

## 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.

Continued technology advancements and collaborations meant that 2007-2008 was another year of growth and excitement at the Broad Institute, and paved the way towards several key discoveries. More efficient genetic analysis methods enabled researchers at the Broad to conduct so-called genome-wide association studies, linking constellations of culprit genes to a diverse range of human diseases. New findings and advances in the HapMap project, cancer research, infectious diseases like tuberculosis and malaria, mitochondrial research, and psychiatric diseases were published by Broad researchers in a variety of prominent journals, including *Nature*, *New England Journal of Medicine*, and *Science*. In addition, Broad researchers garnered accolades that included the Overton Prize of the International Society of Computational Biology, the Ho-Am prize, NIH Director's New Innovator Awards, and more.

### Mission

The Broad Institute's scientific mission is to collaboratively create critical tools for genomic medicine, to apply these tools to the understanding and treatment of disease, and to make these tools and data broadly available to the scientific community.

### Accomplishments and Future Projects

This year, Broad Institute researchers contributed to genome-wide association studies (GWAS) that focused on a myriad of human diseases. Studies revealed genetic variation associated with multiple sclerosis, height, autism, diabetes, Crohn's disease, high cholesterol, heart disease, and other diseases. Recent advances in high-throughput technologies and analytical tools have put GWAS within reach, yielding plentiful results.

Studies of pathogens also abounded. Genetic variations linked to plant pathogens were uncovered; a new study of the parasite that causes malaria revealed which genes are turned on and off during infection; and researchers completed the first genome sequence of an extensively drug-resistant strain of tuberculosis.

In addition, scientific public outreach programs continued to flourish. In addition to continuing the Midsummer Nights Science lecture series, the Broad's Educational Outreach Program supported six high school students who completed successful summer internships in Broad laboratories. The institute also began its artist-in-residence program, with artist Daniel Kohn collaborating with researchers and creating Broad-influenced works of art.

New international collaborations began, and work continued on projects like the HapMap project. This year, researchers at Broad teamed up with scientists nationwide to uncover genes and environmental factors that trigger disease as part of the Genes, Environment, and Health Initiative, and the second phase of the HapMap project

yielded an even denser map of the genome, with three times more markers than the initial version.

A new mapping method was applied to more efficiently map disease genes in dogs in order to understand human diseases faster and an analysis of 12 species of fruit fly was one of the first large-scale comparisons of multiple animal genomes.

A new systematic effort to map genetic changes in lung cancer revealed common genetic variants as well as a critical gene alteration that may underlie some lung cancer cases. Researchers also discovered a culprit gene for the blood disorder known as 5q minus syndrome and new tools used in mitochondrial investigations highlighted the role of this organelle in healthy and diseased cells.

### Major Publications

- Risk alleles for multiple sclerosis identified by a genomewide study, *New England Journal of Medicine* (July)
- A common variant of HMGA2 is associated with adult and childhood height in the general population, *Nature Genetics* (September)
- Natural history and evolutionary principles of gene duplication in fungi, *Nature* (September)
- The *Fusarium graminearum* genome reveals a link between localized polymorphism and pathogen specialization, *Science* (September)
- Efficient mapping of mendelian traits in dogs through genome-wide association, *Nature Genetics* (October)
- Characterizing the cancer genome in lung adenocarcinoma, *Nature* (October)
- Distinguishing protein-coding and noncoding genes in the human genome, *Proceedings of the National Academy of Sciences* (November)
- Distinct physiological states of *Plasmodium falciparum* in malaria-infected patients, *Nature* (November)
- Identification of RPS14 as a 5q- syndrome gene by RNA interference screen, *Nature* (January)
- Association between microdeletion and microduplication at 16p11.2 and autism, *New England Journal of Medicine* (January)
- Polymorphisms associated with cholesterol and risk of cardiovascular events, *New England Journal of Medicine* (March)
- Identification of 10 loci associated with height and previously unknown biological pathways in human growth, *Nature Genetics* (April)
- MicroRNA-mediated control of cell fate in megakaryocyte-erythrocyte progenitors, *Developmental Cell* (June)
- Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease, *Nature Genetics* (June)

## Honors and Awards

- Kerstin Lindblad-Toh, codirector of the Broad Institute's Genome Sequencing and Analysis Program, was awarded a 2007 European Young Investigator award for her work on disease gene mapping in the domestic dog (August).
- Senior associate member Nir Hacohen, associate member Alan Saghatelian, and associate member Levi Garraway were among the first recipients of the NIH Director's New Innovator Award (September).
- Ilan Wapinski was named the inaugural recipient of the Lawrence H. Summers Fellowship (September).
- Cancer Program director and core member Todd Golub received the 2007 Paul Marks Prize for Cancer Research from Memorial Sloan-Kettering Cancer Center (September).
- The Broad Institute received one of seven grants from the National Human Genome Research Institute to support the second phase of the ENCyclopedia Of DNA Elements (ENCODE) project (October).
- Research technician Meghan Bliss-Moreau received second place in the poster competition at the New England chapter of the Lab Robotics Interest Group for her poster describing an innovative solution for managing microscopic data and images (October).
- Three Broad scientists—Director Eric Lander, core member and MPG director David Altshuler, and senior associate member Mark Daly—were among the top 10 most-cited authors of recent papers in molecular biology and genetics according to *Science Watch* (February).
- Core member Aviv Regev was named the 2008 recipient of the Overton Prize of the International Society of Computational Biology (March).
- Associate member Charles Lee received the 2008 Ho-Am Prize for groundbreaking work on human genetic variation (April).

**Eric S. Lander**

**Director**

**Professor of Biology**

*More information about the Broad Institute can be found at <http://broad.mit.edu/>.*