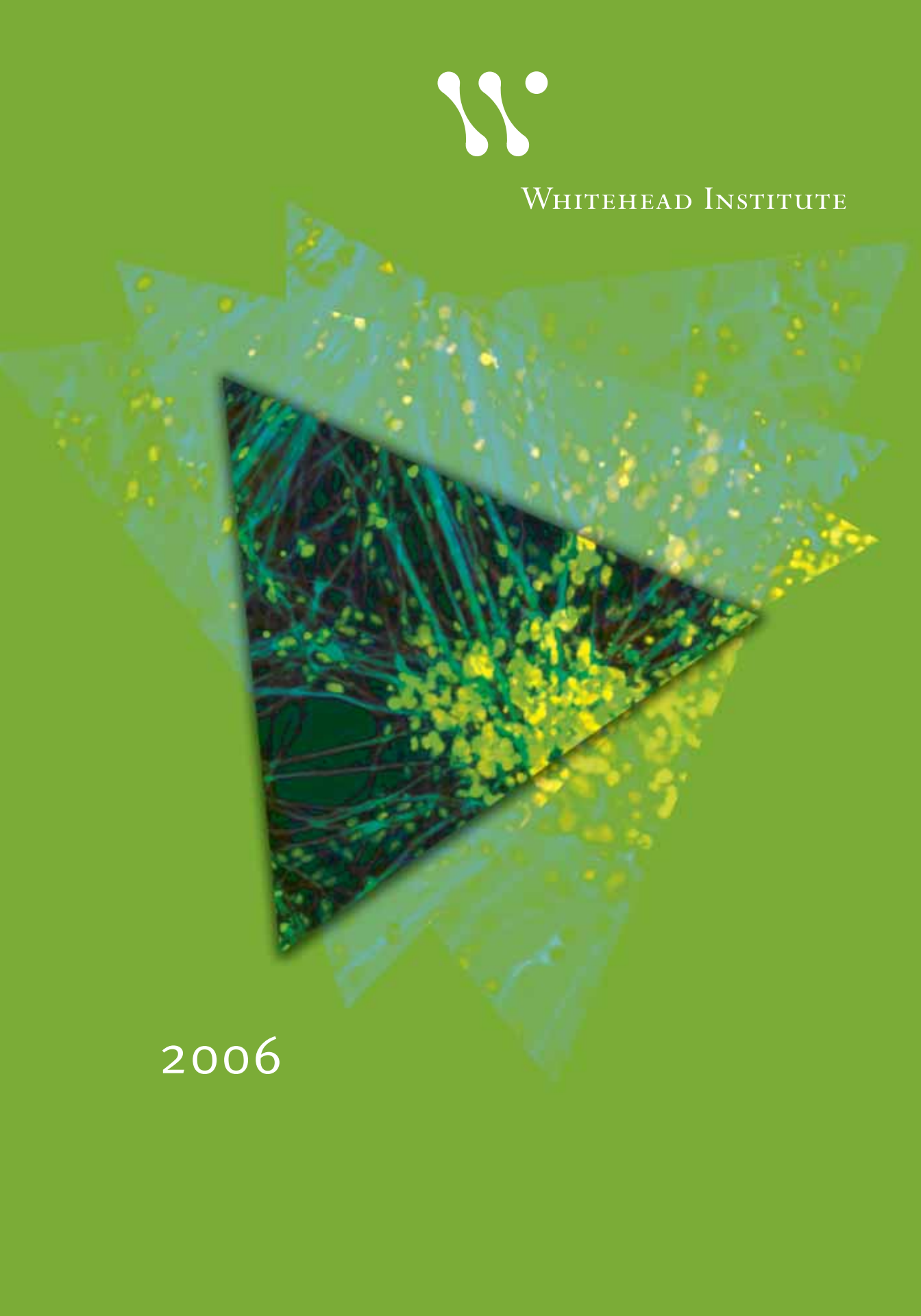


Whitehead Institute

2006

WHAT MAKES WHITEHEAD UNIQUE?

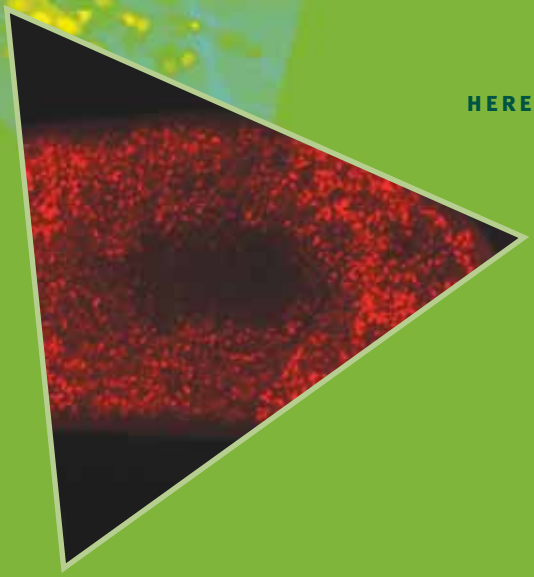
Whitehead Institute for Biomedical Research is a non-profit, independent research and educational institution with research programs in stem cells, cancer, immunology, neurological disorders, developmental biology, regenerative biology, genetics and genomics.

The Institute was founded though the generosity of Edwin C. "Jack" Whitehead, a businessman and philanthropist whose dream was to create an independent research institute that benefited from a full partnership with a world-class academic institution. This dream was realized in 1982 when Whitehead Institute was established with a teaching affiliation with Massachusetts Institute of Technology.

As the Institute marks its 25th anniversary, it houses 21 principal investigators (15 Members and 6 Fellows) and more than 300 postdoctoral fellows, graduate and undergraduate students, visiting scientists and technicians from around the world.

Whitehead brings together a small group of world-class biomedical researchers in a highly collaborative and supportive environment, and empowers them to pursue the questions that intrigue them most.

HERE'S A SAMPLING OF THE STEM CELL-RELATED STUDIES



◀ How do **planarian flatworms** use their adult stem cells (shown here in red) to reconstitute themselves from a tiny sliver? Peter Reddien's lab draws on high-throughput RNA interference and other powerful analysis techniques to address this question.

COVER: Neurons grown at Whitehead from human embryonic stem cells.

THE WHITEHEAD INSTITUTE INITIATIVE IN STEM CELL AND REGENERATIVE BIOLOGY

Embryonic and adult stem cells offer the promise of radically new approaches to heal and renew damaged tissue. Understanding how these cells pull off their astonishing feats may one day transform the way we understand and treat a host of diseases.

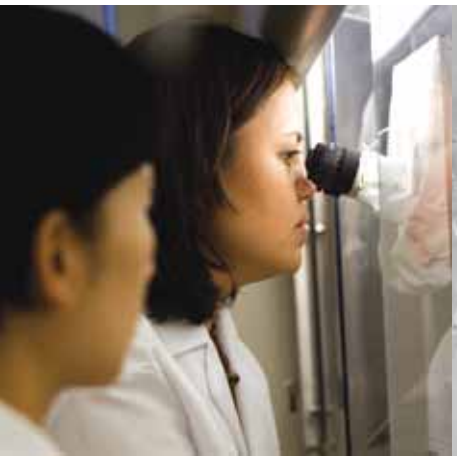
Stem cell research marks a new frontier in biomedical science. But in spite of all the press, politics and hype, surprisingly little is known about the basic mechanisms that empower these cells.

Across Whitehead Institute's eclectic mix of cutting-edge research, more and more projects are opening up the inner world of stem cells.

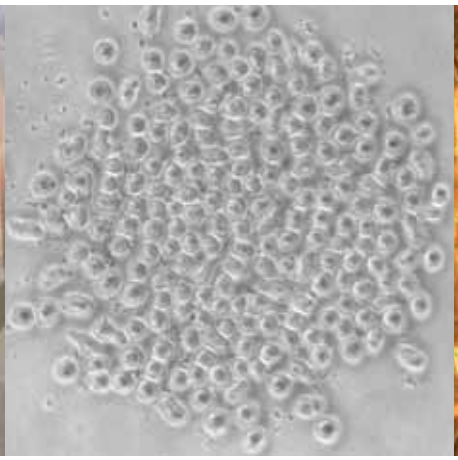
Whitehead's Initiative in Stem Cell and Regenerative Biology will enable these projects—supporting many of the Institute's researchers in exploring embryonic and adult stem cells and the roles they play in development and throughout our lives.

To realize these goals, increased support from foundation, corporate and individual donors will be required to allow Whitehead scientists to pursue promising research efforts that are ineligible for federal research funding.

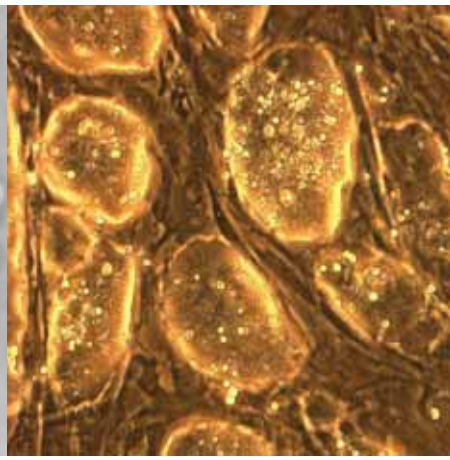
NOW UNDERWAY AT WHITEHEAD



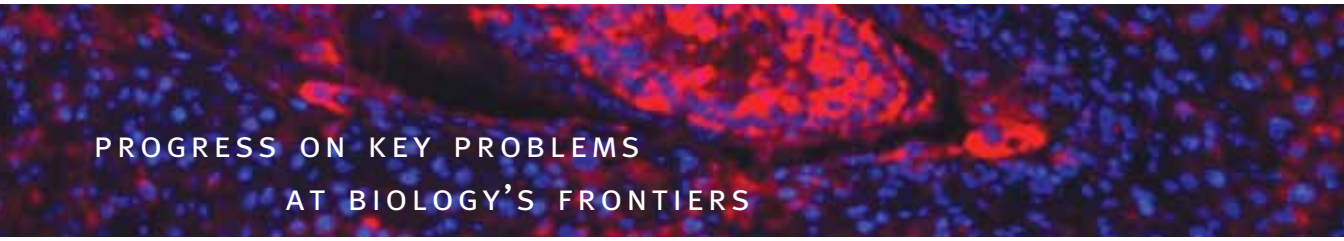
▲ Researchers in the **Human Embryonic Stem Cell Facility** are bringing expertise to the tricky tasks of working with these cells.



▲ **Adult blood stem cells** are extremely difficult to manipulate, but scientists in Harvey Lodish's lab have succeeded in multiplying them 30-fold in mice.



▲ Scientists in the lab of Rudolf Jaenisch work extensively with **embryonic stem cells from mice** (here) as well as humans.



PROGRESS ON KEY PROBLEMS AT BIOLOGY'S FRONTIERS

Whitehead researchers make dramatic findings across a broad range of basic biological phenomena. Among 2006 highlights:

Mapping the foundation of human development: Researchers in the labs of Richard Young and Rudolf Jaenisch and colleagues at MIT and Harvard have mapped how a group of proteins, collectively called Polycomb, controls the genome.

Reversing Parkinson's symptoms in animal models: Researchers in Susan Lindquist's lab and colleagues have identified how traffic jams in a key biological pathway cause Parkinson's symptoms. They also figured out how to repair that pathway and restore normal neurological function in certain animal models.

Discovering a "cloaking device" that helps pathogens evade the immune system: Researchers in Gerald Fink's lab have discovered a network of genes that may help pathogenic fungi hide from the immune system. When this network is disabled, these dangerous fungal invaders are suddenly rendered vulnerable.

Revealing secrets of metastasis by 3D analysis: An advanced three-dimensional imaging study undertaken in the labs of Paul Matsudaira and MIT Bioengineering department head Douglas Lauffenburger highlighted crucial phenomena in how cancer spreads.

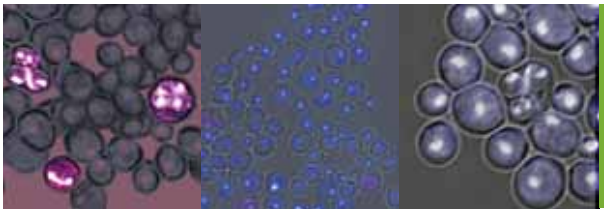
▲ Researchers in David Sabatini's lab study the TOR pathway, aiding investigations of the role nutrients and metabolism play in disease. In this image taken by David Guertin, a mouse embryo shows a high level of mammalian TOR activity (in red, with DNA shown in blue).

Alleviating symptoms of Rett Syndrome in mice: Researchers in Rudolf Jaenisch's lab and colleagues at MIT and Brandeis University have dramatically reduced certain manifestations of Rett Syndrome in mice, marking a path by which to explore possible therapies for this debilitating neurological disorder.

Engineering yeast to speed ethanol production: Scientists from the labs of Gerald Fink and MIT professor Gregory Stephanopoulos have engineered yeast that can improve the speed and efficiency of ethanol production. This may prove to be a key component in making biofuels a significant part of the U.S. energy supply.

Unearthing clues to the immune system: Investigating one form of the herpes virus, researchers in the lab of Hidde Ploegh spotlighted a key component in the machinery with which cells dispose of malfunctioning proteins.

Uncovering a new type of small RNAs: David Bartel's lab located a new class of small RNAs similar to, but distinct from, microRNAs. The uniform structure of these small RNAs strongly indicates an important biological role.



◀ Cintia Hongay in Gerald Fink's lab showed that a class of RNA molecules, thought to have no function, may protect sex cells from self-destructing. In yeast, the *IME4* gene can disable its own ability to make protein with "anti-sense" RNA.

WHITEHEAD FACULTY

David Bartel is a leader in the identification and study of microRNAs, which play important gene regulatory roles in both plants and animals.

Gerald R. Fink, who developed baker's yeast as a model organism, combines genetics, biochemistry and molecular biology to yield discoveries in gene regulation and infectious disease.

Rudolf Jaenisch, a founder of transgenic science, studies the biology of cloning and embryonic stem cells, as well as the way gene expression is regulated in mammalian development and disease without changes to DNA.

Eric S. Lander, who pioneered key tools and discoveries in modern mammalian genomics, studies how genomes function in health and disease.

Susan L. Lindquist conducts research on how changes in protein conformation can govern such diverse processes as stress tolerance, neurodegenerative disease and heredity.

Harvey F. Lodish, a leader in membrane biology research, studies numerous proteins that reside on the surface of cells and may play a role in cancer, diabetes, heart disease and obesity.

Paul T. Matsudaira studies the mechanics of cell motility and develops advanced bioimaging and bioinformatics methods.

Terry L. Orr-Weaver deciphers critical events in cell growth and cell division, helping to reveal new players in birth defects and cancer.

David C. Page, who has overhauled our understanding of the human Y chromosome's structure and operation, studies mammalian sex cells and sex chromosomes.

Hidde Ploegh investigates the molecular mechanisms by which the immune system responds to antigens such as viruses or bacteria.

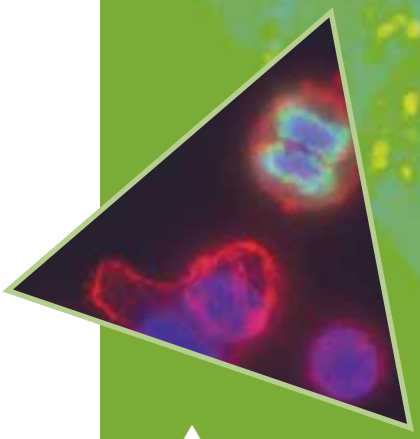
Peter W. Reddien works to understand regeneration through research on planarians, flatworms with regenerative powers that have captured the imagination of biologists for more than a century.

David Sabatini studies the basic mechanisms that regulate cell growth, and has developed technologies to study the functions of large sets of genes in mammalian cells.

Hazel L. Sive studies the earliest stages of nervous system development and primary mouth formation in vertebrates using zebrafish and frog embryos.

Robert A. Weinberg, who discovered the first human oncogene and the first tumor suppressor gene, focuses his attention on how breast cancer cells invade and metastasize.

Richard A. Young is a pioneer in gene transcription (the process by which cells read and interpret their DNA) and maps the regulatory circuitry of human cells.



▲ Jason Moffatt in David Sabatini's lab analyzed cell division by labeling human cancer colon cells for specific genes.

WHITEHEAD FELLOWS

These young researchers skip the postdoctoral stage of their training and are given the space and resources needed to run their own labs and pursue an independent research agenda—without teaching responsibilities.

Thijn Brummelkamp exploits RNA interference, a process that can selectively turn off specific genes, to study genes implicated in cancer.

Fernando Camargo is working to understand the basic molecular mechanisms that control adult blood stem cells.

Hui Ge integrates data from gene expression arrays, protein interaction networks, RNA interference and other high-throughput technologies to study early development in the *C. elegans* worm.

Andreas Hochwagen studies meiosis, the process by which sperm and egg cells are created, and probes the mechanism by which cells prevent genetic damage during the process.

Kate Rubins examines how certain kinds of deadly viruses, such as smallpox, manipulate gene expression within their host cells.

Paul Wiggins works to connect a new generation of quantitative biological experiments with appropriate mathematical models.

SHARING THE WEALTH OF KNOWLEDGE

In 2002, Erika Batchelder really enjoyed the Institute's Spring Lecture Series for High School Students. Afterwards, "I made an hour-and-a-half presentation to my biology class—I just talked and talked," she recalls. Today she has brought her enthusiasm for biology to the Institute's Keck Microscopy Center, helping scientists apply the latest bioimaging techniques for deeper understanding of cell dynamics.

That's a success story for one of Whitehead's core missions: sharing the understanding of research at biology's frontiers with other scientists, students, teachers and the public. This mission becomes ever more crucial as today's life sciences offer an inspiring but daunting mix of power, promise and sheer complexity.

In addition to sponsoring events throughout the year, the Institute spreads the word about advances in biomedical science through its website (www.whitehead.mit.edu) and *Paradigm* magazine. Additionally, the BiologyWeek newsletter (http://biologyweek.wi.mit.edu) alerts the local biomedical research community to scientific talks.

▲ The Spring Lecture Series for High School Students offers students a unique opportunity to learn about today's biomedical research. In 2006, the three-day program covered current research and controversies about human evolution.

▲ This year's Whitehead Symposium, "Bioimaging: Capturing Cell Dynamics," drew over 1,000 registrants, including these students from Gordon College, which sends a group each year.

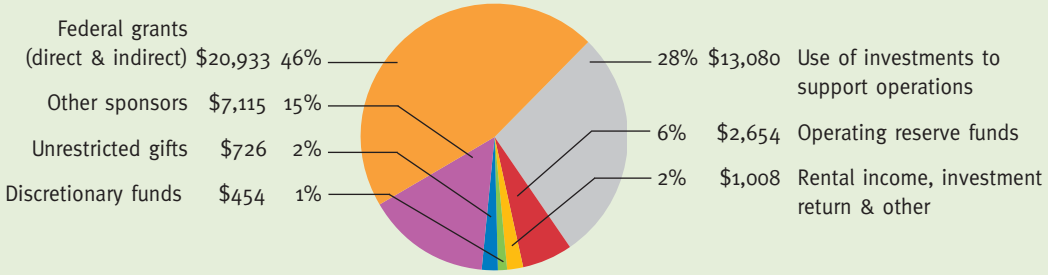
◀ The Lecture Series for High School Teachers brings in world-class researchers to address topics such as personalized medicine for cancer, protein folding and drug development, and the genetics of diabetes. Just as important, the series matches teachers with young Whitehead scientists who serve as resources during the school year.

RESEARCH HONORS AND AWARDS

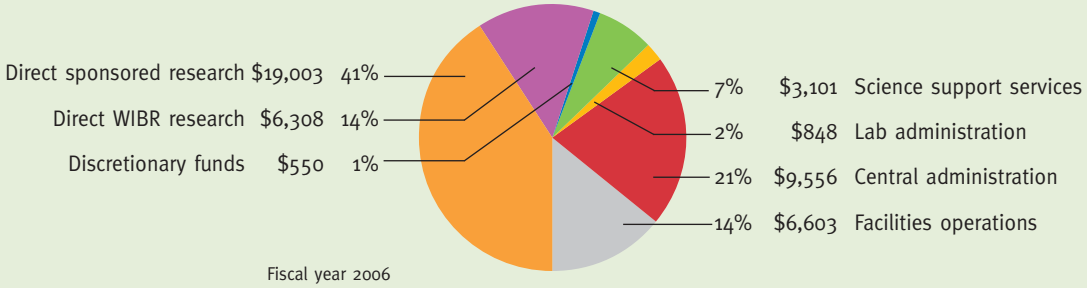
Laurie Boyer, **Susan Lindquist** and **Richard Young** made *Scientific American*'s list of top 50 scientists.... **Thijn Brummelkamp** received a Kimmel Scholar Award... **Gerald R. Fink** was honored with Whitehead's first endowed chair, the Margaret and Herman Sokol Chair in Biomedical Research... **Rudolf Jaenisch** received the Max Delbrück Medal. Along with **Susan Lindquist,** Jaenisch was elected to the Institute of Medicine... **Susan Lindquist** also was appointed a Howard Hughes Medical Institute Investigator.... **Terry Orr-Weaver** was named to the National Academy of Sciences and an American Cancer Society Professor... **Hidde Ploegh** won Belgium's Interbrew-Baillet Latour Health Prize... **Peter Reddien** was named a Searle Scholar and received a Rita Allen Scholar award... **Robert Weinberg** was awarded the Landon-AACR Prize for Cancer Research and was chosen to head the Ludwig Center for Molecular Oncology at MIT.

FUNDING

Sources of funds ($000) **Total $45,969**



Uses of funds ($000)



Fiscal year 2006
July 1, 2005 through June 30, 2006

Whitehead Institute is committed to seeding the most promising, nascent projects. Often, that requires special support for research projects not yet ready for conventional funding—the best of which lead to discoveries that change the very direction of science.

Today, less than half of Whitehead research is funded by grants from the federal government. Whitehead supports the rest through major funding from its endowment and with support from individuals, foundations and corporations. Through efforts such as the Initiative in Stem Cell and Regenerative Biology, Whitehead is seeking new partnerships to ensure scientists the freedom to pursue the most promising research.

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Hui Ge
Andreas Hochwagen
Kate Rubins
Paul Wiggins

CHIEF OPERATING OFFICER

Barbara Siegel

FACULTY AND FELLOWS

Whitehead principal investigators are world-class scientists working at the frontiers of biological research. Under the Institute's close affiliation with Massachusetts Institute of Technology, Whitehead Members also are members of MIT's Biology department or other MIT departments. Created at the Institute's inception, the Whitehead Fellows program allows exceptionally talented young scientists to set up independent research programs without undertaking the full range of normal faculty duties.

FACULTY ACHIEVEMENTS

Whitehead faculty includes the recipient of the 1997 National Medal of Science (Weinberg), eight members of the National Academy of Sciences (Fink, Jaenisch, Lander, Lindquist, Lodish, Orr-Weaver, Page and Weinberg), seven Fellows of the American Academy of Arts and Sciences (Fink, Jaenisch, Lander, Lindquist, Lodish, Ploegh and Weinberg) and three Howard Hughes Medical Institute Investigators (Bartel, Lindquist and Page).

WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH

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