Foundation for NIH

- Established by Congress in 1990; incorporated in 1996
- Supports the NIH mission
- 501(c)(3) non-profit organization
  - Raised over $410M since 1996
  - 50+ projects
- Non-governmental
  - Directly solicits contributions
  - Flexible donor relationships
  - Rapidly makes grants and contracts
- Close relationships with NIH
## Major Foundation for NIH Public-Private Research Partnerships

<table>
<thead>
<tr>
<th>Initiative</th>
<th>Funding</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grand Challenges in Global Health</td>
<td>$200M</td>
<td>Bill &amp; Melinda Gates Foundation</td>
</tr>
<tr>
<td>Collaboration for AIDS Vaccine Discovery (CAVD)</td>
<td>$33M</td>
<td>VRC/NIAID, Bill &amp; Melinda Gates Foundation</td>
</tr>
<tr>
<td>Alzheimer's Disease Neuroimaging Initiative (ADNI)</td>
<td>$27M</td>
<td>NIA/NIBIB &amp; 15 companies/2 non-profits</td>
</tr>
<tr>
<td>Genetic Association Information Network (GAIN)</td>
<td>$26M</td>
<td>NHGRI, NLM &amp; Pfizer, Affymetrix, Broad Institute, Perlegen Sciences</td>
</tr>
<tr>
<td>Observational Medical Outcomes Partnership</td>
<td>$21M</td>
<td>FDA, PhRMA, multiple pharmaceutical partners</td>
</tr>
<tr>
<td>Osteoarthritis Initiative (OAI)</td>
<td>$19M</td>
<td>NIAMS &amp; Pfizer, Novartis, Merck, GlaxoSmithKline</td>
</tr>
<tr>
<td>The Biomarkers Consortium</td>
<td>$12M*</td>
<td>NIH, FDA, CMS, PhRMA, BIO, biopharmaceutical industry/non-profits</td>
</tr>
<tr>
<td>Avon-NCI Progress for Patients Award Program</td>
<td>$12M</td>
<td>NCI &amp; Avon Foundation</td>
</tr>
<tr>
<td>Schizophrenia Metabolic Initiative</td>
<td>$8M</td>
<td>NIMH &amp; Bristol-Myers Squibb</td>
</tr>
</tbody>
</table>

* to date
Goals of The Biomarkers Consortium

- Advance the discovery, development, qualification and regulatory acceptance of biomarkers
- Conduct joint research in “pre-competitive” areas with partners that share common interest in advancing human health and improving patient care
- Speed the development of medicines and therapies for detection, prevention, diagnosis, and treatment of disease
- Make Consortium project results broadly available to the entire research community
### Contributing Members (60)

#### For-Profit Companies (27)
- Abbott Laboratories
- Althea Technologies
- AstraZeneca
- Avalon Pharmaceuticals
- BG Medicine
- Boehringer-Ingelheim Pharmaceuticals
- Bristol-Myers Squibb
- Digilab Biovision GmbH
- EMD Serono
- Genstruct
- GlaxoSmithKline
- GVK Biosciences
- InfraReDx
- Ingenuity Systems
- Johnson & Johnson
- Eli Lilly and Company
- Luminex Corporation
- Lundbeck
- Merck and Co., Inc.
- Metabolon
- Novartis
- Novo Nordisk
- Pfizer Inc
- F. Hoffmann-La Roche
- Rules-Based Medicine, Inc.
- Scout Diagnostics
- Wyeth

#### Nonprofit Organizations (33)
- Academy of Molecular Imaging
- Advanced Medical Technology Association
- Alliance for Aging Research
- Alzheimer’s Association
- American Association for Cancer Research
- American Cancer Society
- American College of Neuropsychopharmacology
- American Health Assistance Foundation
- American Society for Clinical Pharmacology and Therapeutics
- American Society for Therapeutic Radiology and Oncology
- American Society of Clinical Oncology
- Association of Clinical Research Organizations
- Autism Speaks
- Battelle Memorial Institute
- Biotechnology Industry Organization
- Cystic Fibrosis Foundation Therapeutics
- Federation of Clinical Immunology Societies
- The Hamner Institutes for Health Sciences
- High Q Foundation
- Immune Tolerance Institute
- Polo Ralph Lauren Foundation
- Juvenile Diabetes Research Foundation
- Kidney Cancer Association
- The Leukemia and Lymphoma Society
- Lupus Foundation of America
- Lupus Research Institute
- 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 of Nuclear Medicine
- Vanderbilt University
Contributing Membership Program

• Provides operational funds to the Foundation for NIH to operate the Consortium

• Allows all sectors to participate in the activities of the Consortium

• **Membership Benefits**
  – Elect four (4) representatives to serve on the Executive Committee (industry)
  – Nominate individuals to serve on Steering Committees (created to date in cancer, immunity & inflammation, metabolic disorders, and neuroscience) and Project Teams (developing individual projects)
  – Participate in “high-impact biomarkers” prioritization process
  – Propose project concepts/ideas for potential Consortium execution

• **Annual Membership Dues**
  – Companies: $5,000-$100,000 per year (depending on annual sales)
  – Non-profits: $5,000 per year
Private Sector Participation in The Biomarkers Consortium

- Allows for the leveraging of financial and scientific resources from industry, government (FDA, NIH, CMS) and foundations/non-profit organizations

- Industry participation offers new opportunities to
  - pool samples/data from completed trials
  - combine industry, government and academic expertise
  - “piggyback” onto existing research studies and clinical trials
  - spread financial and scientific risk
  - explore scientific basis for new regulatory pathways
Decision-Making Structure

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

Steering Committees
- Cancer
- Inflammation & Immunity
- Metabolic Disorders
- Neuroscience

Project Teams
- Project 1
- Project 2

Project 1 (No SC)
The Biomarkers Consortium
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*

**CMS**
Barry Straube

**FDA**
ShaAvhree Buckman, *Office of Translational Science*
Daniel Schultz, *Center for Devices and Radiological Health*
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 (temporary representative)

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

**Cancer**
Anna Barker, National Cancer Institute
David Parkinson, Nodality, Inc.

**Inflammation and Immunity**
Daniel Rotrosen, NIAID
Bruce Littman, Translational Medicine Associates

**Metabolic Disorders**
Bjorn Carlsson, AstraZeneca
Myrlene Staten, National Institute of Diabetes and Digestive and Kidney Diseases

**Neuroscience**
Huda Akil, University of Michigan
William Potter, Merck & Co., Inc.
2008 Approach: “High-Impact Biomarker Opportunities”

- **Strategic** focus on high impact areas of biomarker development and qualification:
  - **Important:** addresses a significant unmet/scientific need
  - **Translational:** will result in significant improvement in the development, approval or delivery of care to patients
  - **Transformational:** addresses critical gaps
  - **Feasible:** end goals can be likely achieved in a specific timeframe
  - **Practical:** leverages pre-existing resources wherever possible
  - **Fundable:** is capable of generating the required funding/stakeholder support needed
  - **Unique:** not already substantially being done elsewhere
  - **Collaborative:** would uniquely benefit from the multi-stakeholder composition and approach of The Biomarkers Consortium
Principles and Policies

• Key governing policies pre-negotiated prior to Consortium launch 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

• Policies, concept submission forms, and other information available at [www.biomarkersconsortium.org](http://www.biomarkersconsortium.org)
Project Development Process

1. Idea or Concept
   - Scientific merit
   - Pre-competitive
   - Feasibility
   - Initial funding scan

2. Steering Committee
   - Protocol
   - Resources
   - Intellectual property
   - Data sharing and distribution
   - Timelines and milestones
   - Budget
   - Human subjects
   - Privacy
   - Legal review

3. Project Plan
   - Final QA/QC
   - Funding
   - Contracts

4. Executive Committee (and Funders)
   - Project management

5. Project Team

EC/SC, RFA/RFP or External Submission

Steering Committee/Project Team

Executive Committee (and Funders)

Project Team
Current Approved/Active Projects (9)

• **FDG-PET Lung and Lymphoma Projects** (Cancer Steering Committee) – 2 projects
• **Circulating Tumor Cells as Biomarkers of Castration-Resistant Metastatic Prostate Cancer** (Cancer Steering Committee)
• **DCE-MRI Technique Optimization Using Prostate Cancer as a Model System** (Cancer Steering Committee)
• **Utility of Adiponectin as a Biomarker of Glycemic Efficacy** (Metabolic Disorders Steering Committee)
• **Carotid MRI Reproducibility Study via an NHLBI AIM-HIGH Ancillary Study** (Metabolic Disorders Steering Committee)
• **Establish Guidelines and Initial Diagnostic Criteria for the Association of Sarcopenia with Clinically Important Weakness: Evidence for Treatment Benefit** (Metabolic Disorders Steering Committee)
• **Comparison of Two PET Radioligands with $^{11}C$ or $^{18}F$ to Quantify the Peripheral Benzodiazepine Receptor** (Neuroscience Steering Committee)
• **Use of Targeted Multiplex Proteomic Strategies to Identify Plasma-Based Biomarkers in Alzheimer’s Disease** (Neuroscience Steering Committee)
Active Projects:
FDG-PET Lung and Lymphoma Projects (Underway)

FDG-PET Imaging in Non Hodgkin’s Lymphoma to Predict Tumor Response to Treatment
Phase II Study of FDG-PET/CT as a Predictive Marker of Tumor Response and Patient Outcome: Prospective Validation in Non-Small Cell Lung Cancer

Project Goals:
• Determine the linkage of FDG-PET to the effect of therapy and drugs on clinical outcome and survival in lymphoma and lung cancer
• Develop standard protocols for acquiring and evaluating FDG-PET data
• Evaluate robustness and clinical feasibility of protocols

Value:
• More efficient drug development
• Inform the regulatory review process and approval path
• Better early response criteria
• Ability to cost-share the qualification of FDG-PET

Project Duration/Budget:
• 5-year projects; $6.53M raised to date from 9 funders (in addition, $3.75M provided by the National Cancer Institute towards these projects)
Active Project: Utility of Adiponectin as a Biomarker of Glycemic Efficacy (Completed)

- **Project Participants:** Merck, Eli Lilly, Roche, GSK, Quintiles, NIDDK/NIH, FDA, Pfizer

- **Project Goal:** Determine whether adiponectin has utility as a predictive biomarker of glycemic control in normal non-diabetic subjects and patients with Type II diabetes

- **Study Design:** Four pharmaceutical companies shared pre-existing data from clinical trials with two independent statisticians who pooled, blinded and analyzed the data to find whether a relationship between adiponectin and glucose or HbA1C levels can be established

- **Dissemination of Results:** Results to be presented during the 69th Session of the American Diabetes Association Annual Meeting, June 2009
Active Project:
Carotid MRI Reproducibility Study
via an NHLBI AIM-HIGH Ancillary Study

**Project Participants**: University of Washington, NHLBI, Abbott, Merck, Pfizer, FDA

**Project Goals:**
- Establish a standardized carotid MRI protocol at 15 centers with 3T whole body MRI scanners (using GE and Philips scanners)
- Provide training and standardized imaging sequences and carotid phased-array coils to all sites
- Add reproducibility scan at all sites (n=80)
- Determine the impact of site and platform on reproducibility

**Project Duration and Budget:**
- 18-month, $957K study from 3 private funders ($1.02M also provided by NHLBI)

**Dissemination of Results**: Results to be submitted for publication first and then posted on The Biomarkers Consortium website
Active Project:
Use of Targeted Multiplex Proteomic Strategies to Identify Plasma-Based Biomarkers in Alzheimer’s Disease (Underway)

**Need:**
- Simple biochemical tools to identify early AD and monitor treatment effects on disease progression

**Opportunity:**
- Utilize plasma biofluids from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) approved for use in assessing the utility of existing AD biomarker panels as tools for disease progression and identification of early AD

**Objectives:**
- Qualify known plasma-based biomarkers
  - Indicate change in disease progression
  - Serve as useful endpoints to be modified by drug treatment
  - Support disease modification drug trials

**Strategies:**
- Qualify plasma-based (151 analytes) multiplex panel composed of a subset of biomarkers identified in prior proteomic studies (next phase of project (CSF) to be pursued in 2009)
- Characterize the αβpeptide species present in plasma

**Project Duration/Budget:** 6 months / $0.4M
- Results available by April 2009 – funds available in-house at FNIH to conduct this project
Approved Project:  
Comparison of Two PET Radioligands  
Labeled with $^{11}$C or $^{18}$F to Quantify the  
Peripheral Benzodiazepine Receptor

**Need:** New radioligands with higher specific binding to PBR -- Limits to $[^{11}\text{C}](R)$-PK 11195 (prototypical tracer):
- low brain uptake, causing poor signal-to-noise
- amounts of specific binding too low for stable quantitative analysis
- study results difficult to interpret

**Opportunity:** Two new radioligands, $[^{11}\text{C}]$PBR28 and $[^{18}\text{F}]$FBR, have shown significantly higher specific binding to PBR than $[^{11}\text{C}](R)$-PK 11195 in preliminary studies

**Objective:** Develop improved, more sensitive and more quantifiable radioligands

**Project Goals:**
- Assess the utility of these two radioligands to image and quantify inflammation in the periphery and the brain in Alzheimer’s Disease and Atherosclerosis
- Determine the time course/role of inflammation in different brain disorders/periphery and utility as biomarkers to assess the efficacy of agents designed to increase/decrease inflammatory markers

**Project Duration and Budget:**
- Two years, $1\text{M}$ (to be equally funded by NIMH/private sector – 5 companies) – implementation to begin in Q1 2009

**Dissemination of Results:** All results will be published via peer-reviewed journal and/or Consortium website
Approved Project: Circulating Tumor Cells as Biomarkers of Castration-Resistant Metastatic Prostate Cancer

• **Project Participants**: Cougar Biotechnologies, Veridex (Johnson & Johnson)

• **Project Goal**: Circulating tumor cells (CTCs) are very promising as a diagnostic and prognostic and drug-response biomarker; this study seeks to validate this biomarker while testing improved methods to enumerate CTCs

• **Study Design**: This is a companion study, within an ongoing phase 3 clinical trial in advanced prostate cancer, to evaluate the use of CTCs as a diagnostic and prognostic and drug-response biomarker

• **Project Duration and Budget**: Four years, $3M – funds currently being sought

• **Dissemination of Results**: Results published via peer-reviewed journal and/or Consortium website: Q4 2009 for CTC analysis pre-treatment, and Q3 2011 for association between clinical outcome and CTC results
Approved Project:
Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) Technique Optimization Using Prostate Cancer as a Model System

- **Project Participants**: National Cancer Institute (NCI), ACRIN (American College of Radiology Imaging Network), Brown University, University of Pennsylvania

- **Project Goal**: Establish a benchmark dataset that will enable development of a standardized approach to DCE-MRI, facilitating its use in clinical trials for new anti-angiogenesis agents

- **Study Design**: This is an imaging study that will develop an optimized dataset in the context of a prostate cancer clinical trial, analyze these data and use the results to develop a standard approach for widespread use

- **Project Duration and Budget**: 18 months, $1.8M – funds currently being sought

- **Dissemination of Results**: Results published via peer-reviewed journal and/or NCI and ACRIN data warehouses: Q3 2010
Approved Project:

Establish Guidelines and Initial Diagnostic Criteria for the Association of Sarcopenia with Clinically Important Weakness: Evidence for Treatment Benefit

**Project Participants:** NIH, FDA, industry, University of Pittsburgh

**Project Goal:** develop consensus guidelines for the diagnosis of sarcopenia by answering two main questions:

1. What is a clinically important degree of muscle weakness in older adults?
2. Among older persons who are weak, what proportion demonstrate low muscle mass as a potentially treatable contributing cause?

**Project Outline:** existing data from observational and clinical studies will be analyzed to provide the basis for a consensus definition of sarcopenia. Two major phases:

- **Phase 1:** create an RFP and provide 6 research grants to qualified groups of investigators to compile/analyze existing data from observational studies and completed clinical trials
- **Phase 2:** hold a guideline conference in late 2010 to review the analysis findings and create recommendations for the development of a consensus definition of sarcopenia and the criteria for its measurement

**Project Duration and Budget:** 18 months, $463K – funds currently being sought

**Dissemination of Results:** Summary manuscript of the consensus statement via a publication.
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