

TOWARD PRECISION MEDICINE

Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease



*Committee on A Framework for
Developing a New Taxonomy of Disease*

*Board of Life Studies
Division on Earth and Life Studies*

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

Cover Art: Nicolle Rager Fuller, Sayo-Art LLC

Photo: © Graham Bell/Corbis

Statement of Task

At the request of the Director's Office of NIH, an *ad hoc* Committee of the National Research Council will explore the feasibility and need, and develop a potential framework, for creating a "new taxonomy" of human diseases based on molecular biology

Committee on A Framework for Developing a New Taxonomy of Disease

SUSAN DESMOND-HELLMANN, (*CO-CHAIR*), University of California, San Francisco

CHARLES SAWYERS, (*CO-CHAIR*), Memorial Sloan-Kettering Cancer Center

DAVID R. COX, AQC, Pfizer Inc.

CLAIRE FRASER-LIGGETT, University of Maryland, School of Medicine

STEPHEN J. GALLI, Stanford University

DAVID B. GOLDSTEIN, Duke University School of Medicine

DAVID J. HUNTER, the Harvard School of Public Health

ISAAC S. KOHANE, Harvard Medical School

MANUEL LLINAS, Princeton University

BERNARD LO, University of California, San Francisco

TOM MISTELI, National Cancer Institute

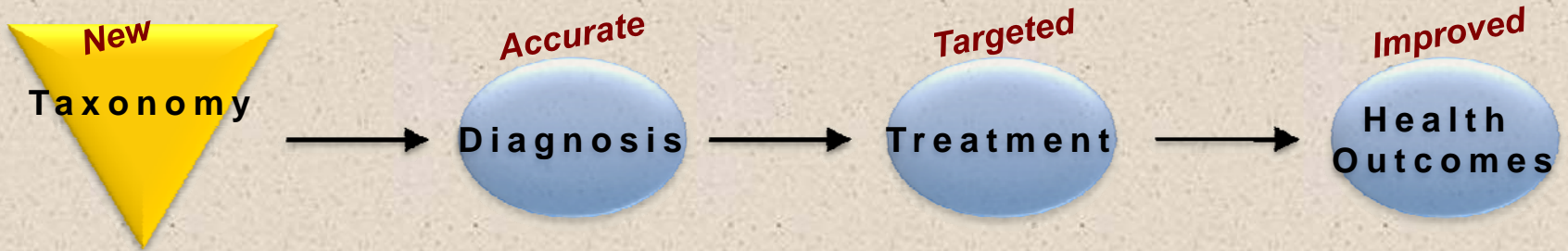
SEAN J. MORRISON, University of Michigan

DAVID G. NICHOLS, the Johns Hopkins University School of Medicine

MAYNARD V. OLSON, University of Washington

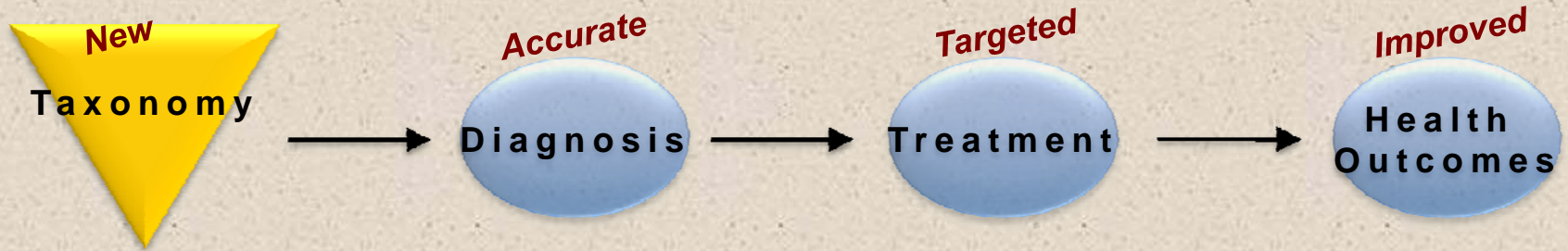
CHARMAINE D. ROYAL, Duke University

KEITH R. YAMAMOTO, University of California, San Francisco



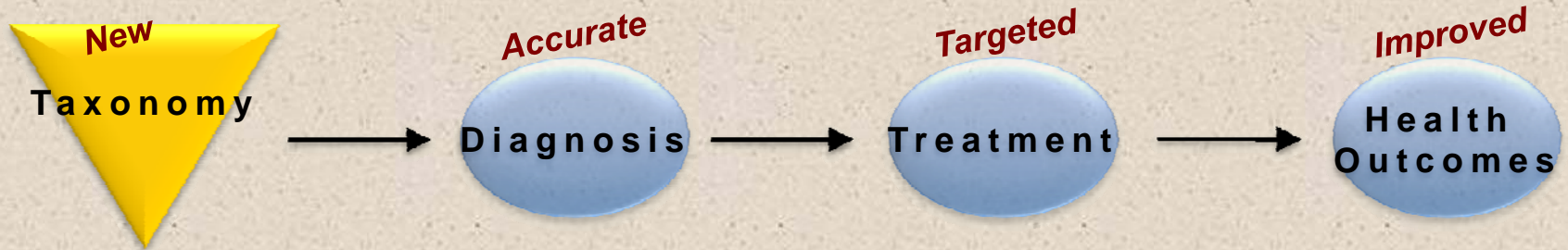
Diagnosis is the foundation of medicine.

Accurately and precisely defining a patient's condition does not assure effective treatment, but it is unequivocally the place to start.



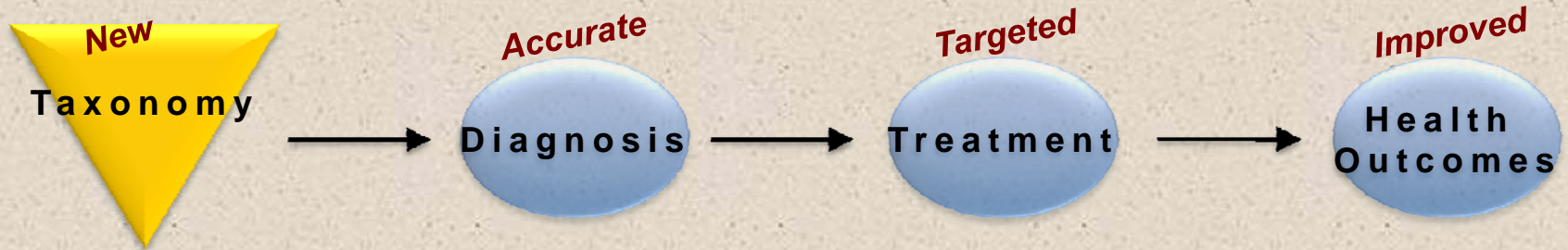
Consider the following clinical scenarios:

in the first example, molecular understanding of disease has already begun to play an important role in informing treatment decisions, while in the second, it has not.



Patient 1: Consulting with her medical oncologist following breast cancer surgery

- **Precise diagnosis based on specific molecular characteristics of patient and her cancer**
- **Physician has multiple therapeutic options available**
- **Therapeutic regimen tailored to focus on her particular tumor markers**
- **Patient's relatives can undergo testing to assess their individual breast cancer predisposition.**



Patient 2: Diagnosed at age 40 with Type II diabetes

- **Imprecise category**
- **Diagnosis gives little insight into mechanism of disease**
- **Little basis for tailoring treatment for this individual patient**
- **Internist has few options --likely prescribe metformin**
- **No concrete molecular information to customize therapy to reduce complications**
- **No tests to measure risk of diabetes for siblings and children.**

Challenge Bigger Than Just a New Taxonomy

Explosion of molecular data

- **Genomics, proteomics, metabolomics, microbiome, systems analyses, imaging, etc.**
- **Improved scientific understanding of fundamental biological processes and insights into human health and disease**

As-yet-untapped opportunities

- **Have begun to yield tangible medical advances in certain diseases**
- **Growing shortfall; information left unused**

Challenge Bigger Than Just a New Taxonomy

Truly historic set of health-related challenges and opportunities

- Higher cost, doesn't always yield better health outcomes
- Pressure on researchers to produce immediate results

Implications for nearly all stakeholders: researchers, clinicians, patients, payers

- Complexity of issues means nearly everyone would be affected – need thoughtful approach
- Each stakeholder would benefit

Integration

The Committee saw its challenge as crafting a framework for integrating the rapidly expanding range and detail of biological, behavioral and experiential information to facilitate basic discovery, and to drive the development of a more accurate and precise classification of disease (i.e., a “New Taxonomy”) which in turn will enable better medicine.

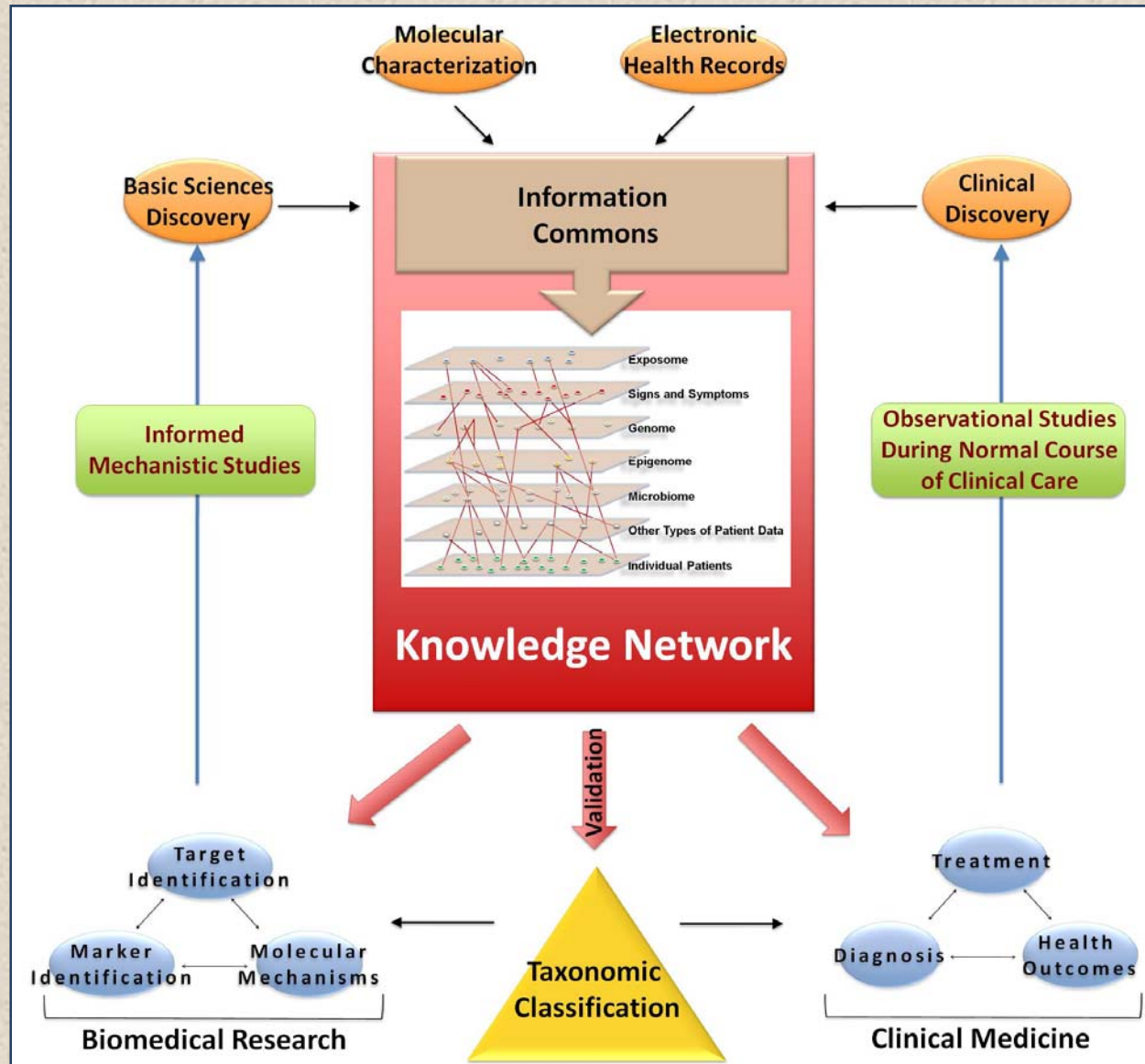
An “Information Commons” and “Knowledge Network” are essential infrastructure – would modernize biomedical research and dramatically improve patient care.

Redirection of resources could facilitate development – shift acquisition of molecular data to point-of-care settings.

Conclusions

- 1. A New Taxonomy will Lead to Better Health Care.**
- 2. The Time is Right to Modernize Disease Taxonomy.**
- 3. A New Taxonomy Should be Developed.**
- 4. A Knowledge Network of Disease Would Enable A New Taxonomy.**
- 5. New Models for Population-based Research Will Enable Development of the Knowledge Network and New Taxonomy.**
- 6. Redirection of Resources Could Facilitate Development of the Knowledge Network – an opportunity to modernize current approaches.**

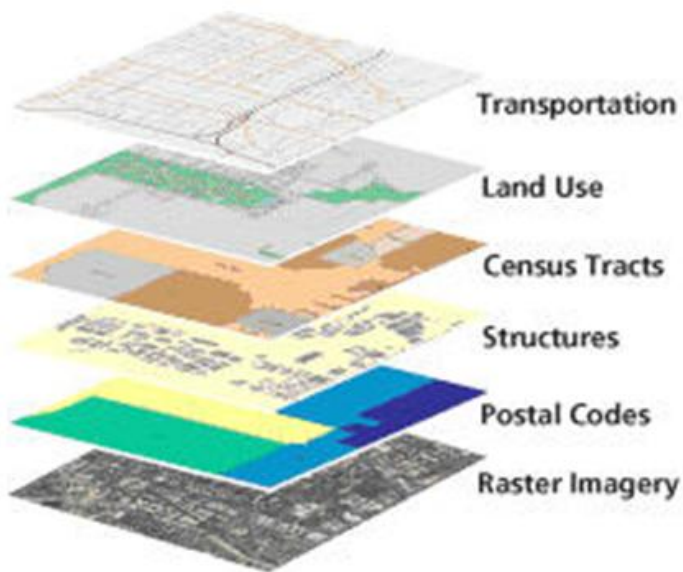
Building a Biomedical Knowledge Network for Basic Discovery and Medicine



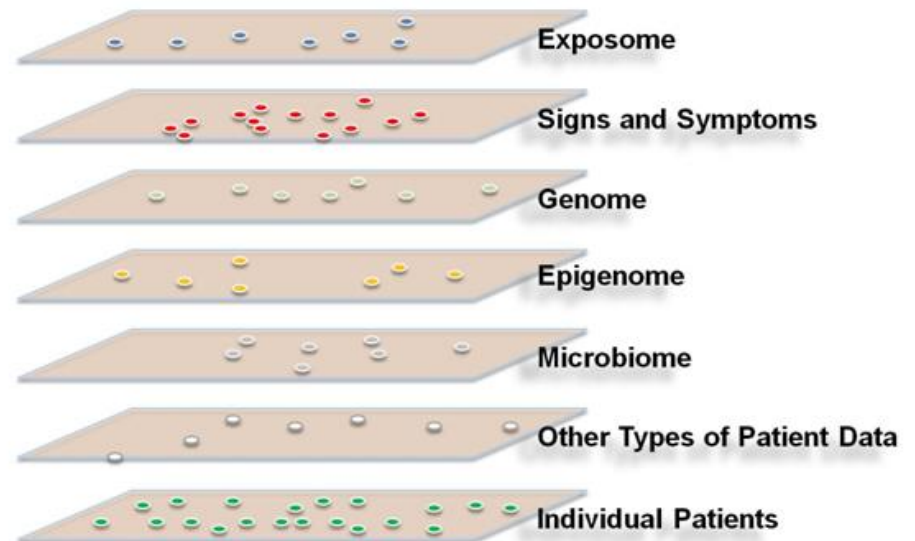
Individual-Centric Information Commons

Google Maps Analogy

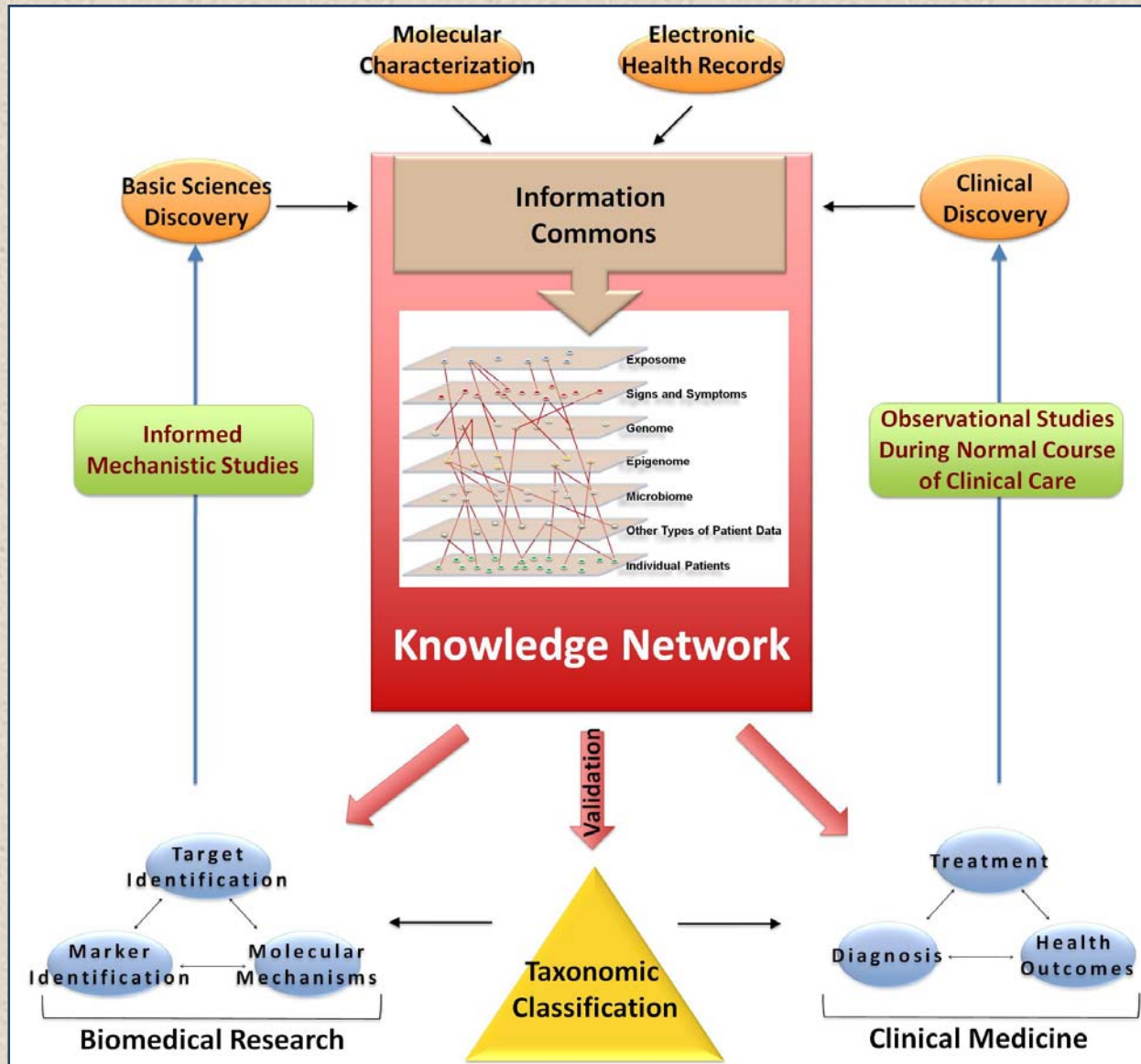
Google Maps: GIS layers
Organized by Geographical Positioning



Information Commons
Organized Around Individual Patients

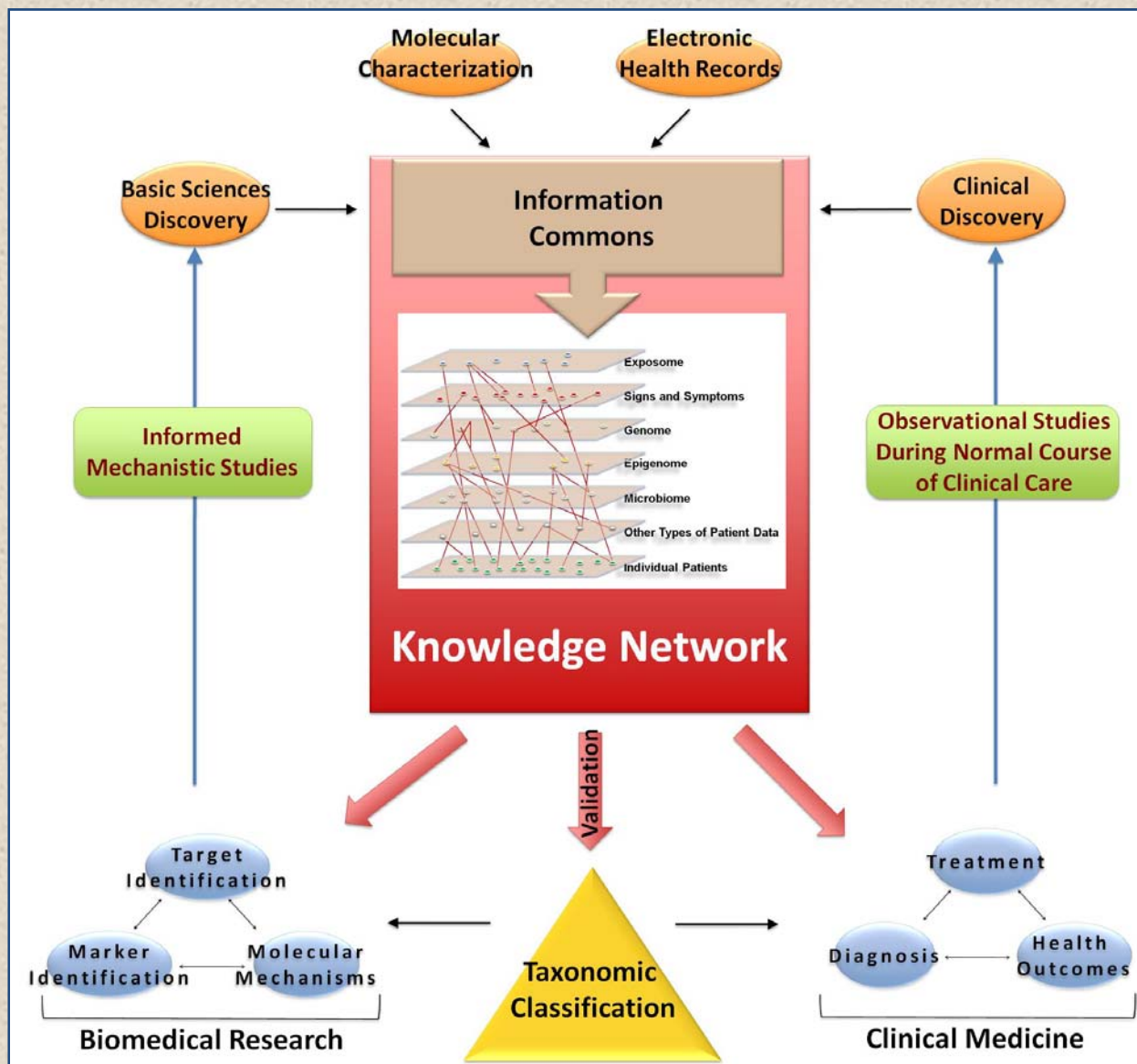


Collect and Integrate Information From Biomedical Research and Clinical Medicine



Knowledge Network Serves Three Key Purposes:

1. Enable Discovery
2. Improve Clinical Care
3. Inform Taxonomy



Recommendations

- 1. Pilot Studies**
- 2. Emphasis on Data Integration**
- 3. Centrality of Privacy Issues**
- 4. Necessity of Data Sharing**
- 5. Validation for Clinical Practice**
- 6. Incentives for Partnerships**

Purpose of Pilot Studies

- **Lead to new connections between molecular (such as genetic or metabolomic) variation and disease sub-classifications, often with implications for disease management and prevention**
- **Provide lessons necessary to facilitate a more rapid transition in the way molecular data are used**
- **Permit many logistical, ethical, and bioinformatic challenges to be addressed**
- **Progress toward the sustainable implementation of point-of-care discovery efforts**

Example Pilot Studies

1. **Million American Genomes Initiative (MAGI)**

- **Sequence the genomes of 1M+ individuals**
- **Grounded in the new discovery model – during normal course of clinical care**
- **Genome sequencing will soon be cheaper than many clinical tests**
- **Makes possible systematic comparisons of the molecular data with electronic medical records**
- **Establishes infrastructure to draw connections between sequence data and the medical histories of the individuals**

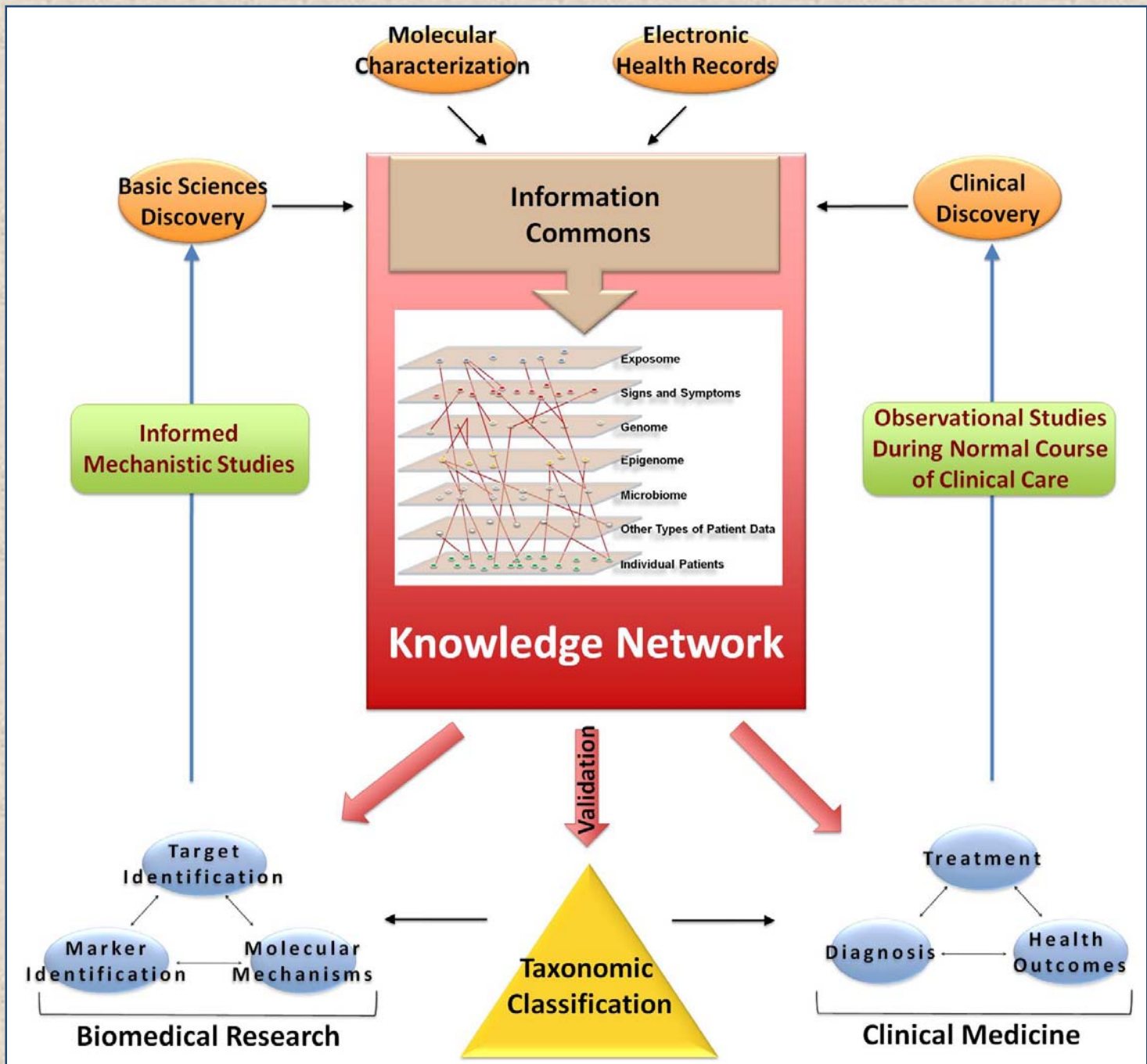
Example Pilot Studies

2. Metabolomic profiles in Type 2 Diabetes

- **Potential of metabolomic analyses to help identify individuals most at risk of developing diabetes**
- **Carry out targeted quantitative metabolomic studies, transitioning towards more comprehensive metabolomic profiles over time**
- **Combined with knowledge gained from MAGI and research from other layers of the Information Commons (such as the microbiome and exposome) could contribute substantially to strategies to delay or prevent the development of type 2 diabetes.**

Toward Precision Medicine

A major beneficiary of the proposed Knowledge Network of Disease and New Taxonomy would be what has been termed “precision medicine.” The Committee is of the opinion that realizing the full promise of precision medicine, whose goal is to provide the best available care for each individual, requires that researchers and health-care providers have access to very large sets of health and disease-related data linked to individual patients.





Cover Art: Nicolle Rager Fuller, Sayo-Art LLC
Photo: © Graham Bell/Corbis

Board of Life Studies
Division on Earth and Life Studies

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES