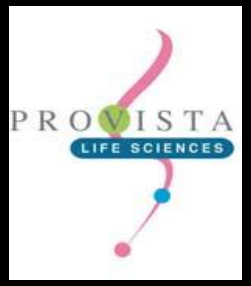
- **solid malignancies**
  - fraction of patients will still present with advanced disease due to failure to use new MDx detection platforms
- **hematopoietic malignancies**
  - distributed nature of malignant cells precludes surgical excision
  - valuable role of MDx in subtyping patients for presence/absence of Rx target(s)

A Momentous Goal:
To Dramatically Reduce The Impact of the Major Cancers

- successful early (pre-metastatic) detection/removal of cancer versus the elusive quest for a ‘cure’ for metastatic disease
  - eliminate 85% of current cancer care costs
  - dramatic reduction of the devastating physical/emotional financial toll on patients/families

Biomarkers, Biosignatures and Molecular Diagnostics: The Key Value Drivers for Personalized Medicine, Improved Healthcare and Maximizing Wellness

Cancer Diagnostics



Diagnostics M&A (2010)

Diagnostics M&A (2011)

NOVARTIS GENOPTIX® MEDICAL LABORATORY

DANAHER BECKMAN COULTER

illumina HELIXIS

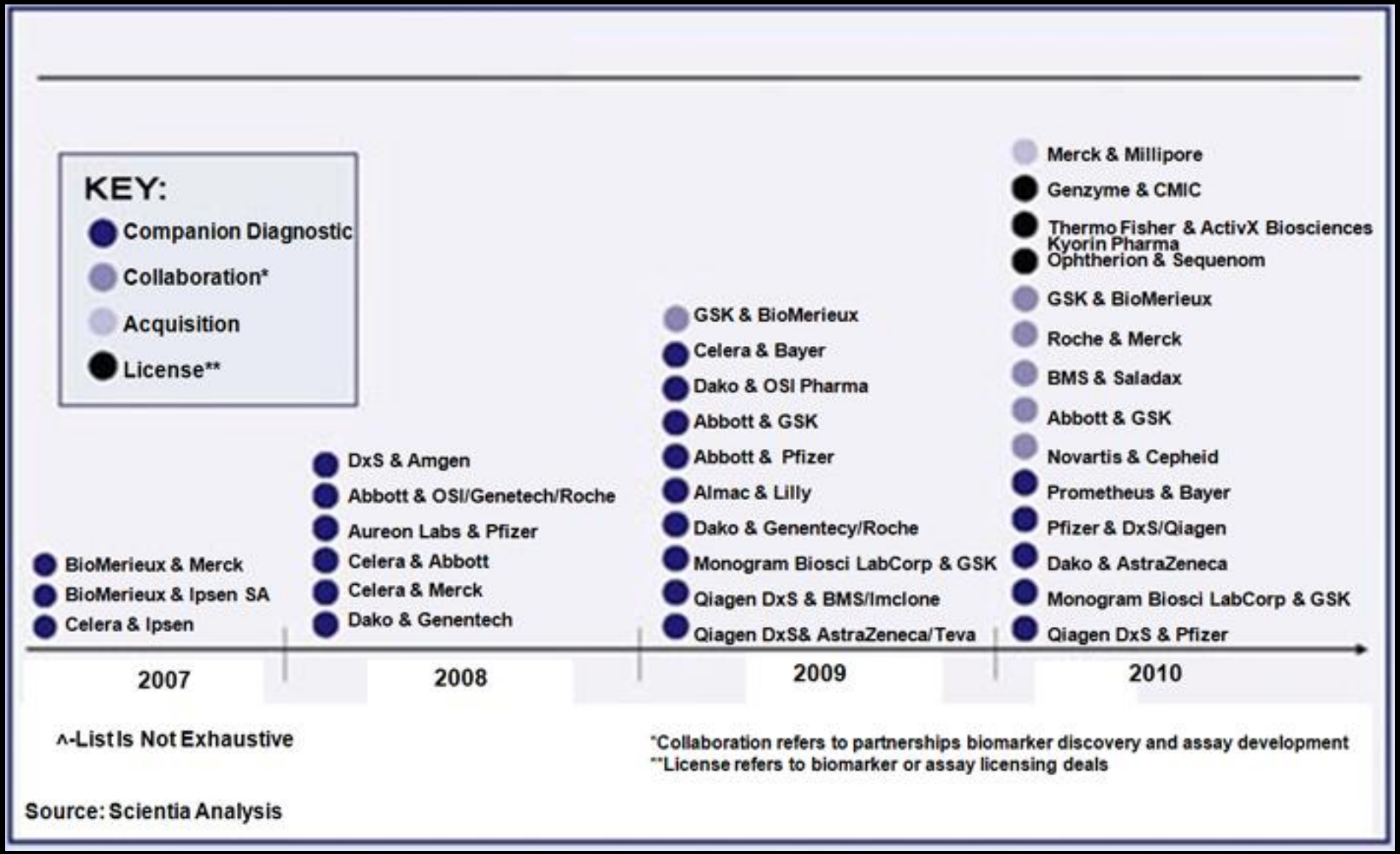
Quest Diagnostics CELERA

illumina EPICENTRE Biotechnologies

Quest Diagnostics athena diagnostics

QIAGEN Alacris Pharmaceuticals

Pharmaceutical-Diagnostics Partnerships

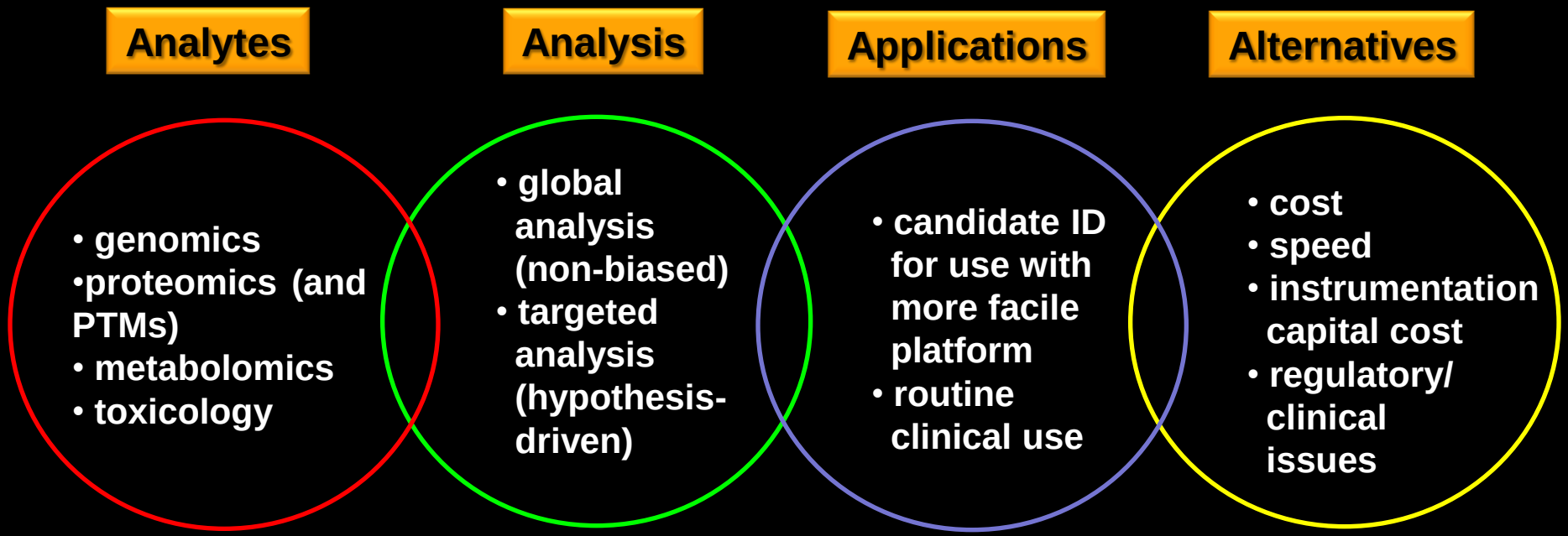


Translation of the Major Potential of Molecular Biomarkers for Diagnosis and Treatment Selection into Routine Clinical Practice

A Complex Multi-Dimensional Challenge

Success Demands a Systems-Based Approach

Platforms for Biomarker and Biosignature Profiling



Standardized Methods, Data Reporting and Database Design

GLP/GMP; LIMS/CTMS; Regulatory Dossiers

Instrumentation: Research Use Only or Approval for Clinical Use

Disease-Associated Biomarkers and Validation of Novel Molecular Diagnostics

- literature dominated by anecdotal studies
  - academic laboratories
  - small patient cohorts
  - lack of standardization
  - poor replication and confirmatory studies
- very few biomarkers subjected to rigorous validation
  - inadequate stringency in clinical phenotyping
  - case-control studies with sufficient statistical power
- widespread lack of understanding of regulatory requirements in academic research community
  - complexities imposed by multiplex tests
  - new regulatory oversight (IVDMIAs)

Biomarkers, Biosignatures and Molecular Profiling of Human Diseases

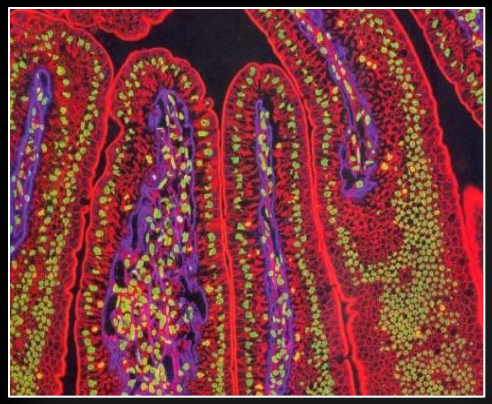
Agnostic

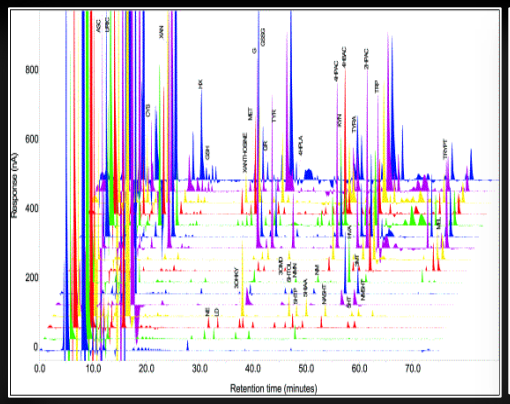
- analytes
- analytical platforms

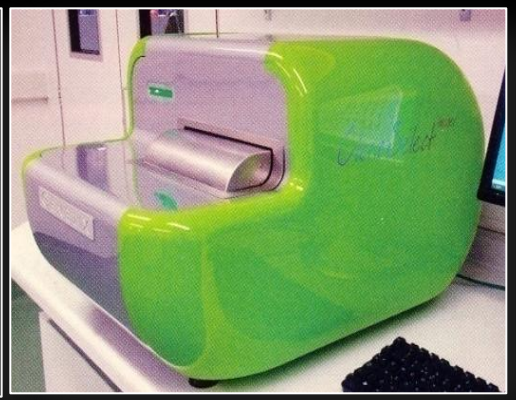
Success Determinants

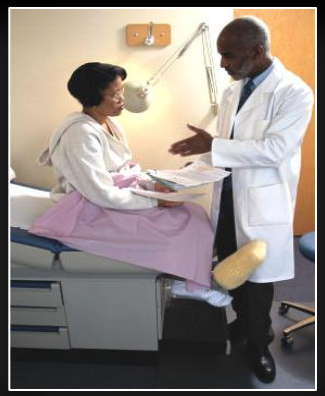
- systems-based strategies
- specimens
- standards/ standardization
- scale/statistics
- silos and sociology
- sustainability

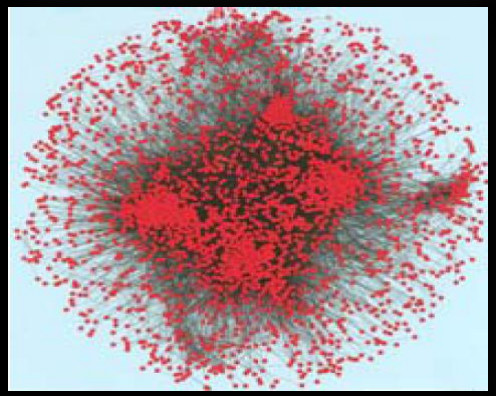
Identification and Validation of Disease-Associated Biomarkers: Obligate Need for a Systems-Based Approaches

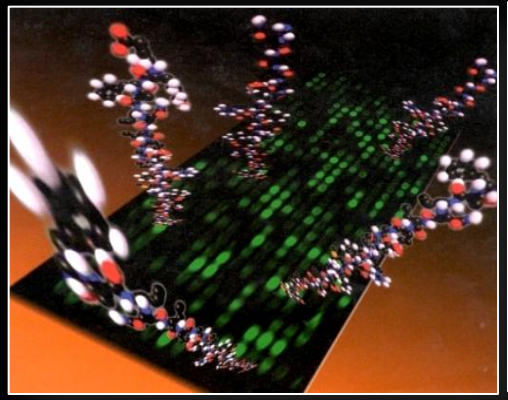


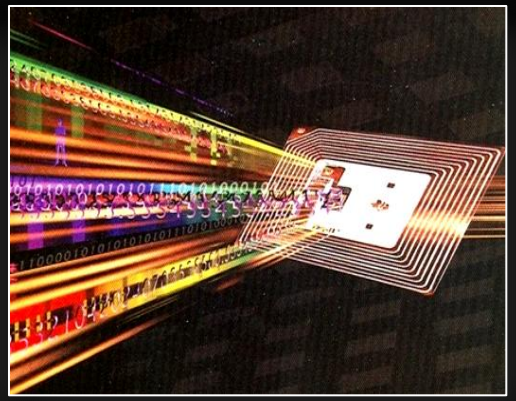












Biospecimens and Molecular Pathway Analysis

Biomarker Validation and Multiplex Assays

Instrumentation and Informatics

Clinical Impact and Patient Monitoring

Access to High Quality Biospecimens

- #1 obstacle to ID and validation of novel biomarkers
- inappropriate ‘turf’ battles over legacy specimens
  - public versus private funding
- unknown or variable quality of legacy biorepositories and limited linkage to clinical records
- historical neglect of national-level leadership/standards for biorepository specimens and management
- poorly developed protocols for systematic classification, coordination or distribution (priorities)

Quotes for Prominent Display in Every Biomarker Research Laboratory

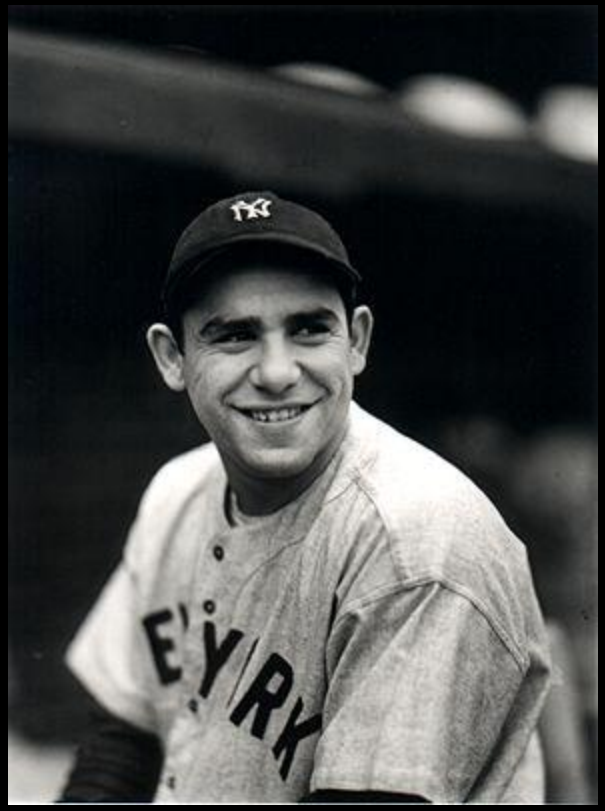
"The technological capacity exists to produce low-quality data from low-quality analytes with unprecedented efficacy."

"We now have the ability to get the wrong answers with unprecedented speed."

Dr. Carolyn C. Compton
Director, Office of Biorepositories and Biospecimen Research
National Institutes of Health
'10M, July 2010'

Validation of Disease Associated Biomarkers

- disease related differences are small compared to biological variability
- many variables behave as QTLs with graded continuum rather than binary normal: disease separation
- the high dimensionality small sample size (HDSS) problem
  - high number of variables (2000-10000) and low sample size (10-100)
  - increased risk of selection of variables due to chance (overfitting)
- standardization and statistical powering of validation studies
  - “the 20:200:2000 rule”
- new regulatory complexities for multiplex ‘signatures’



“We may be lost,
but we’re having a good time”

Yogi Berra

New Diagnostic Technologies: A Neglected Area of Biodefense and Biosurveillance

- faster Rx
- accurate Rx
- prophylactic Rx for incident personnel

- robust triage
  - rationing
  - reassurance of "worried well"
  - quarantine decisions

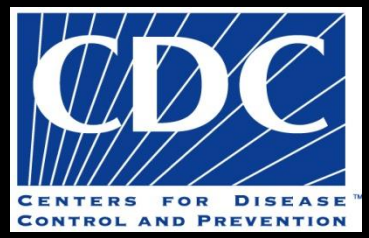
- real time disease surveillance data
- faster ID of incident evolution
- faster incident containment and exposure controls

The Single Most Important Leverage Point For Rapid Mobilization of Resilient Responses to Epi-/Pan-demics and WMD Bioterrorism

Global Surveillance Against Infectious Disease Outbreaks
E.H. Chen et. al. (2010) PNAS 107, 21701

- 398 WHO-verified outbreaks 1996-2009
- median times
  - 23 days for event detection
  - 32 days for public communication
  - 35 days for official laboratory confirmation
  - 48 days for inclusion in WHO Disease Outbreak News

Global Disease Surveillance



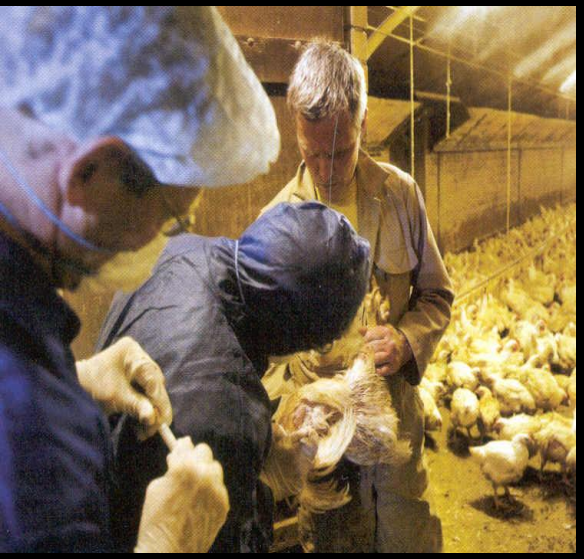
EMERGEncy ID NET

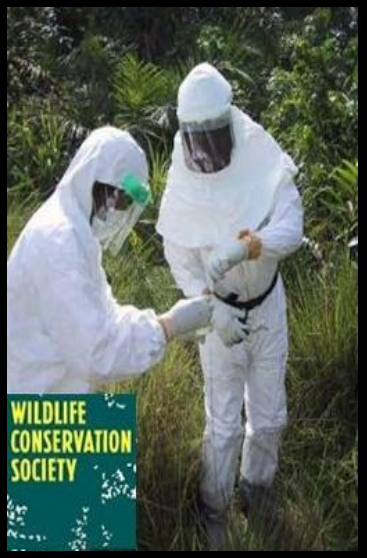
Public Health Department's Surveillance

U.S. Influenza Sentinel Provider Surveillance Network

Quarantine Activity Reporting System (QARS).

Geodemographic Information Systems (GIS): Real-Time, Front Line, Ground Zero Data from Field Sampling and Sentinels

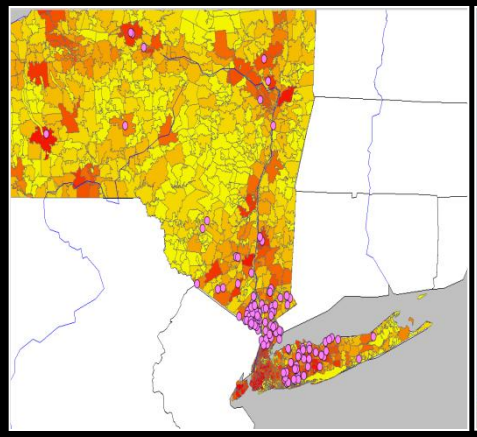


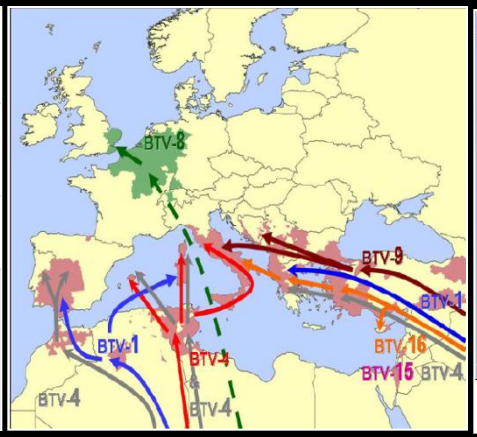


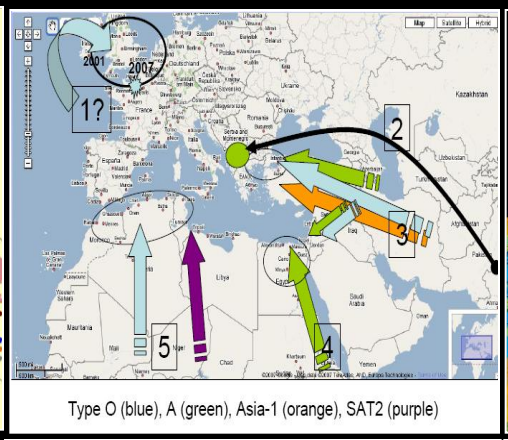
Geodemographic Information Systems: Mapping Disease Patterns and Modeling Trends

Anomaly Detection and Early Alert

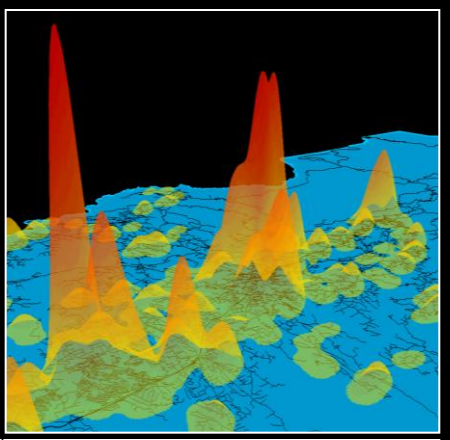
Disease Progression

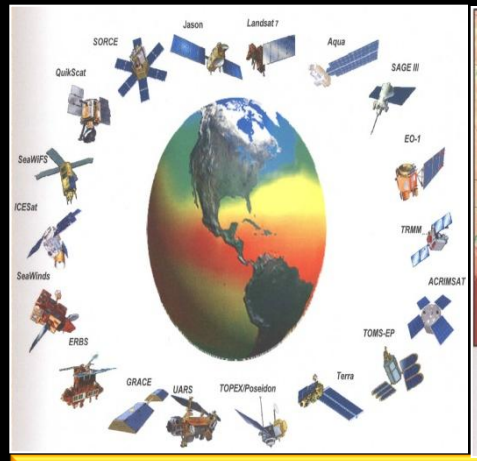


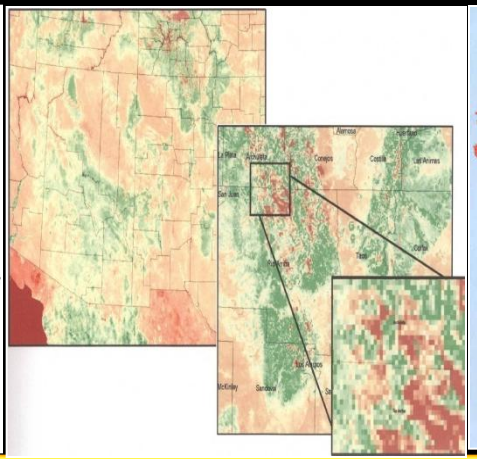


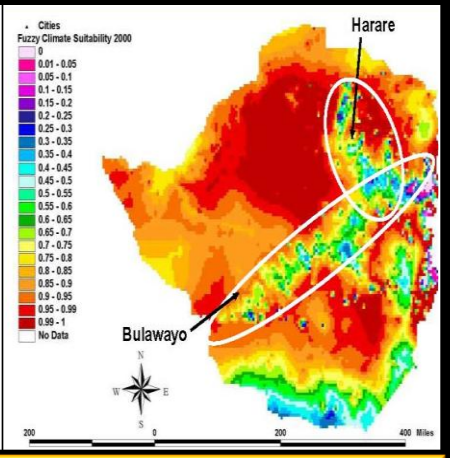


Type O (blue), A (green), Asia-1 (orange), SAT2 (purple)









Satellite Surveillance and Predictive Modeling of Disease Trends


HealthMap
Global Disease Alert Map
English | Español | Français | Português | Русский | 中文 | بية
NEJM H1N1 Case Reports | About | Twitter | Blog | Donate | Store | Feedba
Map
Satellite
Earth
Terrain
Greenland
Iceland
Россия
Russia
Canada
Mongolia
China
North Atlantic Ocean
Algeria
Libya
Mali
Niger
Chad
Sudan
Brazil
Perú
Bolivia
Chile
Argentina
Angola
Madagascar
South Pacific Ocean
South Atlantic Ocean
Indian Ocean
Australia

Remote Health Status Monitoring

Biosignature Profiling Via Sensors and Devices

m.Health

Remote Health Monitoring and Chronic Disease Management

Lifestyle and Fitness

Information for Proactive Health Awareness (Wellness)

Convergence

- MDx, Rx and Ix
- MDx, devices, telecommunications
  - m.Health, remote health status monitoring
- social networks and consumer/patient empowerment
- large scale healthcare data integration, mining and content services
- new players, new partnerships, new delivery pathways

Productivity

Yesterday,
…..it Seems So Far Away”™*

*The Beatles, Apple Records, 1965

Challenges for Sustained Rx Product Flow

- inefficient translation of academic research
  - commercialization education (Kauffman)
- retreat at VC from early stage discovery/pre-POC development assets
  - valley of dea(r)th
- R&D reductions in bigPharma and impact of economic downturn on biotech sector
- complexity of chronic diseases and no prospect of enhancing asset success rate and/or truncation of R&D cycle time
- regulatory uncertainties and increasing hurdles
  - larger trials, risk and REMs
  - increasing inflexibility
  - inadequate budgets, staffing and science

Is the Productivity Decline Due to Organizational/Inefficiencies or Deeper Technological, Economic and Regulatory Challenges?

Shrink It, Cure It!

"Will fragmentation of Big Pharma R&D into multiple small units boost productivity?"

Robert Langreth
Forbes 17 January 2011

Realigning Deck Chairs Without A Map of the Icebergs!

"The core problems afflicting drug firms isn't bureaucracy but a lack of deep understanding of disease biology. How you organize isn't going to solve that."

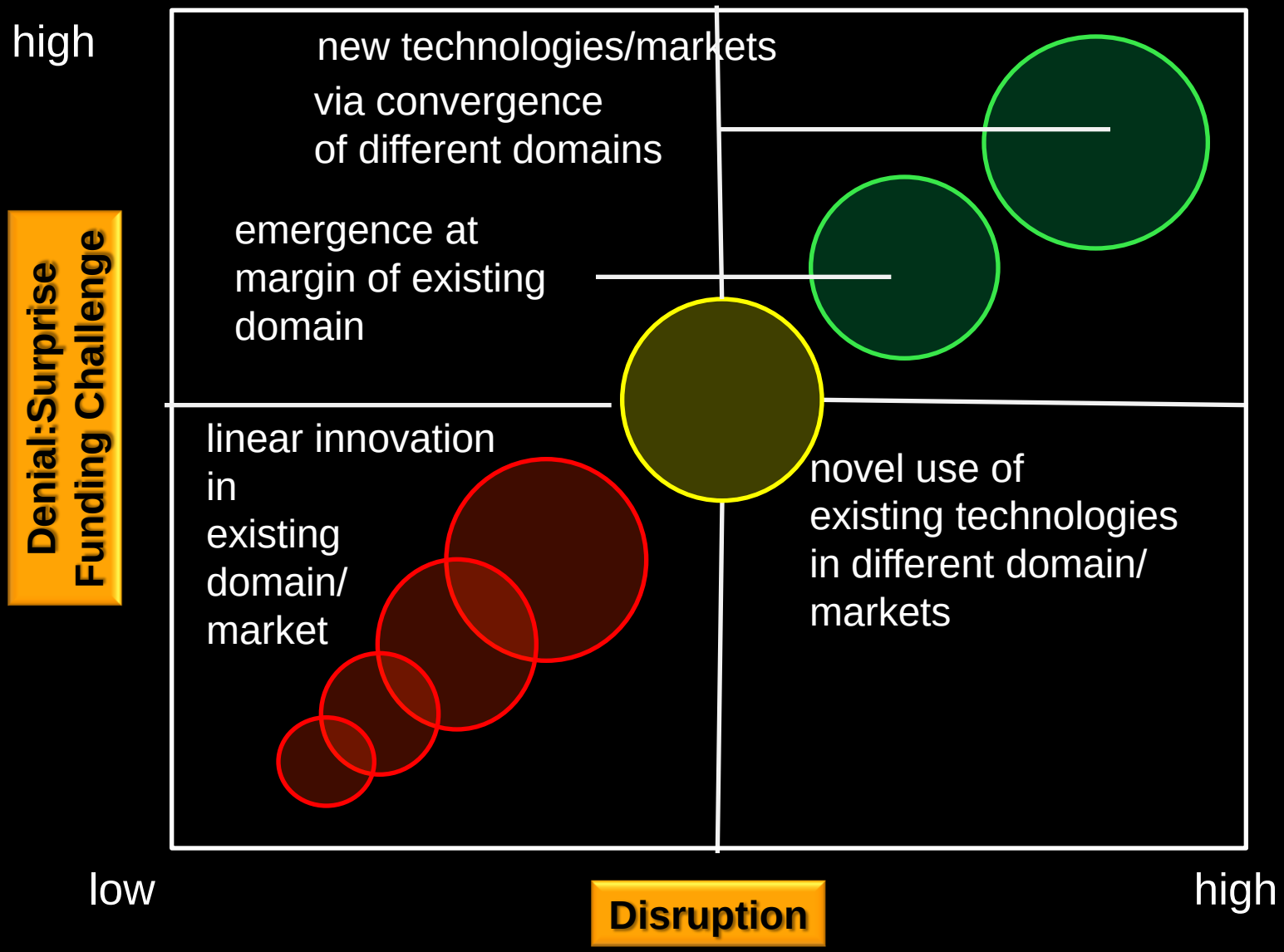
"Biotech companies are no better than Big Pharma at inventing drugs."

Gary Pisano, Harvard Business School
cited in Forbes 17 Jan. 2011

The (Bio) Pharmaceutical Industry and Adapting to New Realities in Healthcare

- from proof-of-concept (POC) to proof-of-relevance (POR)
- increasing emphasis on outcomes and comparative effectiveness as core elements in reimbursement pricing
- focus on outcomes puts further strain of ROI in drug development
- selection of patient populations by MDx profiling is only avenue to address outcomes challenge
  - premium pricing for ‘guaranteed outcomes’
  - use of MDx test post-approval to identify eligibility for Rx

The Innovation Matrix



Disruptive Innovation

- (bio)pharmaceutical and traditional device companies have been slow (and most still are) to recognize the momentum of personalized medicine and the strategic disruption of new diagnostic technologies
- the key components of healthcare (physicians, providers, payors) are ill-prepared organizationally and operationally to respond to intensifying economic and social pressures for better value, improved treatment outcomes and cost control

Disruptive Innovation in Healthcare: Redefining the Value Equation in Healthcare

PRECISION DIAGNOSIS

molecular taxonomy of disease

BETTER CARE AT LOWER COST

managing risk, cost and quality

health status monitoring

EARLIER DISEASE DETECTION AND RESPONSE TO RX

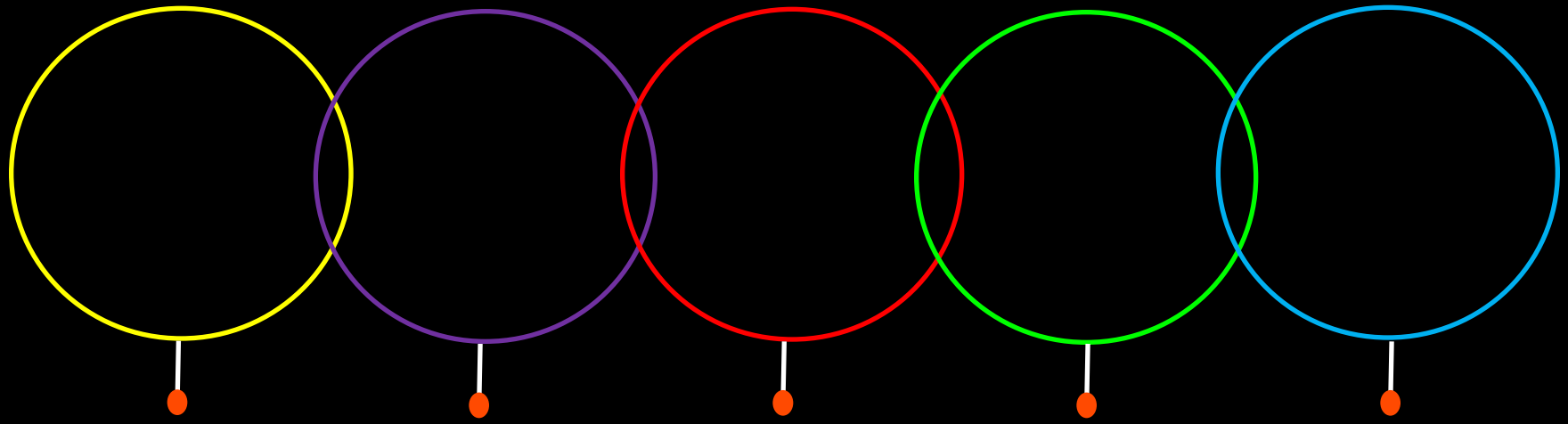
optimized decisions

TREATMENT PERSONALIZED TO THE PATIENT

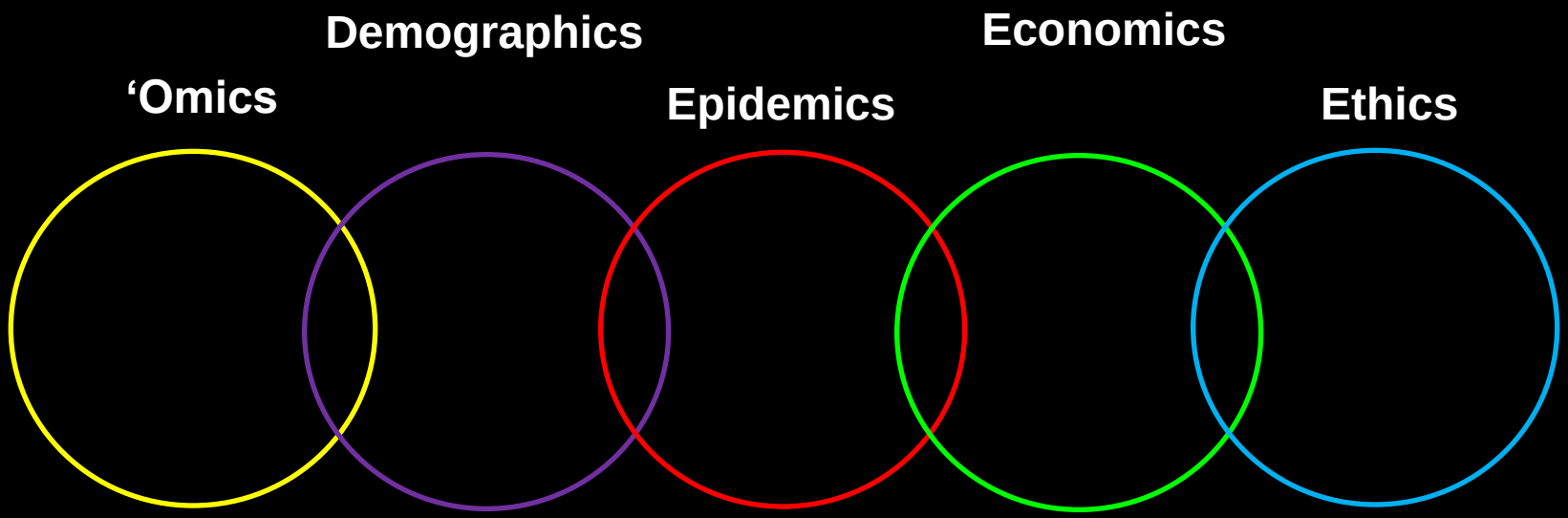
Integration of Previously Separate Domains: Driving Disruption

Informatics:
The Foundation for Greater Efficiency in Healthcare Delivery
and
Improved Translation of Research Discoveries to Clinical Use

Five "-ics"
The Complex Inter-Relationships Shaping the Future of Healthcare



'Omics	Demographics	Epidemics	Economics	Ethics
• mechanisms of disease • molecular diagnostics • rational Rx	• aging • remote health monitoring	• urbanization • food/water resources • instability and conflict	• cost/quality of care • R&D investment incentives	• access to care • affordability • personal accountability for risk mitigation • privacy • behavioral genetics • dual-use technologies
personalized medicine	**m.Health**	**global public health**	**value**	**values**



Informatics

Assembly, Integration and Analysis of Massive Data

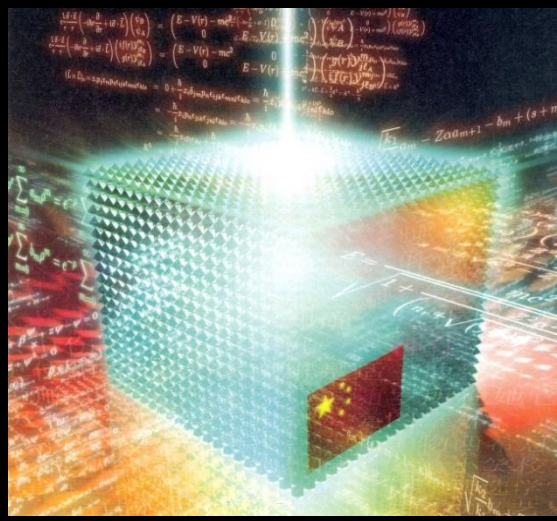
- better diagnosis and treatment decisions (individuals)
- population data and evidence-based guidelines for best practices (health professionals)
- improved allocation of scarce/expensive resources (society)
- global health surveillance and risk reduction (global)
- acceleration of research discoveries and translation for improved care (academia, government, industry)

“Managing Mega-Data”

volume

scale

global networks



multiscale heterogeneity

integration

Big Genomics

- cost reduction and rapid acceleration of sequence datasets
- 1000 Genome Project (2010) generated more data in 6 months than GenBank accumulated in 21 years
- sequence data generation outstripping analytics
- NGS storage as high-resolution images imposes disproportionate archiving burden
  - shift to discard raw data and easier to resequence samples (assumes availability)
- data analytics and bioinformatics personnel as major choke points for using large scale profiling studies
- current software is not scalable
- cloud computing

REPORT TO THE PRESIDENT AND CONGRESS

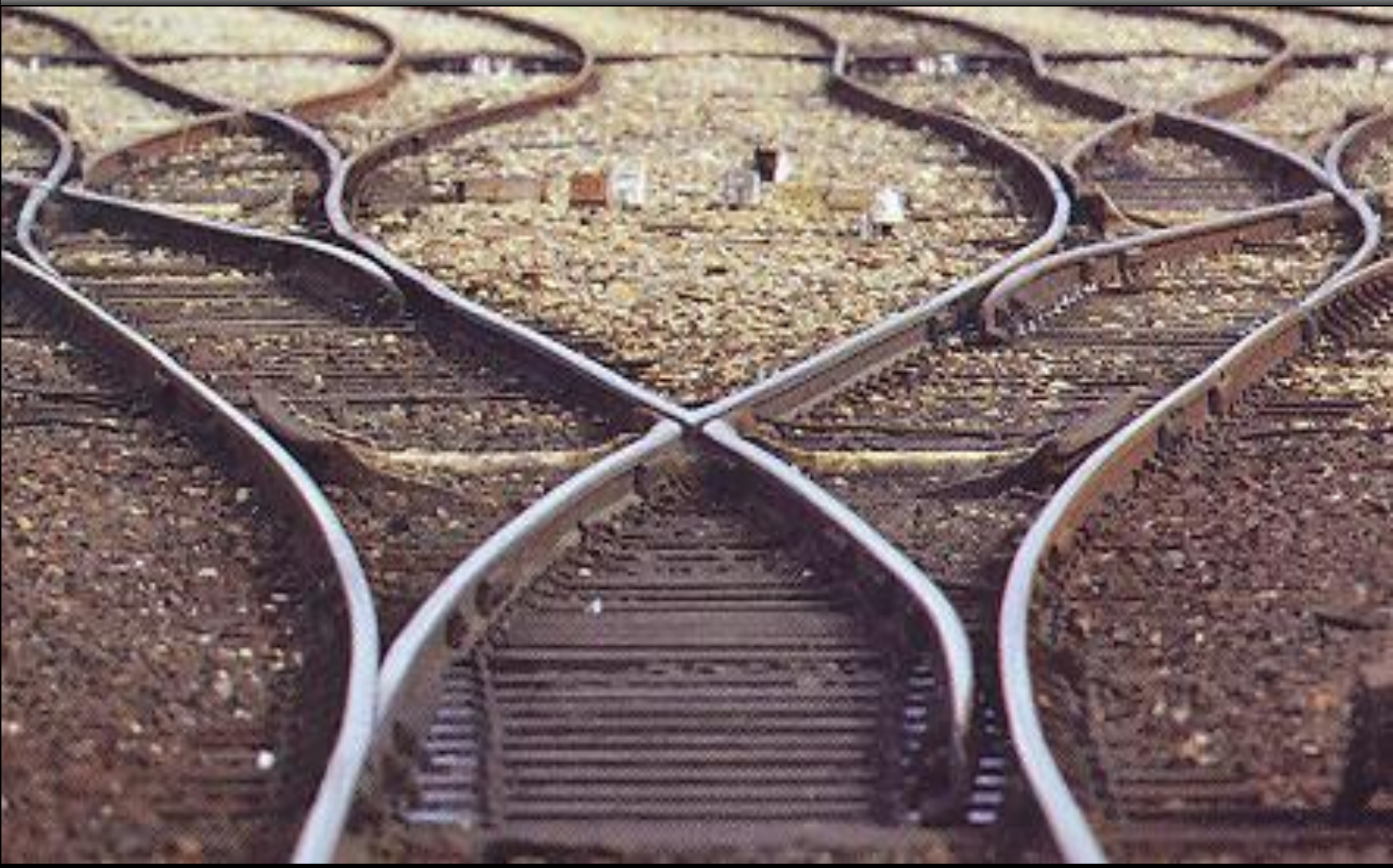
DESIGNING A DIGITAL FUTURE: FEDERALLY FUNDED RESEARCH AND DEVELOPMENT IN NETWORKING AND INFORMATION TECHNOLOGY

Executive Office of the President

President's Council of Advisors on Science and Technology

DECEMBER 2010

thr mst b a futr, rt?



A Strategy for Science & Technology" Soundbite or True Strategic Inflection?

"We need to out-innovate, out-educate and out-build the rest of the world."

"This is our generation's Sputnik moment."

"We need to celebrate not just the super bowl winners but our scientists."

State of the Union Message
January 25, 2011

The Imaginot Line

- leadership delusion that current pre-eminence can be sustained with existing (historical) approaches
- comfort and complacency and catastrophic hubris
- the poverty of imagination and agility
  - ideas
  - incentives
  - institutions
  - ideology

The Missing Near Future: The Futurists Lament

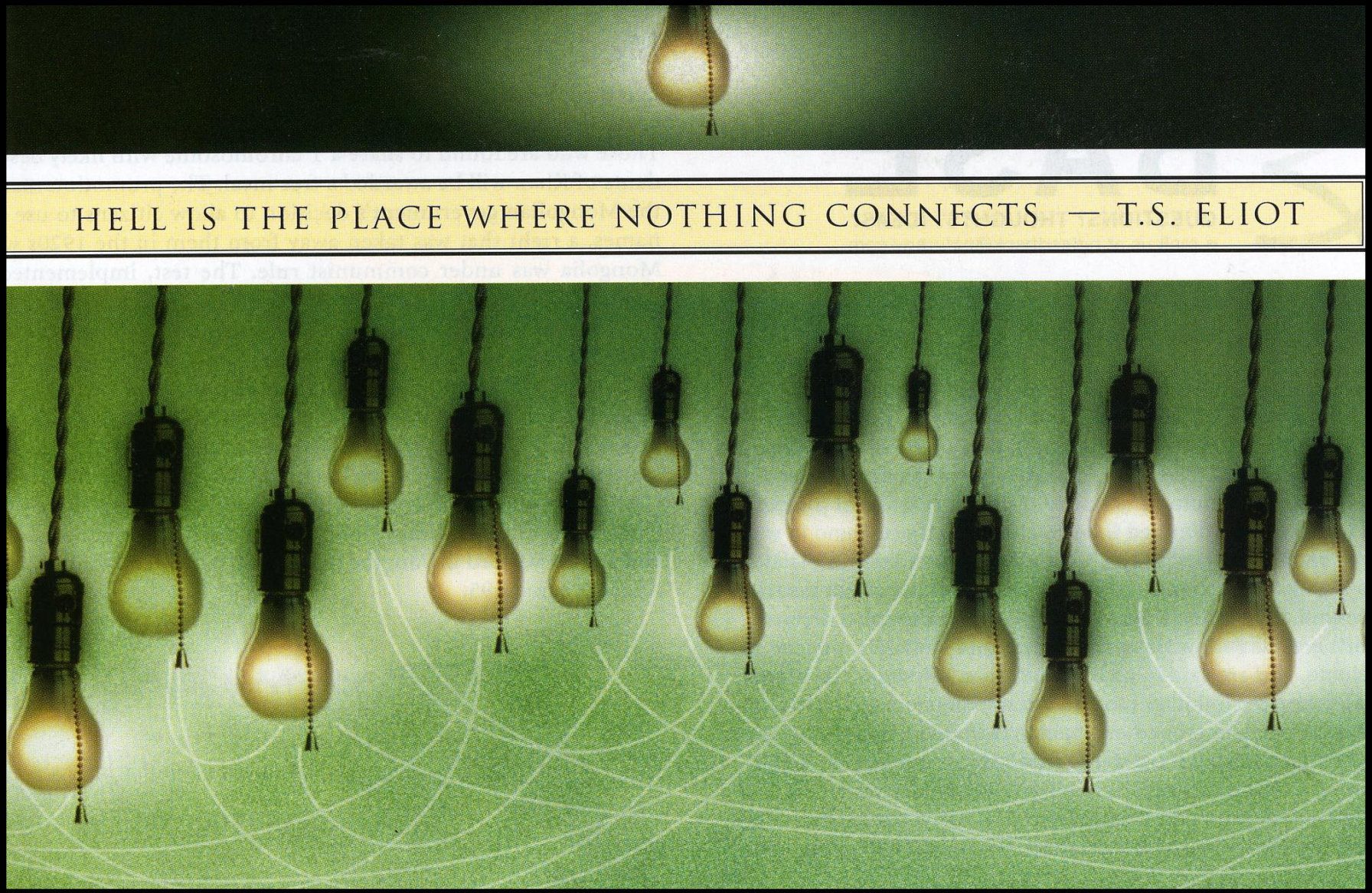
- "why have we lost our ability to imagine the world of the near future (2020)?
  No version (of the near future) seems desirable and plausible."

Kevin Kelly

- "The now is too unstable to provide a satisfactory platform for extension into the future.
  There are too many wild cards too much complexity."

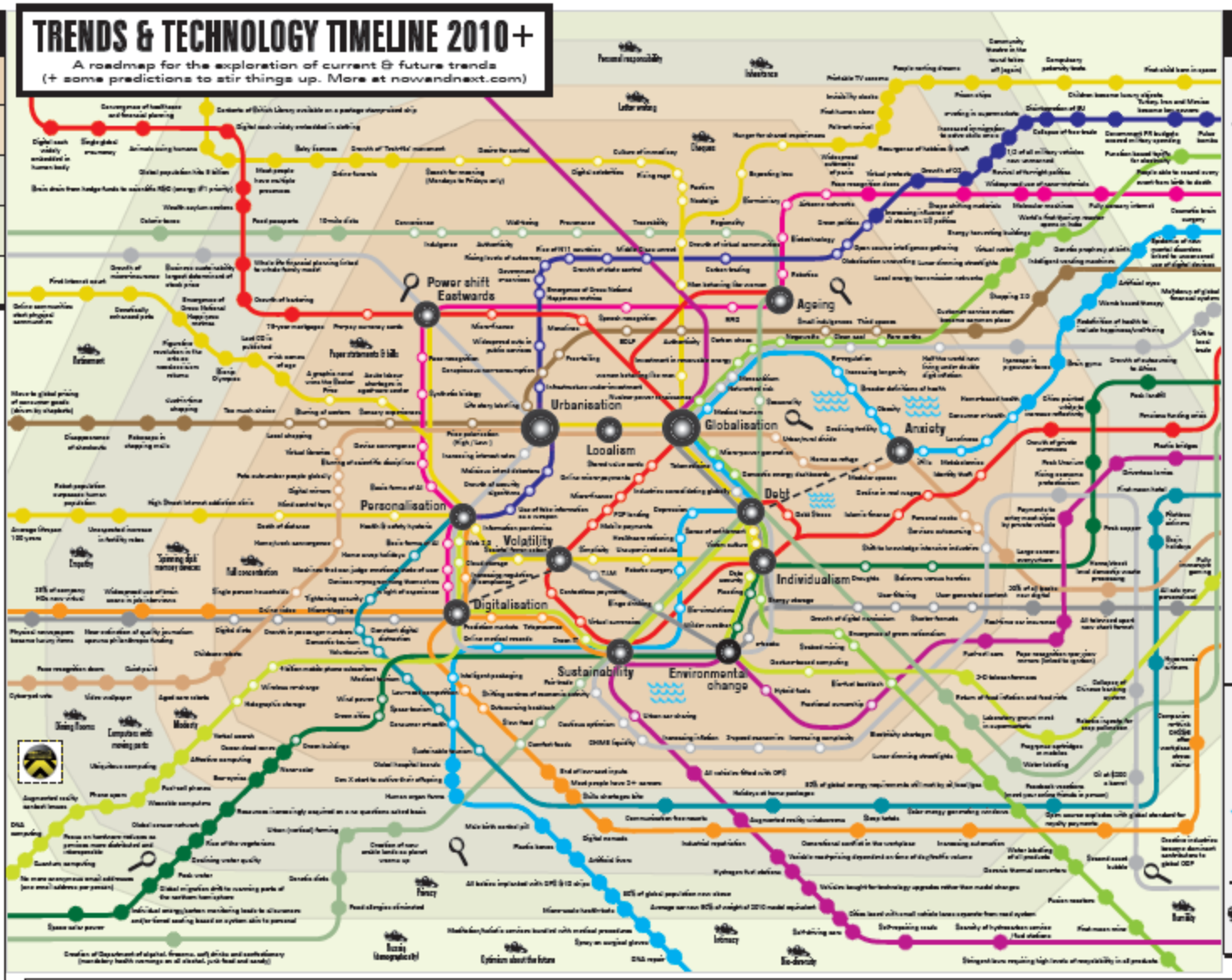
William Gibson

Protecting Turf and Sustaining the Status Quo: Silos Subvert Solutions



TRENDS & TECHNOLOGY TIMELINE 2010+

A roadmap for the exploration of current & future trends
(+ some predictions to stir things up. More at nowandnext.com)



TIME ZONES

- ZONE 1: 2010-2015
- ZONE 2: 2015-2020
- ZONE 3: 2020-2025
- ZONE 4: 2025-2035
- ZONE 5: 2035-2050

Notes on time travel

This map is a broad representation of some of the trends and technologies currently visible. Improvement works are carried out at weekends and travellers should check to see whether lines are still operable before commencing any journeys. Helpful suggestions concerning new routes and excursions are always welcome.

If you wish to travel outside of Zone 1 you are advised to bring comfy shoes and a camera. Travellers are also advised to bring their own supplies of food and water although weapons are unnecessary if you keep to well trodden paths. Also note that travel into Zone 5 is not available for people aged over 75 years of age.

A3 and A2 Prints of this map

Full colour prints of this map are available to anyone that asks nicely. A small charge is levied to cover print and postage costs only. Contact richard@nowandnext.com stating whether you'd like A3 or A2 size and saying which country the map is to be delivered to. Delivery is available to anywhere in the world. Alternatively, just print this out yourself (40 minute recommended)

Sourced

Material for this map has been sourced from a number of publications including Future Files and What's Next

www.futuretrendsbook.com

What's Next
www.nowandnext.com

Acknowledgements

This map was conceived and created by Richard Watson at Nowandnext.com with some help from Benjamin Hirzer at Stop. Also thanks to Oliver Freeman, Mike Jackson and Scott Martin.

LEGEND

1. Society & Culture
2. Geopolitics
3. Energy & raw materials
4. Science & technology
5. Healthcare & Medicine
6. Retail & leisure
7. The Economy
8. Financial services
9. Environment & Climate
10. Food & drink
11. Transport
12. Travel & tourism
13. Home & family
14. IT & telecomms
15. News & Media
16. Work & Business

- Mega trend
- Trend
- Prediction
- Dangerous currents
- Poor visibility
- High-speed link
- Partial ruin

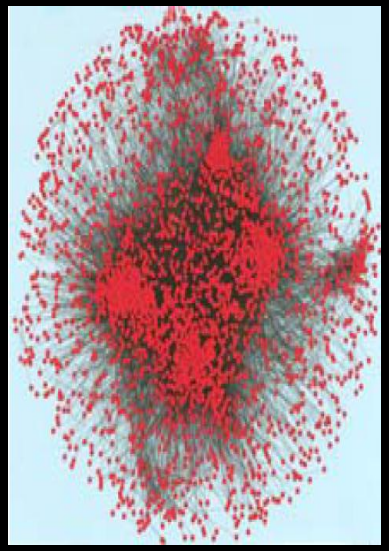
Global risks*

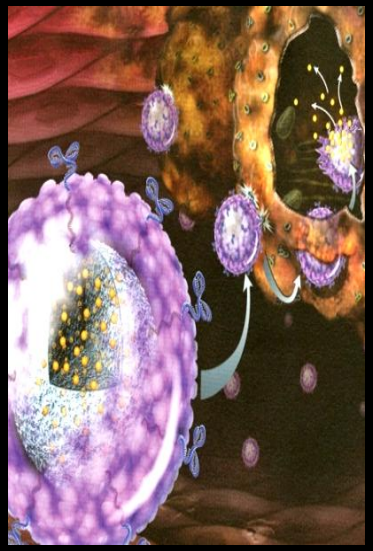
*Low probability/high impact events that could develop off the above timelines and predictions

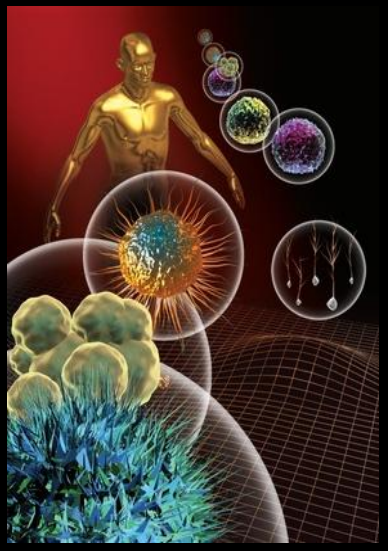
- Commodity price spikes
- Raw materials shortages
- Mass migration of population
- Nuclear terrorism
- Internet brownouts
- Electricity shortages
- Rapid increase in cyber crime
- Critical infrastructure attack
- Rogue stakeholder
- WMD Proliferation
- Green energy bubble
- Genetic terrorism
- Collapse of US dollar
- Global supply chain disruption
- Terrorist attack on urban water supply
- US/China conflict
- Israel/Iran conflict
- Bisphenol A link to cancer
- Geographical expansion of Russia
- Major earthquake in mega city
- Global pandemic
- Conflict with North Korea
- Political disintegration of Saudi Arabia
- Systemic failure of financial system
- Fundamentalist takeover in Pakistan
- Middle class revolution
- Collapse of China
- Mobile phone link to cancer
- Credit Default Swaps
- Rogue asteroid
- Major nano-tech accident
- Space weather disruption to comms
- Aliens visit earth
- Return of the Messiah
- People taking trend maps too seriously

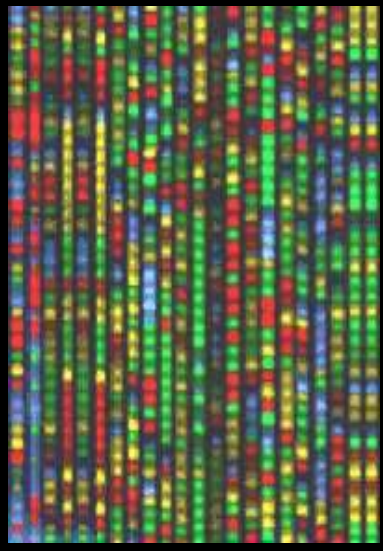
Transcending Boundaries: Emergent Domains Arising from Technology Convergence

Systems and Synthetic Biology	Targeted Rx and Gene Controls	Regenerative Medicine	HPO	Genetic Identity







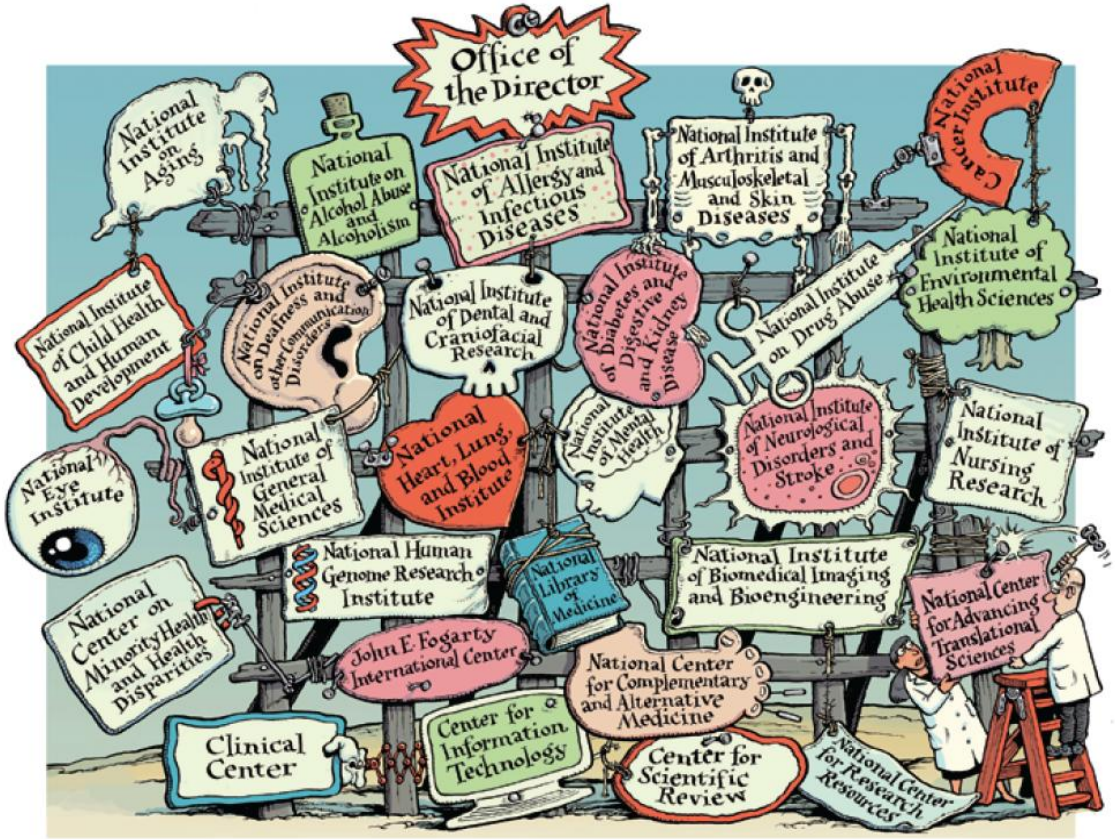


Forging a New Innovation Ecosystem for Biomedical Research and Public Health

- leverage still unique and unmatched capabilities
  - intellectual and cultural capital
  - financial and infrastructure resources
- aggressive reform of national research planning, organization and funding
  - coordinated, multidisciplinary programs with requisite scale
  - increasing standardization as foundation for proficient assembly/analysis of large scale data
  - engagement of private sector partnerships
- imperative for radical and, by definition, disruptive changes

Nature (2011) 471, 569

COMMENT



Time to rethink the NIH

A radical restructure is the only way to solve the systemic problems of the world's biggest funder of biomedical research, argues **Michael M. Crow**.

Adapting to the Scale and Logistical Complexity of Translational Medicine

- single investigator awards and incremental (at best) progress → high risk, high reward projects with prospect of radical, disruptive innovation
- single discipline focus → obligate assembly of diverse expertise for multi-dimensional engagement
- funding agencies ill-prepared to review inter-/cross-disciplinary research → new study sections with broader expertise, including industrial experience
- ‘islands’ of individual datasets with minimal standardization → large scale, standardized, inter-operable open-source databases with professional annotation, curation and analytics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THE PROMISE OF TRANSLATIONAL MEDICINE
With Francis Collins now calling the shots at NIH, will he be able to deliver on the innovations behind the genome?

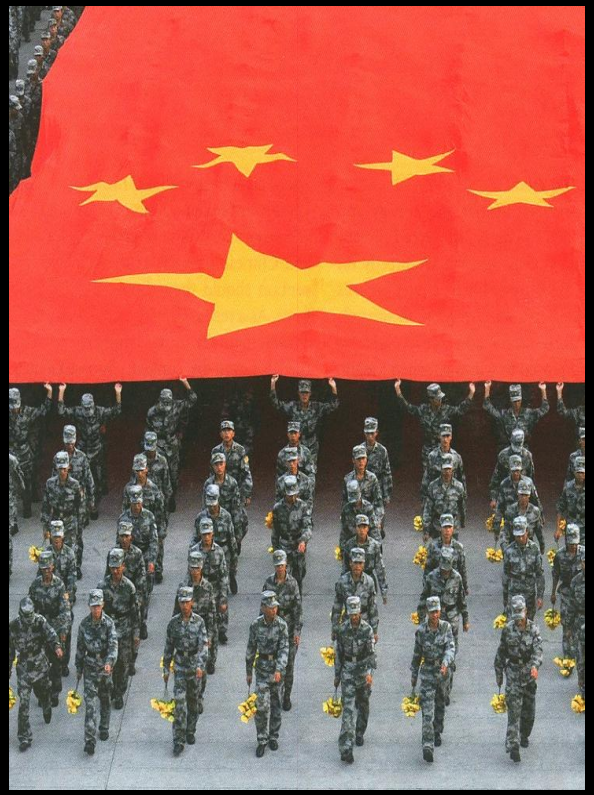
Coordination of the Complex Interactions Required to Build a Productive Translational Medical Research Capacity

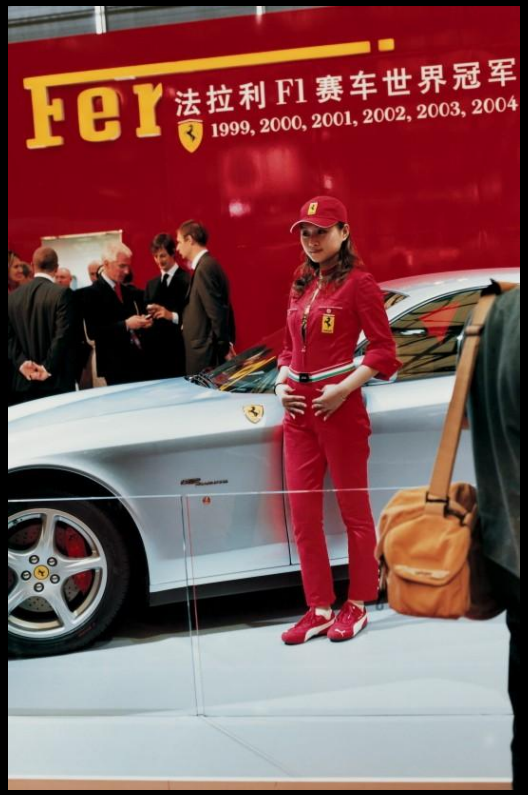
- promulgation of standards and centralized orchestration of resources (national/international)
  - biorepositories and biospecimens
  - 'omics' analytics reference standards
  - informatics platforms (BIX, HIX) for large scale databases and analytics
  - -non-linear dynamics in complex systems
  - ID/recruitment of, relevant case:control patient cohorts
- proactive design of regulatory frameworks to address new technologies
  - complex multivariate assays
  - remote health monitoring
  - review process for combination products
  - new CER tools/metrics and health economics modeling

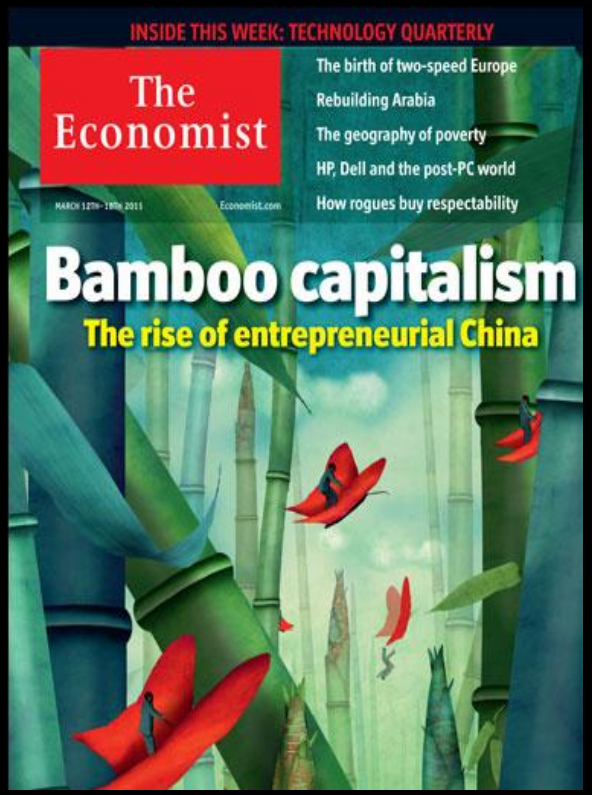
Sic Transit Gloria…..Thus Passes Glory

**“It’s not because things are difficult that we dare not venture.
It’s because we dare not venture that they are difficult.”**

Seneca







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Sustainable Health: Societal and Individual
The Complex Path to Proficient, Personalized Healthcare

- the potential economic and health benefits from biosignature diagnostic profiling transcend any other current category of healthcare innovation
- realization of this potential will depend less on technological advances, albeit crucial, than the circumvention of entrenched economic, cultural and institutional interests in sustaining the status quo

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DISRUPTIVE INNOVATION DEMANDS BOLDNESS