Broad Institute

The Eli and Edythe L. Broad Institute is a collaboration of the Massachusetts Institute of Technology, Harvard University and its affiliated hospitals, and the Whitehead Institute for Biomedical Research.

Officially launched on May 1, 2004, the Broad Institute formally operated for only the last 60 days of the reporting year. This report provides an introduction to the mission and organization of the Broad Institute.

Mission

The Broad Institute's scientific mission is:

- to create tools for genomic medicine and make them broadly available to the scientific community
- to apply these tools to propel the understanding and treatment of disease

Its organizational mission is:

- to enable collaborative projects that cannot be accomplished solely within the traditional setting of individual laboratories
- to empower scientists through access to cutting-edge tools

Research

The Broad Institute is organized around Scientific Programs/Initiatives and Platform Organizations.

Scientific Programs

The Scientific Programs are intellectual communities consisting of faculty, trainees, and professional scientists from groups across the Broad community with a shared biomedical interest. The program is the nucleus for (1) regular scientific meetings among the groups and (2) conceptualization, planning, and execution of major collaborative projects.

There are currently eight programs, including four that are designated as initiatives because they are in the pilot stage.

Cancer Program

The Cancer Program focuses on genomic and computational solutions to problems in cancer biology and cancer medicine. The availability of genomic tools and computational biology present an unprecedented opportunity to systematically study

the biological basis of cancer and to develop new genomics-based therapeutics. Key themes within the program include:

- Development of a molecular taxonomy for human cancer
- Use of genomics to explore the molecular consequences of oncogene activation
- Development of new computational approaches to genomic data analyses
- Identification of therapeutic targets in cancer using chemical genomics
- Development of early diagnostic and prognostic markers for cancer

Cell Components, States and Circuitry Program

The Cell Components, States and Circuits Program focuses on identifying and monitoring functional components of the cell and using such information to understand the basis of human disease. Key themes include:

- Identification of all components encoded in the human genome. Comprehensive identification of the functional elements, including genes, transcripts, and proteins encoded; the regulatory elements that control their expression; and the structural elements in chromosomes.
- Monitoring and modulation of cellular components. Developing tools to monitor levels, modification, and relationships among cellular components (DNA, RNA, protein and metabolites). Develop tools to systematically modulate gene and protein expression.
- Recognition of cellular signatures. Use the tools of monitoring and modulation to collect information about cellular states in health and disease, with the goal of being able to recognize the cellular signatures corresponding to all key cellular states.
- Elucidation of cellular circuitry. Use the tools of monitoring and modulation toward the ultimate goal of understanding cellular circuitry.

Chemical Biology Program

The Chemical Biology Program employs the chemical sciences to understand the principles that underlie biology and to develop approaches to ameliorate disease. Key themes include:

- High-throughput screening capability. Developing capabilities to make high-throughput chemical screening routine in biomedical research and enable access for the community.
- Diversity-oriented synthesis. Developing diversity-oriented synthesis, as well as other types of chemical synthesis, to create the most relevant universe of small molecules for biomedical research —including bioprobes, protodrugs, and research reagents.
- Chemoinformatics tools and databases. Developing suites of informatic tools and federated databases to facilitate the use of small molecules in biology and medicine.

- Target identification. Developing experimental and computational techniques to allow rapid identification of protein targets of small molecule modulators, discovered through phenotypic assays.
- Molecular imaging. Developing non-invasive and revealing techniques for real-time imaging image living systems, including the visualization of single molecules.

Medical and Population Genetics Program

The Program in Medical and Population Genetics is focused on genome sequence variation in the human population and its contribution to disease. The work draws on many disciplines, including population genetics, disease and statistical genetics, epidemiology, analysis of biological pathways relevant to disease, genomic technologies, and bioinformatics. Key themes include:

- Characterization of genetic variants. Comprehensive identification of the common genetic sequence differences between individuals, consisting of single nucleotide polymorphisms (SNPs).
- Haplotype structure of the human genome. Comprehensive characterization of the local structure of genetic variation across the genome, to create a Haplotype Map of the Human Genome to serve as a tool for finding the genes responsible for susceptibility to disease.
- Disease genetics. Individual projects involve the search for genes involved in heritable risk for various disorders, such as type 2 diabetes, inflammatory bowel disease, bipolar disorder and schizophrenia, and cardiovascular disease.

Infectious Disease Initiative

This initiative will explore ways to apply comprehensive tools for genomic medicine to key problems in infectious disease, including screening for chemical and biological modulators of host-pathogen interaction and population genetics of infectious disease. The initiative has particular focus on malaria, tuberculosis, and trypanosomal diseases.

Metabolic Disease Initiative

This initiative will explore ways to apply comprehensive tools for genomic medicine to key problems in metabolic disease. Key themes include using genomic approaches to explore the biology metabolic pathways, using genomic profiling methods to discover biomarkers of metabolic disease in complex samples, and identifying inherited genetic risk factors influencing metabolic traits and diseases in humans and model systems.

Psychiatric Disease Initiative

This initiative will explore ways to apply comprehensive tools for genomic medicine to key problems in psychiatric disease. Key themes include studying the population genetics of common psychiatric diseases, especially depression and schizophrenia; undertaking functional analysis of candidate psychiatric disease genes and their

biological pathways; and screening for small molecule and biological modulators in cell-based and in vivo models of psychiatric disease and related traits.

Inflammatory Disease Initiative

This initiative will explore ways to apply comprehensive tools for genomic medicine to key problems in inflammatory disease. Key themes include population genetics of inflammatory diseases, discovery of biomarkers of immune function and inflammatory disease, and screening for chemical and biological modulators of immune function in cell-based and in vivo models.

Faculty

The Broad Institute involves faculty from throughout its member institutions—MIT, Harvard and its affiliated hospitals, and Whitehead. The Broad Institute investigators include core members, whose labs are located primarily at the Broad, and associate members, whose labs are located primarily elsewhere, but may lead collaborative projects at the Broad. All members have a primary appointment in a "home department" at one of the member institutions.

Core Members

There are currently four core members, with an anticipated total of 12.

Eric Lander is the Broad Institute's founding director. He is a professor of biology at MIT, professor of systems biology at Harvard Medical School, and a member of the Whitehead Institute. He codirects the Broad's program in cell components, states and circuits.

Stuart Schreiber is Morris Loeb professor and chair of the Department of Chemistry and Chemical Biology at Harvard and an investigator at the Howard Hughes Medical Institute. He codirects the Broad's program in chemical biology.

David Altshuler is associate professor of genetics and medicine at Harvard Medical School and the Massachusetts General Hospital. He codirects the Broad's medical and population genetics program.

Todd Golub is associate professor of pediatrics at Harvard Medical School and the Dana-Farber Cancer Institute and an associate investigator of the Howard Hughes Medical Institute. He directs the Broad's cancer program.

Associate Members

There are currently 57 associate members from nine institutions—MIT, Whitehead Institute (WI), Harvard Faculty of Arts and Sciences (HU FAS), Harvard Medical School (HMS), Harvard School of Public Health (HSPH), Massachusetts General Hospital

(MGH), Brigham and Women's Hospital (BWH), Dana-Farber Cancer Institute (DFCI), The Children's Hospital (TCH), and Beth Israel Deaconess Medical Center (BIDMC).

Chris Burge (MIT)
Colleen Cavanaugh (HU FAS)
George Church (HMS)
Jon Clardy (HMS)
EJ Corey (HU FAS)
Mark Daly (WI, MIT)
Gerry Fink (WI)
Jeff Flier (BIDMC)
Bill Gelbart (HU FAS)
Rob Gerszten (MGH)
David Gifford (MIT)
Jim Gusella (MGH)
Daniel Haber (MGH)
Nir Hacohen (MGH)
David Hafler (BWH)
Bill Hahn (DFCI)
Ed Harlow (HMS)
Dan Hartl (HU FAS)
Joel Hirschhorn (TCH)
David Housman (MIT)
Richard Hynes (MIT)
Tyler Jacks (MIT)
Bob Kingston (MGH)
Monty Krieger (MIT)
Doug Lauffenberger (MIT)
Jackie Lees (MIT)
Sue Lindquist (WI)
David Liu (HU FAS)
Jun Liu (HU FAS)
Harvey Lodish (WI)
Gavin MacBeath (HU FAS)
Doug Melton (FAS)
Matthew Meyerson (DFCI)
Megan Murray (HSPH)
David Page (WI)
Aviv Regev (HU Bauer Center)
David Reich (HMS)
Evan Rosen (BIDMC)
Gary Ruvkun (MGH)
David Sabatini (WI, MIT)
Leona Samson (MIT)
Ed Scolnick (HU, MIT)
Christine Seidman (BWH)
Jonathan Seidman (HMS)
Bill Sellers (DFCI)
David Sinclair (HMS)
Pamela Sklar (MGH)
Peter Sorger (MIT)
Alice Ting (MIT)
Bob Weinberg (WI)
Ralph Weisleder (MGH)
Forest White (MIT)
Dyann Wirth (HSPH)
Wing Wong (HU FAS)
Mike Yaffe (MIT)
Rick Young (WI, MIT)
Xiaowei Zhuang (HU FAS)

Facility

The Broad Institute will occupy a new building currently being constructed at 7 Cambridge Center, opposite the MIT Biology Department and next to the Whitehead Institute. Construction is expected to take two years, with occupancy expected in spring 2006.

The Broad Institute is currently located in temporary quarters at 320 Charles St. and One Kendall Square.

Eric S. Lander
Director
Professor of Biology

More information on the Broad Institute can be found online at http://www.broad.mit.edu/.