Health Technology Acceleration and Convergence: Implications for Personalized Medicine

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San Francisco, CA, 9 November 2009
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
Reforming health care
This is going to hurt
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
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
Dominate Themes in Biomedical R&D

- technology acceleration
- technology convergence
- new cross-disciplinary, cross sector partnerships
- data standards
- data volume
- data diversity and integration
- information infrastructure
Dominant Themes in Biomedical R&D

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The Strategic Triad:
• diagnostics (Dx), therapeutics (Rx) and informatics (Ix)
Technology Convergence

- Biotechnology, Systems Biology and Synthetic Biology
- Nanotechnology, Materials Science and Miniaturization Engineering
- Advanced Computing and Knowledge Management

• technologies with radical, pervasive and enduring impact

Integration of Dx, Rx and Hlx
Personalized Medicine: Progressive Evolution Based on Increasingly Comprehensive Profiling of Disease Risk and Health Status

- Targeted Care
  - rational Rx based on profiling of underlying molecular pathology
  - MDx and disease subtyping

- Individualized Care
  - rational Rx based on comprehensive molecular profiling of individuals
    - disease subtypes and optimum Rx
    - Rx AE risk
    - disease predisposition risk and mitigation

- Personalized Care
  - integrated framework of care and longitudinal data on individual health status
  - real time remote health status monitoring
  - transition to disease prediction and preemption
Personalized medicine: Key Drivers

Science

Policy

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

Dx Platforms

- massive parallelism
- miniaturization
- automation
- rapid
- POC

RIGHT Rx for RIGHT DISEASE SUBTYPE
The Emergence of Drug: Diagnostic Combinations

- **Selzentry** (maraviroc) tablets
- **trofile** CO-RECEPTOR TROPISM ASSAY
- **CAMPTO** irinotecan
- **Invader® chemistry**
- **Pfizer**
- **Coumadin** (Warfarin Sodium Tablets, USP) Crystalline
- **Verigene® System**
- **5-Fluorouracil**
- **Xeloda® capcitabine**
- **TeraGuide 5-FU**
- **AMGEN**
- **Vectibix™ (panitumumab)**
- **Nanosphere**
- **DXS Diagnostic Innovations**
● 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)

- full or partial refund for non-responders

- four Rx cycles
- 50% reduction in serum M protein
- NHS continues to fund
- <50% response company refunds cost of Rx
Outcomes-Based Risk-Sharing Agreements (ORBAs) Come to the USA

- reimburse average treatment cost (not just Rx) for fractures incurred after 6 months therapy
- improved Hb1Ac levels in diabetics over one year increases Rx discount to Cigna
The Conceptual Foundations of Drug Discovery

- from empiricism to rational therapeutics
- from ambiguity to predictability
  - mechanism(s) of action
  - clinical efficacy and safety
  - healthcare outcomes and value

Drug-Target Networks for FDA Approved Rx
Molecular Pathways and Network Analysis: Systems Pharmacology

Deconvolution of Signaling Networks in Disease

Identification of ‘Fragile’ Nodes/Pathways for Targeted Rx
Molecular Pathways Network Analysis and Systems Pharmacology

- ‘connectivity’ maps
  - correlations between genomic signatures and sets of proteins involved in Rx action
- Rx ‘promiscuirty’
  - spectrum of ‘target’ effects required for optimum efficacy
- Rx ‘pleiotropy’
  - undesirable off-target effects and adverse event risk
- ‘synthetic lethal’ screening
  - ID new Rx oncology targets in co-dependent genes required for cell survival
- ‘minimum knockout’ modeling
  - ID/predict smallest number of drug targets to fully block a cellular process
Pharmacogenetic Predisposition to Adverse Drug Reactions

- 1.5 to 3 million annual hospitalizations (US)
- 80 to 140 thousand annual deaths (US)
- est. cost of $30-50 billion
update labeling for Abacavir (Ziagen) to require pre-therapy screening for HLA-B*5701 allele to avoid fatal hypersensitivity

Table of Valid Genomic Biomarkers in the Context of Approved Drug Labels

http://www.fda.gov/cder/genomics/genomic_biomarkers_table.htm
broader, more complex profiling platforms than MDx assays for ID of drug targets
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
complex patterns of ethnic variation and haplotype associations impose continuum of metabolic phenotypes
The Human Microbiome: A Barely Understood Influence in health

- complex meta-system
  - host, microbes, viruses, other organisms, metabolites, xenobiotics
  - is there a core microbiome?
  - how do perturbations affect disease and vice-versa?
  - does the microbiome influence xenobiotic metabolism and the metabolite spectrum?
The Trajectories for Molecular Medicine

Exponential growth of research data

Technology convergence
- Life sciences
- Engineering
- Computing

Data

Time
The Trajectories for Molecular Medicine

Addressing the Void in Translation and Design of New Delivery Models

Data

Time
The Trajectories for Molecular Medicine

- Time
- Data
  - translational medicine and clinical validation
  - regulatory standards
  - clinical utility and reimbursement
  - routine clinical adoption
Adoption of New Technologies in Healthcare

- not merely innovation in technology
- parallel evolution and adoption of new business, financial and organizational models
- harmonizing incentives for diverse constituencies
- critical role of public policies in defining market entry barriers
  - regulation, reimbursement
  - professional standards and sustaining status quo
  - changes in administrative procedures
- cost-based, event-/procedure-based incentives versus value-based pricing, integrated care and disease management
The Evidence Dilemma in Adoption of Next-Generation Molecular Diagnostic Tests and the Evolution of Personalized Medicine
“The stark reality is that although academic conception of new biomarkers is fertile, their gestation is generally interminable”

Dr. Janet Woodcock
FDA
useful only when correlated with additional parameters
– clinical outcomes
– clinical utility
– actionable information
– demonstrable economic value
Disease-Associated Biomarkers

- Literature dominated by anecdotal studies
  - Academic laboratories
  - Small patient cohorts
  - Poor replication and confirmatory studies
- Lack of standardization
- Very few biomarkers subjected to rigorous validation
  - Case-control studies with sufficient statistical power
  - Inadequate stringency in clinical phenotyping
- Widespread lack of understanding of regulatory requirements
  - Complexities imposed by multiplex tests
  - New regulatory oversight (IVDMIAs)
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
The Imperative for Rigorous Clinical Sampling Protocols in Biomarker Profiling and Validation of IVD Tests

- statistical powering
- rigorous case-control studies
  - retrospective
  - prospective (piggy back on clinical trials)
- prospectively defined endpoints
  - diagnostic marker(s)
  - Rx responsiveness and resistance markers
  - staging, stratification, progression markers
- regulatory validation of software algorithms for multiplex tests
Sample Sizes Required to Render False Positive Results Unlikely When Testing Association Between a Genetic Variant and Cancer

<table>
<thead>
<tr>
<th>Genetic relative risk†</th>
<th>Probability of association</th>
<th>Sample size for cases‡</th>
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<tbody>
<tr>
<td>1.25</td>
<td>0.001</td>
<td>2128</td>
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<tr>
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<td>2580</td>
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<td>1.15</td>
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<td>7022</td>
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<td></td>
<td>0.00001</td>
<td>8234</td>
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from: S.G. Baker et al. (2006) BMJ 332, 1150

*Based on a two sided type I error of 0.05, a power of 0.90, and a false positive report probability of 0.05
†Relative risk of cancer in people with genetic variant compared with those without.
‡An equal number of controls is also needed.
Development of Molecular Diagnostics and Biomarkers for Personalized Medicine: The Need for End-to-End R&D Solutions

### Complex Biosignature Profiling

<table>
<thead>
<tr>
<th>genomics</th>
<th>proteomics</th>
<th>immunosignatures</th>
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<tbody>
<tr>
<td><img src="image1" alt="Genomics" /></td>
<td><img src="image2" alt="Proteomics" /></td>
<td><img src="image3" alt="Immunosignatures" /></td>
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### Signature Detection, Deconvolution and Multivariate Analysis

<table>
<thead>
<tr>
<th>multiplex assays</th>
<th>novel test devices (POC)</th>
<th>new algorithms</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image4" alt="Multiplex Assays" /></td>
<td><img src="image5" alt="Novel Test Devices" /></td>
<td><img src="image6" alt="New Algorithms" /></td>
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</table>
Increased Legislative Interest in Standards, Oversights and Regulation of Molecular Diagnostic Testing

- (2008) In Vitro Diagnostic Multivariate Index Assays (IVDMIAs)
- (2009) Quality, Regulation and Clinical Utility of Laboratory-Developed Tests
- (2009) Secretary’s Advisory Committee on Genetics, Health and Society (SACGHS)
- (2009) SB 42: Post-CLIA Bioinformatics Services
“Under the current CLIA framework, only the analytical validity of the test is assessed, while the clinical validity and clinical utility of the test are not”

DHSS Agency for Healthcare Quality and Research Report on Laboratory Developed Tests September 2009
“Our ignorance of the laws of variation is profound”

Charles Darwin
Mapping the Allelic Architecture of Common Traits and Gene Constellations for Disease Predisposition and Progression

- family-based linkage studies and 'candidate genes'
- SNPs, haplotypes and genome-wide association studies (GWAS)
- Common variants confer small risk increments (OR 1.1 to 1.5)
- Explain only small component of disease risk
- Majority of associated loci in intronic and inter-genic regions of unknown function
- Relationship of CNVs to associated loci yet to be defined
- Focus on larger number of variants with low minor allele frequencies (MAF) and smaller effects
Mapping the Allelic Architecture of Common Traits and Gene Constellations for Disease Predisposition and Progression

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- comprehensive exome and whole genome sequencing
Daunting Scale, Time and Cost of Comprehensive Mapping of Loci Associated with Complex Human Diseases

- high cost GWAS studies on few thousand individuals
  - largely uninformative in identification of the collective actions of multiple rare alleles with individual weak effects
- very large sample sizes needed for adequate statistical power to identify low frequency loci
  - 200,000 – 500,000 ($1-3 billion)
- skepticism that coarse-grained nature of routinely collected clinical/lab/billing metrics are insufficient to establish research-quality phenotypes for robust correlative whole genome sequencing
The Imperative for New Initiatives to Establish Large Scale, Standardized Scientific and Clinical Resources for Translational Research
The Rise of Big Biology: Nature Genetics (September/October 2009)

Genomic-wide association study identifies variants in the ABO locus associated with susceptibility to pancreatic cancer

Laury Amundston1,2,*, Peter Kraft1,2,*, Rachel Z. Stolzenberg-Solomon1,3, Charles S. Fuchs2,*, Gloria M. Petersen1, Alan A. Kreiger1,4, H. Ran Bueno-de-Mesquita1, Myron Green1, Kathy Hedblom1, Eric J. Jacobs1, Andrea Lacroix1, Wei Zheng1, Dominique Alvarado1, William Bnder1, Christiane D Borg2, Franco Berrebi1, Mila Bhargava1, Julie E. Burton1, Faig Marie2, Federico Canziani1, Francisco Canale-Chapoz1, Sandra Chipot1, Michelle Gottschalk1, Mario de Andrade1, Eric J. DeFronzo2, Rudolf Kansikas1, Alison P. Klein2, Charles K. Kooperberg1, Robert C. Kurtz1, Dongfeng Gu1, Shannon M. Lynch1, Margaret Maclver1, Robert R. McWilliams1, Julie B. Mendelsohn1, Dominique S. Michael1, Sara H. Moser1, Kim Oversæde1, Alpa V Patel1, Petra H. M Peeterson1, Alexander Rakhit1, Elke Ribordy1, Harvey A. Blaker1, Xiaozhao Guo1, Elke Sohrab1, Dimitrios Trichopoulou1, Stephen K. Vos Kerdijk1, Jarmo Virtamo1, Jan Wactawski-Wende1, Brijen M. Wolk1, Herbert Yu1, Kai Wu1, Anne Zemelich-Jacquiss1, Stephan J. Chanou1,2, Patrick Hartshorne1, Robert N. Hoover1

Genomic-wide association study identifies variants at CLU and CR1 associated with Alzheimer’s disease

Jean-Charles Lombert1,*, Simon Hart1, Gad Enn1,*, Dominique Campist1, Kristel Soghe1,*, Mikko Hiltunen1, Costas Gkourtso1, Dimosthenis Karalis1, Maria Baldovin1, Marie Enevoldsen2, Iris Leutenegger1, Karolin Betjeman1, Fabio Filippini1,* Jose A. Fernandez1, Andrea Patrone1, Frank H. Flier1,*, Charles K. Kooperberg1, Robert C. Kurtz1, Dongfeng Gu1, Shannon M. Lynch1, Margaret Maclver1, Robert R. McWilliams1, Julie B. Mendelsohn1, Dominique S. Michael1, Sara H. Moser1, Kim Oversæde1, Alpa V Patel1, Petra H. M Peeterson1, Alexander Rakhit1, Elke Ribordy1, Harvey A. Blaker1, Xiaozhao Guo1, Elke Sohrab1, Dimitrios Trichopoulou1, Stephen K. Vos Kerdijk1, Jarmo Virtamo1, Jan Wactawski-Wende1, Brijen M. Wolk1, Herbert Yu1, Kai Wu1, Anne Zemelich-Jacquiss1, Stephan J. Chanou1,2, Patrick Hartshorne1, Robert N. Hoover1

Genomic-wide association study identifies variants at CLU and PICALM associated with Alzheimer’s disease

Denise Harold1,*, Richard Abraham1,*, Paul Hollingsworth1,*, Rebecca Sim1, Amy Gerich1,*, Marian L. Hampson1, Josép Pagès1,2, Valentine Moskvin1, Kimberly Dowell1, Amy Williams1, Nicole Iosip1,*, Charles Thomas1, Theresa Strepton1, Angharad R Morgan1, Simon Lovestone1, John Powell1, Petrovna Prat1,*, Michael E Lipton1,*, Carol Brayne1,*, David C Rubinshtein1,*, Michael Giff1, Brian Lawlor1, Aboobaker1,*, Kevin Morgan1,*, Kristie S Brown1,*, Peter A Passmore1, David Craig1, Bernardette McGinnity1, Seppan Tod1,*, Clare Holton1,*, David Mame1,*, David Smith1,*, Seth Love1,*, Patrick Gleeson1,*, John Hardy1,*, Simon Mead1,*, Nick Fox1,*, Martin Rossor1, John Collinge1,*, Wolfgang Maier1,*, Frank Jessen1, Brita Scherrmann1,*, Hendrik van der Bussche1,*, Isabella Heres1,*, Johanne Korsnes1,*, Jens Witting1, Markus Nyberg1,*, Arne Thele1,*, Peter M. Holt1,*, Richard Kjar1,*, John S Krause1,*, Carlos Gracuraga1,*, Petr Novotny1,*, John Kavanagh1,*, Kevin Mee1,*, Kristin Sleegers1,*, Karin Beie1,*, Sebastian Rottschäfer1,*, Patrick Kiel1,*, Christian van Broeckhoven1,*, Nicholas Bavo1,*, Hugh Crichton1,*, Andrew McQuillin1,*, Rhian Coupland1,*, Benno Deckers1,*, Anuar Al-Chalabi1,*, Christopher E Shaw1,*, Magda Todd1,*, Andrew Singleton1,*, Britta Couperus1,*, Theophrastos W Maraziotis1,*, Mark Derkits1,*, Simon Niederreither1,*, Marie-Francoise Scholl1,*, Norman E Klop1,*, Eric Weissenberg1,*, Minorea M Carrau1,*, Vahan Panosian1,*, Steven G Younkin1,*, Peter M Holmes1,*, Michael O’Donovan1,*, Michael J Owen1,*, and Julie Williams1

Genomic-wide association study identifies a new ovarian cancer susceptibility locus on 9p22.2

Hongmin Song1,*, Susan J Rimm2,3, Jonathan Tyrol1,*, Kelly L Belton1,4, Aleksandra Gentsy-Aharon1,*, Eva Wimw1,*, Hoda Ashton-Cleary1,4, Jenny Chang-Claude1,4, Daniel W Craner1,*, Richard DiCato3,*, Thilo Drk1,*, Ellen I Good1,*, Marc T Goodman1,2,*, Jolleen M ChildsK1, Thomas Sellers2,*, Laura Bagliet1,2,*, Matthews W Beckmann1,*, Jonathan Beesly1,*, Ian Blakie1,*, Michael E Carney1,*, Stephen Chase1,*, Zhilin Chen1,*, Julie M Cunningham1,*, David A Jackson1,*, Matthias Drees1,*, Arif E Er2,*, Daniel Fennemore1,*, Bruce L Froelicher1,*, Graham Giles1,*, Martin E Gore1,*, Immunoula De Veir2,*, Peter Hillermann1,*, Claus Hoppel1,*, Kari Heilig1,*, Edith S Iverson2,*, Ian J Jacobs1,*, Anna Idhunok1,*, Dong Li1,*, Johanna Ilosvay1,*, Jan I Ljubkovic1,*, Galina Litle1,*, Valerie McGuire1,*, Michael Mekalanos1,*, K耳 Frerik Meier1,*, Patricia G Moorman1,*, Kirsten M Norris1,*, Catherine Phelan1,*, Carlo Pecy1,*, Harvey Risch1,*, Ingo B Ronnebaum1,*, Gianluca Servetti2,3,4,*, Melissa Southby1,*, Daniel O Steen1, *, Fall C Thie1,*, Kathryn L Terry1,*, Ya-Tai Tien1,*, Shelley S Vogt1,*, John J Van Den Berg1,*, Robert A Vedder1,*, Shih Wang1,*, Gareth Wang1,*, Jennifer M Wells1,*, Anna H Wu1,*, Hannah Yang1,*, Wendy Wenstrom1,*, Argeiros Ziga1,*, Australian Ovarian Cancer Study Group1,*, The Ovarian Cancer Association Consortium1,*, Richard Hoads1,*, Ian Thomas1,*, Alice S Whittemore1,*, Mary Anne Rossing1,*, Bruce A J Foster1,*, Celeste Leigh Pearce1,*, Robert B Neils1,*, Usha Menon1,*, Suzanne Krenger1,*, Jacob Grendahl1,*, Montserrat Garcia-Christafari1,*, Peter A Fasching1,*, Douglas F Eastern1,*, Georgia Cottrell-Trench1,*, Andrew Berchuck1,*, Pant D P Bhattacharya1,*, and Simon A Gaylor1

Genomic-wide association study identifies 1p31.3 (UNC13A) and 9p21.2 as susceptibility loci for sporadic amyotrophic lateral sclerosis

Michael A van Engeland1,*, Jan H Veldink1,*, Christian G Jarris4,*, Hylke M Blauw1,*, Paul W Van Vliet1,*, Anna Riva1,*, Robin Lemmens2,*, Helene Vreffo1,*, Erez N / Giessing1,*, Bernard van den Broek1,*, Albert Hofmans1,*, Michiel J Zwarts1,*, Perry J van Duijvenb1,*, Dan Russek1,*, Eric Stengen1,*, Lisa Geiniger1,*, Perdita van Megchelen1,*, Barbara Vorvik1,*, Agnieszka Wolny1,*, Andre G Underwood1,*, Corinna Hendrik1,*, Stefan Wall1,*, Therese Boysen1,*, Patrick Börger1,*, Jennifer D Gage1,*, Steven Pare1,*, Sirer Cildir1,*, Meinolf M. Richters1,*, H-Erich Wichmann2,*, Stefan Zimmermann2,*, Sven Hennies1,4,*, Jeroen Cramer1,*, Vincent Meininger1,*, Judith Merki1,*, P Nigel Leigh1,*, Christopher E Shaw1,*, John E Frontera2,*, Jannes Al-Chalabi1,*, Robert H Brown Jr2,*, Roel Ilofsen1,*, Peter M Anderson1,*, Rod A Ophoff1,*, Rleenard L van den Berg1
HIPAA fails to protect privacy and impedes research

- consent does not protect against security breaches

- proposal that research be exempt from HIPAA

- adopt prior federal standard for human subjects research: The Common Rule

- eliminates need for reconsent and reauthorization for future and use of sample/data
Standards for ‘Omics’ Data Cross-Domain Integration, Open-Source Data Sharing and Computational Analysis
The Rise of Open-Source Networks and Consortia

- NCBI
- Entrez, The Life Sciences Search Engine
- ToPaz
- caBIG
- International HapMap Project
- PLoS ONE
- ALLEN INSTITUTE for BRAIN SCIENCE | Allen Brain Atlas
- W3C
- World Wide Web Consortium
- PubMed
- The Cancer Genome Atlas
- BROAD INSTITUTE
- Diabetes Genetics Initiative
- Science Commons
- The Neurocommons
- CRITICAL PATH INSTITUTE
- PhRMA
- Creative Commons
- Clinical Semantics Group
- Genes, Environment and Health Initiative (GEI)
# OBO Foundry Ontologies

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

<table>
<thead>
<tr>
<th>The Open Biomedical Ontologies</th>
<th>Gene Ontology (GO)</th>
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<tr>
<td><strong>Cell Ontology (CL)</strong></td>
<td><strong>Chemical Entities of Biological Interest (ChEBI)</strong></td>
</tr>
<tr>
<td><strong>ZFIN</strong></td>
<td><strong>Disease Ontology (DO)</strong></td>
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<tr>
<td>Zebrafish Anatomical Ontology</td>
<td><strong>Ontology for Clinical Investigations (OCI)</strong></td>
</tr>
<tr>
<td><strong>Plant Ontology (PO)</strong></td>
<td><strong>Sequence Ontology (SO)</strong></td>
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<tr>
<td><strong>Phenotypic Quality Ontology (PATO)</strong></td>
<td><strong>OBO Relation Ontology</strong></td>
</tr>
<tr>
<td><strong>Protein Ontology (PRO)</strong></td>
<td><strong>RNA Ontology (RnaO)</strong></td>
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http://www.nature.com/nbt/journal/v25/n11/fig_tab/nbt1346_T2.html
Creating a New Network of Connected Expertise to Accelerate Innovation in Healthcare R&D

- ever faster generation of new information
- diversification of innovation sources
- current R&D ecosystem is too fragmented to fully leverage novel content and shared learning
- global sourcing
- rise of new business models of ‘expertise networks’ that eclipse current monolithic single company innovation models
If You Build It Will They Pay?
Adoption of Disruptive Innovation

- new technology/service that simplifies a complex/costly problem
- business model that allows market adoption of the simplified solution at low(er) cost
- incentivized supply and demand to networks to reinforce the disruption
Reimbursement for Diagnostic Tests

The Imperative for Value-Based Pricing versus Current Cost-Based Models

- inadequate US Medicare coding and payment mechanisms
  - out moded, out-dated, lacking in transparency, inconsistently applied
- inappropriate assignment of existing CPT codes to new tests
- engagement of third party payers who derive economic/clinical value from new Dx
The CMS Date of Service Rule (Implemented 1/08) 
a.k.a The ‘14 Day Rule’

- “presents a barrier to the use and development of personalized medicine”
- Senate Finance Committee Proposed Amendment (10/09) to eliminate and allow non-hospital labs to bill Medicare

- “We couldn’t support a bill that would disadvantage hospital labs”
  Amy Miller, Policy Director

- “This will lead to closing and down-sizing of academic labs. It would benefit a very small number of laboratories and harm a very large number of hospitals”
  Mary Williams, COO
Demonstrating the Clinical Utility of Diagnostic Profiling

- right disease (subtype)
- **right risk: benefit decision**
- right treatment
- right patient
Have We Ignored the Biology of Tumor Progression in Our Approaches to Cancer Screening

Prostate
Breast
Colon
Cervix
Have We Ignored Differences in Patterns of Tumor Progression in the Design of Breast and Prostate Cancer Screening Programs?

- L. Esserman et. al. (2009) JAMA 312, 1685-92
- Gil Andriole (2009) NEJM 360, 1310
- screening increases detection of early disease
  but
  incidence of regional disease not reduced commensurately
- suggests potential overtreatment for low risk indolent lesions
  and
  screening intervals insufficient to detect aggressive lethal tumors arising as ‘inter-interval’ events
- concept consistent with detection of small fraction of small, early breast cancers classified as low risk by NCI criteria but high mortality risk by NKI 70 gene test
  and
  I-SPY trial data with 85% malignancies were inter-interval cancers and only 15% detected in routine screening
Effectiveness of Cancer Screens Based on Different Patterns of Tumor Biology and Screening Intervals

- metastatic
- regional
- localized
- microscopic

Time

screening intervals

Tumor Progression
How Much New Technology Can We Afford?
Does Comparative-Effectiveness Research Threaten Personalized Medicine?

Alan M. Garber, M.D., Ph.D., and Sean R. Tunis, M.D.
UK National Institute for Health and Clinical Excellence (NICE)
Nice Gets Nasty (or Rational?)
Promotion of Wellness

- increased consumer responsibility for wellness
- remote monitoring of individual health status
- crucial role of healthcare information systems
  - integrated Rx care for complex chronic conditions
  - outcomes and comparative effectiveness
  - earlier detection of disease episodes and risk mitigation
  - wellness versus illness
Annual Excess Healthcare Costs Related to Consumer Behavior

- Conditions related to obesity and overweight: $200 billion
- Smoking: $191 billion
- Non-adherence to drug regimens: $177 billion
- Alcohol abuse: $2 billion

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

- remote monitoring of health status

**Applications**

- multi-feature monitoring and broadband wireless networks
  - ubiquitous sensing
- enhanced autonomy for in-home aged
- proactive alerting and intervention to mitigate health incidents
- monitoring of patient compliance
- coupled linkage to remote Rx dispensing for efficient disease management
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)
Paper Kills!:
The Inefficiencies and Risks Created by Sustained Dependence on Paper Healthcare Records
The Infocosm: Emerging Networks of Global Connectivity
Wireless Technologies: Consumer and Clinical Markets Converge
Connecting Patients (and Consumers) to Optimum Healthcare Resources

PMRs and patient support networks for linkage to clinical trials and expertise

Integrated care of chronic conditions and specialty Rx distribution
Pharma and Healthcare Social Media (Non-Brand Sponsored) Patient Communities

- **CancerCompass**: social network about Empowering cancer patients to make informed decisions
- **Face to Face Health**: healthcare social utility designed to connect people
- **Depressiontribe**: community network share stories, encouragement and friendship
- **CAREFLASH**: place to submit, retrieve and share information and well-wishes surrounding a loved one's health circumstances
- **CureTogether**: expert-guided communities where you have access to authoritative information about health topics
- ** Autism111**: campaign to pull our community together and offer a brighter, more positive view of autism
- **Advanced Breast Cancer Community**: information source online community advanced (metastatic) breast cancer patients, caregivers
- **Be Well**: discussion board featured on cancer survivors
- **Cancer Survivors Network**: discussion board anonymously share health information
- **Daily Strength**: safe, anonymous online support groups focused on over 500 specific challenges
- **Circle of Sharing**: helps cancer patients and caregivers get personalized information about the disease, and share that information
- **healia**: discussion board featured on cancer survivors
- **Depression.Understood**: social network where like-minded people can communicate with each other and offer peer support
- **eDrugSearch**: search engine for Americans interested in purchasing safe, low-cost prescription drugs from prescreened international pharmacies
- **CROHN'S & COLITIS FOUNDATION OF AMERICA**: discussion groups and forums
- **Crohn's & Colitis Foundation of America**: discussion groups and forums
Pharma and Healthcare Social Media Brand
Physician and Nurse Communities

ASK LEPIOS
HCPs' social network operated by the Canadian Medical Association

coliqio
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

doc2doc
UK-registered doctors in primary and secondary care

Doctors.net.uk
medical and healthcare communities

Doctrs
exclusive social network for Physicians

DoooX
connects physicians with information, opportunities, and each other.

DOKCTORNETWORKING.COM
Network for physicians

DoctorsHangout.com
Personal & Professional Networking for Doctors & Medical Students Worldwide

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

MedicSpeak

MedicalExchange
interactive platform on web for the medical professionals

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

Medscape Physician Connect
Engage your peers through our FREE global physician community

New Media | Medicine

OBGYN.net
research and support community

Ozmosis
Trusted Physician’s Network

Present Diabetes
multi-disciplinary diabetes Learn, share, collaborate

Podiatric Residency Education
Online community
The Expanding Universe of Health Information Resources: Redefining Physician:Patient Relationships

- MD-centric monopoly
- paternalistic decisions and passive patients
- institutional control
- paper records
- fragmented information and portability barriers
- centralized testing analysis and expert interpretation

- patient-centric markets
- engaged patients/consumers
- individual custody
- EHR/PMRs
- seamless integration and mobility
- increasingly decentralized, automated analysis and decision algorithms
- remote health status monitoring
Changing Minds and Changing Behaviors

- improvement methods and metrics
- evidence and best practices
- human factors

Resistance:
- delusional merits of status quo
- unwarranted external scrutiny
- claimed risk by change
- loss of status, income, autonomy
- skepticism
- ‘victims’

Adoption:
- incentives
- alignment
- ownership
- tangible individual/group rewards
- political/media/public pressures
New Vistas in Biotechnology with Potential for Major Therapeutic Advances

- selective modulation of gene expression via siRNA
- regenerative medicine: programming cellular differentiation and autologous cell therapy
- synthetic biology: cells as novel Rx/vaccine delivery systems or diagnostic sentinels
- tissue engineering: novel biomatrices for repair and remodeling
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
- 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