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

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Medical Progress:
From Superstitions to Symptoms to Signatures
the potential economic and health benefits from biomarkers transcend any other current category of healthcare innovation
- increased diagnostic accuracy
- rational treatment selection
- monitoring treatment efficacy
- health monitoring and optimized wellness
- earlier detection of treatment resistance
Identification and Validation Biomarkers: A Complex, Multi-Dimensional Challenge

- Biomarker profiling technologies
- Multi-disciplinary data integration
- Validation, evidentiary standards and regulation
- Clinical utility and adoption
- Value and reimbursement
Identification and Validation Biomarkers: A Complex, Multi-Dimensional Challenge

OPTIMIZED DECISIONS FOR IMPROVED OUTCOMES AT LOWER COST
The Evolution of Clinical Diagnostic Testing in The Pending ‘Omics Era and New Device Technologies

- **Unianalyte Tests**
  - Centralized Testing, Large Capital Base Instrumentation

- **Multianalyte Biomarkers**
  - New Regulatory and Reimbursement Policies
  - On-Body: In-Body Sensors
  - Portable, Point of Need Diagnostic Devices

- **Whole Genome Sequencing**
  - Increasingly Distributed Data Feeds and Real Time Health Monitoring
The complexity of multiplex biomarker discovery, clinical validation and regulatory oversight is comparable to (bio)pharmaceutical R&D.

In common with R&D for drugs and vaccines, solutions to complex multi-dimensional technical challenges require systems-based approaches.
Sloppy and Unstandardized Science: The Growing Problem of Poor Reproducibility in Biomedical Publications
● publish and vanish: disturbing low reproducibility of academic publications
● poor access to rigorously annotated biospecimens from stringently phenotyped patients plus outcomes data
● insufficient control of pre-analytical parameters and poorly standardized analytical methods
● idiosyncratic ‘lab-specific’ analytical methods
● ‘small N’ studies lacking statistical power
chaotic data reporting formats and poor database interoperability

pressure to publish

poor compliance with funding agency/journal policies on open data sharing and full data disclosure

failure to work to (or understand) industry and regulatory standards
Access to High Quality Biospecimens, Biobanks and DNA Repositories:
An Obligate Prerequisite to Productive Validation of Putative Causal Disease Markers

academic anecdotes and wasted investment?

or

requisite scale and stringent QA/QC standards?
Data Silos and Data Tombs

HELL IS THE PLACE WHERE NOTHING CONNECTS — T.S. ELIOT
Data Silos and Data Tombs

WELCOME TO BIOMEDICAL RESEARCH AND PATIENT MEDICAL RECORDS

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

- are we building systems and infrastructure that merely support the collection of data?
  
or

- systems to integrate data from early discovery to patient care?
  
and

- support data validation, sophisticated analytics, evidence generation and decision support systems to optimize patient care and drive a learning healthcare enterprise?
The Need for Facile, Seamless Data Exchange Formats for Large Scale Biomedical Data Systems
● the demise of the all-comers trial design?
● new trial designs based on biomarker-selected patient cohorts and Rx response evaluation
  – enrichment trials, adaptive trials
  – multi-agent trials and more agile shifts in combination Rx
● regulatory engagement and leadership
The Vital Role of Patients and Patient Advocacy Organizations
Interactive Patient-Centered Initiatives (PCI)

- new opportunities to share, mine and integrate data on a larger scale
  - research, clinical trials, outcomes analysis
- build new biorepository networks of well curated and standardized samples to support research
- faster accumulation of large sample collections to achieve necessary statistical power
- “matchmaking” for more proficient research study/clinical trial recruitment
The Pending Zettabyte Era
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Managing Big Data in Biomedicine is Not a Simple Extrapolation from Current Practices

Current Institutional Structures and Competencies Are Ill-Prepared for Pending Disruptive Change
Technology Acceleration and Convergence: The Escalating Challenge for Professional Competency, Decision-Support and Future Education Curricula

Data Deluge

New Science and Cognitive Bandwidth

Automated Analytics and Decision Support

Facile Formats for Actionable Decisions
21st Century Knowledge Networks versus 20th Century Organizational Structures
Cross-Domain Convergence, Complexity in Biomedicine and Increasing Dependency on Data-Intensive Methods and New Knowledge Networks

multi-disciplinary, systems-focused, big data sets

reductionist, investigator-centric, single discipline datasets

unbiased datasets and new analytics for pattern mining

hypothesis driven research
From Silos to Systems

- single discipline, single investigators
- single institution activities/resources
- academic isolation
- erratic quality qualitative data
- fragmented data
- incompatible data formats
- multi-disciplinary teams
- large scale collaboration networks
- academia-industry-healthcare provider networks
- reproducible quantitative data
- integrated data
- data interoperability from discovery to clinical care
From Silos to Systems

- Unshared data: “data tombs”
- Dominance of ROI grant policies
- Passive patient engagement
- Cost-based reimbursement for molecular diagnostics

- Open, shared data and compliance with deposition commitments
- Redirect more grants to networked systems projects
- Engaged patient advocacy groups for faster progress: biorepositories/ clinical trials/ outcomes analysis
- Value-based pricing for molecular diagnostics and information services
Realizing the Potential of Biomarkers in Healthcare

- more than proficient adoption of new technologies
- depends equally on major reforms in current approaches to the organization and funding of biomarker discovery and validation
- new reimbursement and market incentives for commercial investment
• completed two year in-depth analysis of obstacles and opportunities for biomarkers in biomedicine

• multi-sector engagement
  – researchers, clinical trialists, statisticians, informaticians
  – healthcare providers and patients
  – regulators and payors
  – private sector (Rx, MDx, computing)

• urgent imperative for strategic vision and national leadership to integrate cross-disciplinary and trans-sector actions

• new framework for long overdue change