Precompetitive Collaboration in Biomedicine: The Biomarkers Consortium

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Institute of Medicine
National Cancer Policy Forum
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A convergence of multiple factors has led to the emergence of public-private partnerships in biomedicine.

- Decline in NIH budgets → funding gap
- Declining productivity in biopharma R&D → “externalization” of research
- Regulatory challenges → increasing complexity, limited budgets

Increased Need for Public-Private Partnerships

- Escalating complexity of biomedical science and technologies
- Emergence of viable collaborative models → e.g., SNP Consortium, Gates Foundation
- Expansion of “pre-competitive” field
FNIH is the sole organization authorized by the U.S. Congress to support the mission of the NIH by creating and managing public-private partnerships

- 501(c)(3) non-profit organization
  - Raised over $460 million since 1996
  - Activities include major research partnerships plus scientific education/training, conference, and facilities programs
  - 100+ currently active programs

- Non-governmental
  - Independent Board of Directors
  - NIH Director/FDA Commissioner *ex-officio* Board members
Foundation for NIH Overview

- Creates innovative public-private biomedical partnerships that complement NIH priorities and advance the public health
  - Partners include industry, academia, other federal agencies, and the philanthropic community
  - Provides a neutral forum able to engage all partners to work together
- FNHIH’s structure enables efficient, effective collaborations
  - Directly solicits contributions
  - Flexible donor relationships
  - Focused grants, contracts, and project management capabilities
  - 96 cents of every dollar directly supports programs
- Has received a 4-star Charity Navigator rating for the past four years
  - #1 among 64 medical research organizations; #3 among 582 health category organizations
  - Ranked among the ten fastest growing charities in 2009
Some Major FNIH Research Partnerships

Grand Challenges in Global Health
Partner: Bill & Melinda Gates Foundation

Collaboration for AIDS Vaccine Discovery (CAVD)
Partners: VRC/NIAID, Bill & Melinda Gates Foundation

Alzheimer's Disease Neuroimaging Initiative (ADNI)
Partners: NIA/NIBIB & 20 companies/2 non-profits

Genetic Association Information Network (GAIN)
Partners: NHGRI, NLM & Pfizer, Affymetrix, Broad Institute, Perlegen Sciences

Observational Medical Outcomes Partnership
Partners: FDA, PhRMA, multiple pharmaceutical partners

Osteoarthritis Initiative (OAI)
Partners: NIAMS & Pfizer, Novartis, Merck, GlaxoSmithKline

The Biomarkers Consortium
Partners: NIH, FDA, PhRMA, CMS, BIO, biopharmaceutical industry/non-profits
Biomarkers are seen as key to reducing the time and expense required to bring new drugs to market

• The 2004 FDA Critical Path Initiative, which challenged the pharmaceutical industry to reduce the time (12-15 years) and expense (~$1-2 billion) to bring a drug to market, emphasized the utility of biomarkers in meeting these goals

• Cancer biomarkers have led the way via high-profile successes such as Herceptin

• However, despite such success and promise, much remains to be done…
Out of 1,261 putative cancer protein or peptide biomarkers described in the literature*, only 9 are FDA approved as “tumor associated antigens”

- Fewer than 1 per year have been approved by the FDA since 1998
- This high percentage of un-validated biomarkers is generalizable to other diseases
- This “biomarker barrier” in which candidate biomarkers have not been validated needs to be overcome

Goals of The Biomarkers Consortium

- Facilitate the development and validation of biomarkers using new and existing technologies in a precompetitive context
- Help qualify these biomarkers for specific applications in diagnosing disease, predicting therapeutic response, or improving clinical practice
- Generate information useful to inform regulatory decision-making
- Make consortium project results broadly available to the entire scientific community
For-Profit Companies (22)
Abbott Laboratories
Amgen
AstraZeneca
BG Medicine
Boehringer-Ingelheim
Bristol-Myers Squibb
Genstruct, Inc.
GlaxoSmithKline
InfraReDx, Inc.
Johnson & Johnson
Eli Lilly and Company
Merck and Co., Inc.
Meso Scale Discovery
Metabolon, Inc.
NextGen Sciences
Novartis Pharmaceutical Group
Orasi Medical, Inc.
Pfizer, Inc.
F. Hoffman-LaRoche
Scout Diagnostics
Sepracor
XOMA, Ltd.

Non-Profit Organizations (30)
Academy of Molecular Imaging
Advanced Medical Technology Association
Alliance for Aging Research
Alzheimer's Association
American Association for Cancer Research
American College of Neuropsychopharmacology
American Health Assistance Foundation
American Society of Clinical Oncology
American Society for Clinical Pharmacology and Therapeutics
American Society for Therapeutic Radiology and Oncology
Association of Clinical Research Organizations
Autism Speaks
Avon Foundation
Battelle Memorial Institute
Biotechnology Industry Organization
CHDI Foundation
Cystic Fibrosis Foundation Therapeutics
Federation of Clinical Immunology Societies
The Hamner Institutes for Health Sciences
The Immune Tolerance Institute, Inc.
Juvenile Diabetes Research Foundation
Kidney Cancer Association
The Leukemia and Lymphoma Society
Michael J. Fox Foundation for Parkinson's Research
Ontario Cancer Biomarker Network
Pharmaceutical Research and Manufacturers of America
Radiological Society of North America
Ryan Licht Sang Bipolar Foundation
Society for Nuclear Medicine
University of Illinois
Governance Structure

Executive Committee
NIH / FDA / Industry / Foundation for NIH
CMS / Public-Patient Representative

Steering Committees

Project Teams
Executive Committee

**Chairman**
Charles Sanders, Foundation for NIH

**NIH**
Thomas Insel, *National Institute of Mental Health*
John Niederhuber, *National Cancer Institute*
Lawrence Tabak, *National Institute of Dental and Craniofacial Research*

**Public Member**
Mary Woolley, Research!America

**FDA**
ShaAvhree Buckman, *Office of Translational Science*
Janet Woodcock, *Center for Drug Evaluation and Research*

**Industry**
Stephen Eck, Eli Lilly & Co.
Gary Herman, Merck & Co., Inc.
Garry Neil, Johnson & Johnson
Sara Radcliffe, BIO

**Foundation for NIH Board**
Steve Paul, Eli Lilly & Co.
Ellen Sigal, Friends of Cancer Research

**CMS**
Barry Straube
Project Development Process

1. Initial Idea or Concept
   - EC/SC, RFA/RFP or External Submission
   - Scientific merit
   - Pre-competitive
   - Feasibility

2. Approved Project Concept
   - Steering Committee

3. Project Plan
   - Steering Committee/Project Team
   - Protocol
   - Resources
   - Intellectual property
   - Data sharing and distribution
   - Timelines and milestones
   - Budget
   - Human subjects
   - Privacy
   - Legal review

4. Approved Project
   - Executive Committee (and Funders)
   - Final QA/QC
   - Funding

5. Launch
   - Project Team
   - Contracts
   - Project management
Progress to Date

• Announced October 2006, launched in 2007
• 7 projects funded and launched to date @ ~$14 million total cost
  – 1 project completed
• 8 additional projects fully planned and approved
• 4 additional project concepts in near-term development pipeline
Consortium Governing Policies

• Key overarching governing policies pre-negotiated with principals/legal counsel representing the Foundation for NIH, NIH, FDA, PhRMA and BIO:
  – Intellectual property and data sharing
  – Antitrust
  – Selection and award of grants/contracts
  – Confidentiality
  – Conflict of interest

• Specific policies for each project developed on a project-by-project basis

• Policies available at www.biomarkersconsortium.org
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<thead>
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<th>Affiliation</th>
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CSC Evaluation Criteria for Prioritization of Cancer Biomarker Project Concepts (summary)

- Fits biological mechanism(s) of neoplastic progression
- Biomarker measurement has potential impact
- Biomarker measurement clinically feasible
- Feasibility of evaluation/use
- Feasibility of commercialization
**Example: I-SPY 2 Trial**

*(Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And molecular Analysis)*

- Paclitaxel ± Herceptin +/- New Drug A, B, C, D, or E (12 Weekly Cycles)
- AC (4 Cycles at 3 weeks each)
- Surgery

**Probability of Randomization to Treatment Arm**

HER2 +/- Randomize

- Biopsy
- Blood
- MRI

*Primary endpoint of the trial: pathological Complete Response for each treatment arm*

- Up to 12 new Phase II agents will be tested
- Patients will be assigned to an agent based on specific biomarker signatures
- As each patient moves through treatment, their response feeds back to the probability of the next patient who enters the trial (adaptive design)
I-SPY TRIAL 2

Will allow faster development of better targeted treatment for breast cancer:

• Demonstrate how adaptive design can streamline clinical trials, enabling Phase II decisions in months instead of years, with significantly fewer patients

• Graduate each agent with data about efficacy for each biomarker profile, so that phase III studies for successful agents can be performed with hundreds rather than thousands of patients

• Help establish and demonstrate new regulatory pathways, using a master IND with the FDA, held by the FNIH

• Further validate known stratifying biomarkers in breast cancer and progress several qualifying biomarkers toward qualification; provide platform for additional exploratory biomarker work

• Improve outcomes for the highest-risk breast cancer patients for whom successful treatments promise the greatest chance of saving lives
Intellectual property will be handled according to Biomarkers Consortium policies

- No single company stands to be the sole beneficiary of the I-SPY 2 project
- Pre-existing IP related to agents contributed by companies will remain with the company owning that IP
- Pre-existing IP related to biomarkers and platforms will remain with those companies, and be licensed for use in the Project. In some cases the tests have been published and are available commercially
- New IP will be managed by the FNIH, acting as a trusted third party to hold and license the new inventions
- Results are expected to be broadly applicable and will be made broadly available
IP Plan

FNIH will act as trusted third party to ensure fair and appropriate licensing of new inventions arising from I-SPY 2

1. Inventing Organizations grant exclusive licenses to new IP to FNIH

2. FNIH prosecutes and manages resulting patents

Medical Center A
Medical Center B
Laboratory C

FNIH returns a fair share of royalties (less expenses) to Inventing Organizations

Drug Co. A
Drug Co. B
Dx Co. C

3. FNIH markets and licenses IP to interested parties
   • Will negotiate exclusive or non-exclusive commercial license with limited field of interest

4. $$
Contact Information

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