In February 2011, the world celebrated the 10th anniversary of the completion of the draft sequence of the human genome – an achievement in which many Broad Institute scientists played a central role.

When the Human Genome Project (HGP) was first proposed some 25 years ago, the notion was so foreign to biology that commentators had to resort to metaphors from physics. The HGP was biology’s Manhattan Project, biology’s Moon Shot, biology’s Superconducting Supercollider particle accelerator.

Ultimately, the HGP yielded discoveries as remarkable as any atom-smasher or deep-space telescope. It revealed that the spectrum of protein-coding genes is far smaller than imagined, that physiology depends on a vast universe of regulatory controls and noncoding RNAs, that diseases arise from many unsuspected genes and pathways, that so-called junk DNA may be the mother of much invention.

In the end, though, the HGP might indeed best be viewed as a “high-energy accelerator” – not of particles, but of scientific work and scientific imagination. Today, biomedical researchers can carry out projects that were once inconceivable: they can readily assay thousands of genes, millions of genetic markers, billions of nucleotides; they can interpret their findings in the context of public datasets representing tens of thousands of experiments worldwide and billions of years of evolutionary information. These capabilities have liberated them to think creatively and boldly about important biomedical challenges.

In the wake of the HGP, young biomedical scientists feel an urgency about finding new ways to accelerate science. They are impatient with technological limits that stand in the way of knowledge. They transcend disciplinary boundaries, fusing experimental, computational, and clinical science into a new biology. They roll up their sleeves to create vast datasets and powerful new methods – and they share them freely. They embrace teamwork, which is often essential to truly changing the world.

Nowhere in the world is this spirit more evident than at the Broad Institute. Walking around the Broad, you hear scientists brimming with vision and energy about: predicting all ways in which tumors can become resistant to a therapy; unraveling the molecular basis of psychiatric diseases; creating a comprehensive catalog of all cellular circuitry; and devising general methods to speed the development of new therapeutics.

Our mission is to accelerate science through a new research model and to tackle the most important challenges in biomedicine. This Annual Report aims to give a glimpse of what this means to the Broad Community – and to highlight the important support from our larger community of friends that makes it possible.

To learn more, come visit!

Eric S. Lander
President and Director
Those who look back decades from now at the history of this remarkable institute will surely mark the period since July 2009 as a crucial transitional phase. The Broad Institute, Inc., with roots dating back to 2002, is now firmly established as a separate and permanent 501(c)(3) organization pursuing a soaring vision. The Broad is stepping up to a challenge that has become conceivable only in the past decade: the transformation of medicine for the next generation – and beyond.

Such a bold and ambitious vision would be daunting if not for the inspiring spirit of collaboration and possibility that infuses the Broad. Whenever I visit, I can see, feel, and hear the music of this collaborative spirit in the Broad’s lovely atrium, in hallways, elevators, conference rooms and labs, on whiteboards and in common spaces. Here geneticists, chemists, physicians, biologists, computational scientists, and many novel combinations of these and other disciplines come together to pool their knowledge, puzzle over their newest data, and share their emerging hunches about the underlying mechanisms of some of the world’s most frightful illnesses: cancer, diabetes, heart disease, infectious disease, major psychiatric disorders, Crohn’s Disease ... many others.

What does it mean to transform medicine? For all the stunning advances we have seen in our lifetimes, physicians remain handicapped, all too often, by treatments for their patients that are still blunt instruments, the “halfway technologies” Lewis Thomas lamented years ago. In some cases, the underlying cause of a disease remains shrouded in full or partial mystery; in others the diagnostic and predictive tools are crudely inadequate. The passion that drives Broad researchers is the opportunity they see to organize bold, transformative projects to tackle what have been insurmountable problems in science and medicine, all in the hope of creating a new world of options for patients. The many Broad scientists who are practicing physicians at partner institutions are witnesses to the immediacy of their patients’ struggles and a bridge to the yearnings for promising new discoveries.

The institute itself is a bridge – a horizontal connector – across multiple institutions: Harvard, MIT, and the Harvard teaching hospitals, as well as partners in industry. While no one anywhere can predict precisely how, where, and when the foundations of modern medicine will be reshaped by the cascade of new insights from genomic studies, “Broadies” are energized by the unknown, eager to surmount constraints, undeterred by orthodoxy and traditional boundaries. It’s the really hard questions that rally the whole community.

Broad scientists work at warp speed and the relatively new Board of Directors, after its inaugural meeting in September 2009, has rapidly hit its stride. Comprising experienced leaders from academia and industry, the board, like the Broad, integrates scientific vision and industrial-strength teamwork. At the start of this year we welcomed a new director, Louis V. Gerstner, Jr., former chairman and CEO of IBM Corporation. Now, at year’s end, we express our deep gratitude, as his term draws to a close, to William F. Lee, Co-Managing Partner of WilmerHale, whose distinguished service as board vice chair and chair of the Audit, Risk, and Compliance Committee helped set the board on a firm footing in its critical start-up phase.

As I recently wrote on behalf of the board to our gifted president and director, Eric Lander, we are excited about the Broad’s progress this past year and about the impact the institute is poised to have on human health around the world. It’s a pleasure and a privilege to be sharing this grand adventure with Eric and his many partners, supporters, and colleagues.

Thanks to each and every one of you, Broadies all.

Diana Chapman Walsh
Chair of the Board of Directors
Psychiatric diseases such as schizophrenia, bipolar disorder, and major depression afflict millions, disrupting lives and families. Over the last 40 years, however, progress in understanding the underlying biology of mental disorders has been slow.

Edward Scolnick, one of the 20th century’s leaders in cancer research and the pharmaceutical industry, holds a clear and far-reaching vision of how to crack open the field of psychiatry and accelerate research by employing the tools and knowledge of the genomic era.

Arriving at the Broad in 2004 after stepping down as president of Merck Research Laboratories, Dr. Scolnick launched a third career in a lifetime of scientific achievement. As director of the Psychiatric Disease Program, he devoted himself to improving the diagnosis and treatment of major psychiatric diseases such as schizophrenia, bipolar disorder, obsessive-compulsive disease, severe anxiety syndrome, and major depression.

In early 2007, Dr. Scolnick became director of the newly formed Stanley Center for Psychiatric Research at the Broad, which was launched with generous support from Ted and Vada Stanley, founders of the Stanley Medical Research Institute in Bethesda, Maryland. Dr. Scolnick is also a core faculty member of the Broad Institute.

“Five years ago, the field of severe mental illness really had no approach to try to figure out what’s causing diseases like schizophrenia, bipolar disorder, obsessive-compulsive disease, severe anxiety syndrome, and major depression,” Dr. Scolnick explains.

Research into mental disorders has long been limited by a basic fact: It is difficult to study the living brain. But expanding genetic knowledge and sophisticated technology allow scientists to peer more deeply into the human genome to gain new insight, much as Dr. Scolnick envisioned.

“Psychiatry is undergoing and will undergo a profound change over the next decade. I don't think you'll recognize the field in 10 years,” Dr. Scolnick says. “For schizophrenia and bipolar disorder, the single largest known risk is genetics,” he says. “The genetics are complex and therefore really couldn’t be approached until four or five years ago, building on the sequencing of the genome and then the mapping of the genome – work which many people at the Broad really helped pioneer.”

He adds: “It's safe to say that progress in the field of severe mental illness is [now] only limited by money and time.” Over the past four years, major findings have been made in understanding the underlying causes of schizophrenia, bipolar disorder, and major depression. “The field is no longer stuck,” he explains. “There are ideas and approaches to try to figure out these diseases and do something better about both their diagnosis and treatment.”

Stanley Center scientists are also working to stimulate a flow of fresh ideas for potential new drugs. Janice Kranz, assistant director of the Stanley Center, notes that over the last 60 years, only one drug with a distinctively new mode of action has emerged for psychiatric disease.

“For high cholesterol and heart disease, the number of new drugs from the 1950s to the 2000s has grown,” she says. “But for psychiatric disease, the only mechanistically distinct drug that has been developed is the SSRI category – selective serotonin re-uptake inhibitors like Prozac. Ed’s whole approach to science is that if you understand the mechanism, you can tease it apart and make something that will have an effect. He proved that in his work on [cholesterol-fighting] statins, for example.”
Using the Broad's powerful technology platforms to screen thousands of chemical compounds, Edward Holson, the Stanley Center's Director of Medicinal Chemistry, looks for “keys” that fit into a specific “lock,” allowing scientists to alter the functions of specific genes. “What’s also key for us is to integrate with all the biologists and the geneticists, feeding off their techniques, and their data, to find a target and develop a chemical compound that will have a series of characteristics that we think we need,” Dr. Holson says. “The end game is to make a medicine.”

Deep collaboration with other institutions is crucial to this work. “We've catalyzed the way the field approaches the understanding of the disease; getting large groups to work together was critical,” Dr. Holson says. “In that way, the Stanley Center is very complete,” says Li-Huei Tsai, director of the Picower Institute for Learning and Memory, who began working with the center five years ago. “Any other psychiatric disease center or department covers one particular aspect of the disease,” she says.

Building on recent genetic studies, researchers are beginning to understand what accounts for behavioral changes and are studying potential connections and pathways – from genes to the brain's cells and circuits – and their role in psychiatric disorders. “We really have a lot of the different pieces available, especially in this community, for a very detailed, complete analysis and study of these disease genes,” Dr. Tsai explains.

Because Dr. Scolnick's long-range goal is to have an impact on clinical psychiatry, the Stanley Center's collaboration with treatment centers at Massachusetts General Hospital and McLean Hospital have provided crucial access to patient samples and other clinical data. In fact, Dr. Scolnick has been a member of McLean's Board of Trustees.
Working at McLean Hospital’s main campus in Belmont, clinical and research psychiatrist and Stanley Center collaborator Bruce Cohen notes the importance of a broad approach that can harness emerging technologies to analyze “a lot of genes, a lot of people, a lot of illnesses. Ed Scolnick and I were of a mind about this.” Dr. Cohen, who also served as president of McLean, is now director of the Shervert Frazier Research Institute at the hospital.

While historically researchers once hoped that simple associations could be made between a small set of genes and common mental illnesses, the reality has proven more complex. “It just doesn’t look like that,” Dr. Cohen says. “The brain is remarkably complex; electrical activity matters, chemical activity matters. It’s got so many cells with so many connections, and it’s all plastic, or malleable – always changing with time. It looks like lots of genes are involved in explaining whether you’re at more risk or less risk. Except in rare instances, none of them are absolute. The best way to come at a problem like that is probably going to be multidimensional, multidisciplinary, involving people with different interests, different laboratories.”

In addition to Dr. Scolnick, two more of the nine Broad core faculty members in 2011 are focused on neuroscience: Myriam Heiman, who also holds appointments at MIT’s Department of Brain and Cognitive Sciences and the Picower Institute for Learning and Memory, and Feng Zhang, who holds a joint appointment at the McGovern Institute for Brain Research at MIT.

Although much work remains, Dr. Scolnick says, it is clear that psychiatric research has entered the genomic era. That, in turn, will attract talented scientists and clinicians who will carry on a revolution in research for years to come.

“I think the real take-home message is that the vision is paying off,” Dr. Scolnick says. “The vision was the right vision. It still is the right vision. It needs to be constantly refined in the particular technologies that are applied to it, and the approaches. But there’s absolutely no longer a shred of doubt in my mind that if the funding is available for the full application of the technologies of human genetics to this field, you will not recognize the field of psychiatry, and how psychiatric diseases are diagnosed and treated, in decades to come.”
After a storied career running a multimillion-dollar business, Ted Stanley and his wife, Vada, anticipated a new chapter in their lives. They were setting up a philanthropic foundation in the 1980s to invest in good causes – and to help people who through no fault of their own faced trouble in their lives.

“We were feeling our way on what those causes were going to be,” Mr. Stanley says now. Then, with one phone call, their focus became clear. Their son Jonathan, then a junior at Williams College, developed bipolar illness and needed treatment. Despite that troubling news, the Stanleys considered themselves fortunate that the drug lithium successfully addressed his symptoms – and they want to make sure that someday, there is a much wider range of options for others with psychiatric illness.

Sitting in their light-filled Frank Lloyd Wright-designed home in Connecticut, the couple talks about that period with a shared voice and vision. Jonathan returned to Williams, finished law school and built a successful career of his own, lobbying to reform laws affecting those with psychiatric illness. Jonathan has committed his life to making it easier for families to get their loved ones into treatment and is a member of the board of directors of the Treatment Advocacy Center, a national nonprofit organization dedicated to eliminating barriers to the treatment of severe mental illnesses.

“Our hope,” says Mr. Stanley, “is that researchers in this field can discover and add medications that will help.”

That central hope – to see clinical impact for a wide range of psychiatric patients – has motivated their philanthropy. In 1989, the Stanleys founded the nonprofit Stanley Medical Research Institute, supporting research on the causes of, and treatments for, schizophrenia and bipolar disorder. Since it began, SMRI has supported more than $300 million in research in more than 30 countries around the world, and is the largest nongovernmental source of funds for research on these diseases in the United States.

The Stanleys’ interests span basic science as well as translational research that can eventually lead to new treatments. When Ed Scolnick’s work came to their attention, Mr. Stanley was impressed by his credentials as a scientist and a manager. Dr. Scolnick’s experience, along with the Broad’s industrial-strength technology, set the Broad apart from a purely academic setting. In early 2007, the Stanleys made an extraordinarily generous commitment of support, creating the Stanley Center for Psychiatric Research at the Broad with a $100 million grant. Pleased with the progress that Dr. Scolnick and his team are making, in April 2011 the Stanleys pledged to extend their support through 2022. Their partnership will continue accelerating scientific research at crucial junctures.

“We feel the Broad is developing a new paradigm for medical research.” – Ted Stanley
If family has been a central part of their lives together, so has business: Ted and Vada met more than a half-century ago at Procter & Gamble in Cincinnati. Both had taken entry-level jobs in P&G’s brand management groups. (They will celebrate their 50th wedding anniversary in 2011.) He left P&G for a marketing consulting group, and, in 1969, launched a business developing memorabilia for collectors. His company, now a $400 million a year concern known as MBI, began under the name The Danbury Mint. He remains as chairman, while still working part-time.

The Stanleys are also stewards of one of the last private homes built by renowned architect Frank Lloyd Wright. The house, cut into a rolling swath of land near a brook, has been restored with the same passion the couple applies to other endeavors. Wright’s furniture, his signature touches in Cherokee red, and his wood-and-concrete-block construction feel fresh more than 50 years later. Leather-bound books from the Stanleys’ Easton Press line mahogany shelves.

Reflecting on their hopes for the future of psychiatric research, the Stanleys draw on their experience in business. “In business, you are focused on the bottom line, and you want to earn profits and be a leader in your field. In medical research, basic science is quite necessary, but research also needs to focus on the real world, on patients, and potential treatments. And that’s what Eric Lander and Ed Scolnick are doing: managing scientific research that, in part, helps people who have psychiatric disorders, through basic research that might lead to development of new medications.”
Kent Dauten, managing director of Keystone Capital, Inc., was on a business trip to Boston in 2005 when he first met Ed Scolnick, who was embarking on a mission of his own: to crack open the field of psychiatric research.

A native of Illinois, Mr. Dauten has intellectual roots in New England. He graduated from Dartmouth College in 1977 and earned an M.B.A. from Harvard Business School in 1979, before returning to the Midwest to launch a distinguished career in business. A close friend from business school knew that Kent and Liz Dauten had two children with bipolar disorder, and also knew of Dr. Scolnick’s reputation and his research in the field. Dr. Scolnick met the Dautens and a partnership was forged.

In an interview in their home near Chicago, the Dautens shared their family’s journey, as well as their passion for the vital research at the Broad. It is this nexus that led them to provide crucial financial support that catalyzed the scientific research in the early days of the institute.

“The whole world of mental illness is not very well understood. But this area of research is clearly how science will come up with more effective treatments: by targeting the specific genes.” – Liz Dauten

Mr. Dauten adds that as a businessman, he was drawn to Dr. Scolnick’s background as president of Merck Research Labs. His experience “allocating resources and assessing the risks and returns they would get from research bets that they were placing was a unique combination.”

The Dautens have four children, two of whom were diagnosed with bipolar disorder at the same point in their lives, when they were sophomores in high school.

“It was a total shock to us,” Mr. Dauten says, “because they had a totally normal childhood and we have no known family history with this illness. It was quite a surprise to have one diagnosed. But with the second child, we said, ‘We’ve seen this before so we know what we’re up against.’ We’ve both become as knowledgeable as we could, attending seminars, visiting specialists, learning more and more about the illness in order to be helpful to our kids.”

Mrs. Dauten reflects that she was a psychology major at Dartmouth (where she and Kent met) and adds, “It stood us in good stead. We have learned through firsthand experience a lot more about the world of mental illness than we ever expected to.”

Research to address bipolar disorder more directly, by targeting specific genes, is important to both of them – and it has focused their philanthropy. “We’ve had a lot of ups and downs,” Mr. Dauten says. “At least we have the resources and hopefully the intellectual stamina and strong relationship between the two of us to get us through all of it.”
Asked about her hopes for the future, Mrs. Dauten sketches a picture of an era when psychiatric diagnosis and treatment will be more tailored to each unique patient—“Because bipolar disorder is a brain illness, every individual responds differently.”

She adds: “I am quite honestly hoping that we can keep our own children healthy and able to manage their illness and function independently. I would like to see, in our lifetime, an era when people with psychiatric illness can receive the medical care they need to function normally without worrying that the illness is going to take over their lives.”

Mr. Dauten sounds a hopeful note, saying, “I would like to think that in our kids’ lifetimes, there will be very meaningful progress in identifying the genetic causes of bipolar illness, and that will lead to meaningful progress in treatment. Certainly, the kind of research that the Broad is conducting and that we are helping to fund leads you to believe that the progress will continue to accelerate, and hopefully achieve this goal.”
A cancerous tumor develops along a twisted evolutionary path, growing rapidly without the controls that keep cells functioning normally. “We know that cancer is a genetic disease, meaning that all tumors, all cancers, are caused by mutations in genes,” says Todd Golub, a founding core member of the Broad Institute and director of the Cancer Program. But for most of its history, cancer research has been “hit or miss,” Dr. Golub says, “with researchers discovering a mutation here or there.”

When the nation launched the war on cancer in 1970, in fact, researchers did not know that cancer was caused by mutations in genes. The prevailing theory was that viruses caused cancer. By the late 1970s scientists began to figure out the genetic link, and that realization was one of the motivations for the groundbreaking Human Genome Project, which provided the first look at the contents of the human genetic code in 2001.

Although sequencing an entire genome was still a daunting project in 2001, Dr. Golub believed that the power of genomics ultimately would allow researchers to attack cancer on a grand scale. “The idea was that if you could systematically develop the ability to discover all of the mutations in a given tumor, then you’d be able to have clarity around the mechanisms by which tumors develop,” he explains. “You’d have clarity around what would be promising therapeutic approaches; you’d have a full deck of cards.”

Using the Broad’s new massively parallel sequencing technologies that can read DNA rapidly and deliver huge amounts of data, the Broad Institute’s Cancer Program is now unveiling comprehensive genetic blueprints for deadly cancers such as multiple myeloma, prostate cancer, melanoma, and breast and ovarian cancer.

“This is a special moment. Now there is really an international effort to write this ‘book’ of the cancer genome,” says Dr. Golub. “The Broad took a leadership role in making the case that this was an important effort for the world to take on. And the Broad has taken a leadership role in developing experimental and analytical methodologies to make it possible – and in actually executing certain projects.” Having this genetic framework for cancers will change the way cancer is diagnosed and treated, scientists believe, by precisely targeting the molecular pathways that go awry as cancer develops.

The Broad Cancer Program goes beyond simply cataloguing the mutations in cancer. Broad scientists have mapped out three pillars of cancer research designed to accelerate progress toward better treatments for patients with cancer:

- **Develop a comprehensive catalogue of all mutations in a tumor, to understand how genes collaborate to drive the disease;**
- **“Turn on” and “turn off” all the genes in many cancer cell lines, to understand the genetic vulnerability of cancer; and**
- **Apply genome-inspired thinking to cancer drug discovery.**

The first pillar, which involves systematically cataloguing all mutations in a tumor, will allow scientists to understand the genes that are the true “drivers” of cancer – knowledge that will be useful therapeutically.

Broad associate members Lynda Chin, Levi Garraway and Matthew

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Cancer Program

Writing the ‘book’ of the cancer genome

Microscopic images of breast cancer, lung cancer, and leukemia.
Meyerson (all of the Dana-Farber Cancer Institute) are leading this effort, which is an integral part of The Cancer Genome Atlas (TCGA) project and the International Cancer Genome Consortium (ICGC). Data generated by the Broad are expected to be used by scientists throughout the worldwide cancer research community.

“While it is still early, we are learning already that there is great diversity across different tumor types, in terms of how many mutations there are, how many genes are mutated in one tumor type versus another,” says Dr. Garraway. “For example, in tumor types like multiple myeloma, we see mutations piling up in genes we never thought of before. We’re also discovering that there are molecular mechanisms and pathways that cut across different tumor types, so a subset of breast cancer looks like a subset of prostate cancer, for example,” he adds. “In the long run, having this genetic framework for cancers will likely result in rewriting the taxonomy of cancers.”

The second pillar is based on the observation that the mutated cells in tumors often create special vulnerabilities – they make the cancer addicted to certain cellular processes. “To learn about those vulnerabilities requires turning on or off every gene in the genome – and observing which of them matter. Until recently, that would have been a thought experiment,” says William Hahn, senior associate member leading this effort, referred to as Project Achilles. “But it is now possible to think about doing that, not only in a single cancer cell but in over 100 human cancer cell lines.”

Using tools developed at the Broad, researchers can shut off individual genes one at a time. If a gene is turned off, and a cell dies, that gene might be an “Achilles heel” that makes for a promising drug target.

The third pillar involves the discovery of chemical compounds that can induce changes in cancer cells. “Could we screen a collection of chemical compounds – small-molecules – for their ability to kill tumor cells of a particular molecular type, but not others?” Dr. Golub asks. “Could we find chemical compounds that induce a cancer cell to do something that we want it to do, to stop being a cancer cell and be more like a normal cell?” Accomplishing these goals involves close collaboration with scientists within the Broad Chemical Biology Program and Platform, and necessitates innovative approaches to both cancer biology and chemistry. For example, new types of chemical compounds (Diversity-Oriented Synthesis or DOS) developed by founding core member Stuart Schreiber are proving particularly powerful.

An important task for the future, Dr. Golub says, is to use the genetic makeup of tumors to ask which genes are important for the survival of cancer cells following drug treatment. Scientists at the Broad are testing this idea by looking for genetic predictors of drug sensitivity across a large panel of human cancer cell lines. If those experiments prove successful, extending the findings to patient samples would be the next step. These types of studies are expected to pave the way for personalized cancer medicine, whereby patients and their doctors choose treatments using the genome as a guide.

In a related effort, the Broad has created a public resource of cellular response following drug treatment. This project, called the Connectivity Map, and led by Justin Lamb and Aravind Subramanian, involves the systematic measurement of gene expression signatures (which genes are activated or repressed) following treatment with a wide variety of compounds, including most FDA-approved drugs. The Connectivity Map approach holds promise for discovering previously unknown effects of existing drugs, some of which might prove unexpectedly useful in treating disease.

The Broad Institute environment allows scientists to develop and deploy powerful new technologies on an industrial scale to tackle some of the most pressing problems in the cancer field. The institute also allows integration that cuts across traditional divisions in academic research and in medicine. “That, in some ways, is what’s most special,” says Dr. Golub. “From the clinical questions – because we have oncologists in our community – to the genetics of cancer to the functional genomics of cancer to drug discovery for cancer. To really make progress, you need a structure that allows projects to transcend those different areas, where no individual is able to be expert in everything. The Broad is set up to do exactly that. What is also unique about the Broad is that the culture, by design, is meant to support integrative, ambitious, bigger-than-yourself kind of thinking.”
The cell – the central component of every living organism – is abuzz with activity. Cells use a complex network of connections to make a constant array of decisions about their surrounding environment: Is it time to grow? Is it time to change into a different type of cell? When a cellular component or connection is missing or defective, disease takes hold.

The Human Genome Project, which was proposed twenty-five years ago, yielded great riches in terms of systematically understanding cellular components - genes and proteins. Now, Broad core faculty member Aviv Regev and her colleagues are writing an important second chapter: they are making a systematic effort to define the cellular circuits that underlie human health.

Dr. Regev, a computational biologist who joined the Broad Institute in 2006, devotes much of her research to understanding just how complex cellular networks work – or don’t. Because cells play such an important role in biology, her work touches nearly every aspect of research at the Broad.

Until recently, the study of cellular circuits required painstaking research that examined connections one “wire” at a time – sometimes requiring up to a decade of work to put together all the pieces of a circuit. Over the past two years, however, Dr. Regev and other scientists at the Broad have jump-started the process by developing ways to rapidly characterize circuits.

“In disease, some pieces of our circuits break down,” Dr. Regev says. “Maybe a component is missing. Maybe you have a wire that shouldn’t be connected. If you can figure out which part is wrong, then you may be able to come in and fix it.”

Reconstructing cellular circuits on a large scale requires a new paradigm. Dr. Regev and her colleagues have developed a four-step approach:

- Observe and measure the internal state of cells by using powerful tools to study tens of thousands of components at once;
- Create a computational model to explain the data;
- Use experimental tools to interfere with genetic function, and observe what happens; and
- Repeat and refine the model.

A computational biologist by training, Dr. Regev has nonetheless invented new laboratory methods to delve into the function of cellular circuits for numerous cell types; she has discovered scores of circuits that regulate different types of blood cells and immune cells. Working with the Broad’s RNA interference (RNAi) Platform, Dr. Regev and her colleagues use chemical and molecular methods to eliminate many components in a circuit in parallel to analyze how that component affects the cell’s function.

“If we cycle through this many times, we can figure it out,” she says. Drawing a comparison to an electrical circuit in a computer or cell phone, she adds: “It’s the same as taking an electrical circuit and saying, ‘Hmmm, I wonder what this wire does.’ You cut it, and all of a sudden you can no longer have outgoing calls.”

Much in her background has prepared her for this moment. At Tel Aviv University, Dr. Regev focused on biology, computer science, and mathematics, and in her Ph.D. research there and at the Weizmann Institute in Israel she developed a language for molecular processes based on computer algorithms. In the past several years, Dr. Regev has worked on the reconstruction of cell circuits from genomic data as a fellow at the Bauer Center for Genomics Research at Harvard University.
Her lab also focuses on the evolution of gene expression – looking across the evolutionary scale to see what important functions have been conserved across multiple species – and how functions might differ. “For example,” she explains, “if you look at an infectious organism and you see a drug-resistant variant and a non-drug-resistant variant, and you can tell how they evolved from one to the other, you can then find new cures for important clinical challenges.”

Dr. Regev aims to approach the puzzle of cell circuitry on a large scale. “I wanted to take the general approach that the Broad has to problems, which is to scale up and say, ‘Let’s just take it and do it right.’ And sometimes that involves doing things on a scale that people have not thought about before.”

A generous gift from the Richard Merkin Foundation for Stem Cell Research at the Broad Institute supports her work, with a goal of advancing the study of the circuits that control stem cells and the way stem cells differentiate to become new cells. “One of the biggest decisions that the cell has to make is which cell type it should be, and then maintain this identity,” she says.

She and her colleagues accomplish this research on two levels: by studying embryonic stem cells and focusing on how to reprogram them; and by conducting research to decipher how stem cells in the bone marrow make new blood cells. “The Merkin Foundation gift has allowed us to conduct research that is hard to fund through regular agencies. We have also been able to develop new lab technologies and computational algorithms, which can be used for many different applications. It has been tremendously enabling.”

Dr. Regev collaborates with a number of the Broad’s platforms and programs. Understanding how different genetic variations interact with cellular circuits can provide important context that will allow a deeper understanding of the disease process, and may ultimately lead to new therapies. “One of the great strengths here is the informal network. People here like rallying around good problems. It changes everything.”
Richard Merkin – physician, entrepreneur, and inventive thinker – believes that the best way to predict the future is to create it.

Trained in emergency medicine, Dr. Merkin is now focused on developing a coordinated care system that is collaborative, efficient, and centered on the patient. As president, CEO, and founder of Heritage Provider Network, he is attempting to break down some of the silos in medical care “so the patient doesn’t feel like an island, and certainly doesn’t feel abandoned. That’s what we think is going to be the future of medicine in this country.”

Frequently, he observes, no one coordinates care during a hospital stay, or after a patient is discharged. “If you can eliminate duplication in the health care system and preserve resources, those resources can be redirected to places like the Broad – not to provide care, but to provide cures. Ideally, we can redirect those resources to research and translational medicine.”

As a donor, Dr. Merkin has provided fuel to accelerate new research into stem cells and the circuits that control them. The foundation he created – the Richard Merkin Foundation for Stem Cell Research at the Broad Institute – supports the work of Aviv Regev, a computational biologist and core faculty member who is deciphering cellular circuits.

“The idea was to fund science before it was ready for prime time with the NIH, to develop great, transformative ideas,” he says. “I thought the Broad was a wonderful collaboration of brilliant people in the right environment.”

Dr. Merkin likens biological research to a tree: “Stem cells are at the root, and they differentiate into different branches. Those branches differentiate into leaves. If there’s a problem anywhere along that path, it leads to disease. If we can clarify and understand the functioning of the circuitry at the initial site of the stem cell, we may be able to reprogram it to cure an enormous number of different diseases.”

A philanthropist who serves on the boards of numerous private healthcare organizations, Dr. Merkin believes in the inherent power of teamwork, particularly in science. “Many organizations segment and silo the different sciences,” he says. “Interdisciplinary discussions are rare. At the Broad, there is a wonderful collaboration where someone with a physics background might be in close geographic proximity to someone in biology. They might discuss a problem and say, ‘We can work on this together.’ ”

Donor profile

Richard Merkin: Creating the future

‘The idea was to fund science before it was ready for prime time with the NIH, to develop great, transformative ideas. I thought the Broad was a wonderful collaboration of brilliant people in the right environment.’

– Dr. Richard Merkin
Crohn’s Disease, an inflammatory bowel disorder first observed in the 1930s, has long been thought to run in families. Until recently, though, little more was known about the specific genes and mechanisms that underlie susceptibility.

Recent genomic advances at the Broad Institute and elsewhere have sped the pace of discovery, breaking open the biology of the disease by identifying genes and biological processes that go awry. Scientists have now pinpointed 100 genetic loci – up from two just a decade ago – involved in different “pathways” that place a person at risk for developing Crohn’s.

Crohn’s is just part of the story. A number of the same genetic regions and immunological pathways are also altered in another disease without a cure: Type 1 Diabetes. Moreover, the same tools and approaches that have been successfully pioneered in Crohn’s Disease can productively be applied to Type 1 Diabetes. That’s why Crohn’s and Type 1 Diabetes – and their combined 200 genes – are being tackled in tandem through a project at the Broad supported by The Leona M. and Harry B. Helmsley Charitable Trust.

Drawing on his clinical experience treating Crohn’s Disease, Ramnik Xavier, a senior associate member of the Broad Institute, is determined to find better options for patients.

“We have the genetics,” says Dr. Xavier, who is also chief of gastroenterology and director of the Center for the Study of Inflammatory Bowel Disease at Massachusetts General Hospital. “The next challenge is to find out what the genes do. Then, the hardest challenge, but one we are committed to achieve, is to find drugs that correct the underlying defect.”

Starting with genes identified from patient samples, scientists have marshaled technologies at the Broad to map the biological pathways, or chains of molecular events, these altered genes set in motion. Understanding these pathways is essential to finding more finely calibrated targets for potential drugs. One crucial pathway uncovered in Crohn’s Disease is autophagy, the cellular digestive process that also repels infectious invaders. Other pathways lead to other fronts in the body’s complex immune defenses, including one that amps up inflammation and another that turns it down.

Crohn’s, Type 1 Diabetes, and other immune-mediated diseases require more than just a genetic defect before they emerge. As the name implies, both a problem with the immune system and some kind of environmental or microbial trigger are needed to move the needle from predisposition to actual disease. Some people who carry the same altered genes that are a signature of Crohn’s do not develop symptoms. While Type 1 Diabetes often appears in children, it can remain dormant into adulthood, when the immune system suddenly turns on the body, destroying its insulin-producing cells as if they were threats.

Dr. Xavier has recreated inflammation similar to Crohn’s in mice genetically engineered to have the human gene variants implicated in faulty autophagy and other components of immunity, strongly suggesting that these mutations are responsible for the disease. His work builds on dozens of new genetic variants revealed just three years ago, as well as earlier Broad-related discoveries, says Mark J. Daly, co-director of the Program in Medical and Population Genetics at the Broad, a member of the Center for Human Genetic Research at Massachusetts General Hospital, and a key player in those discoveries. Last fall, Dr. Daly was named the first chief of the new Analytic and Translational Genetics Unit, a unit within the Department of Medicine at MGH. ▶
“This is the proving ground for the value of what we’ve discovered from the genetic studies from the past decade,” he says. “It can change the way we think about the disease; it can change the way we think about developing therapies for the disease.”

Following the same philosophy, researchers at the Broad, led by Stuart L. Schreiber, a founding core faculty member and director of the Chemical Biology Program, have tracked pathways important in Type 1 Diabetes — and discovered a way to work around them in experiments with mice. Searching libraries of small molecules using a technology called high-throughput screening, they discovered a small-molecule probe (probes are compounds that are used to test emerging hypotheses in biology and can be precursors to drugs) that could induce alpha cells in the pancreas to take over insulin production from beta cells destroyed by a faulty immune response.

The intent of the Helmsley project at Broad is to turn these new discoveries from human genetics into knowledge about how normal functions go wrong to cause disease, and then to use Broad’s chemical expertise to discover new compounds that tilt the system back towards normal function.

“This project is bringing to bear a lot of Broad approaches in a parallel way to accelerate discovery,” says David Altshuler, a founding core faculty member of the Broad and co-director of the Program in Medical and Population Genetics.

“It has to be done at the Broad,” Dr. Xavier says. “It cannot be a one-lab initiative. It has to be a community initiative.”

Dr. Schreiber believes the Broad approach will hasten the day when such diseases will be laid bare by learning from their genetics.

“At the Broad, we can do these experiments rapidly and comprehensively, which enables actionable hypotheses for human health,” he says.
When David Panzirer became a trustee of The Leona M. and Harry B. Helmsley Charitable Trust after the death of Leona Helmsley, his grandmother, he was taking on a deeply personal mission. Not only was he accepting the responsibility of continuing a philanthropic legacy, he was also making a commitment to change the course of a destructive disease. Five months before his grandmother’s death, one of Mr. Panzirer’s daughters was diagnosed with Type 1 Diabetes, a lifelong ailment that puts her health – and life – at risk daily. As a trustee, he now had the power to do something significant for his daughter and for others living with the disease.

“As difficult as it was to learn that our daughter has Type 1 Diabetes, the gift from my grandmother gives us the opportunity to make a real difference in the lives of the many people affected by this disease,” says Mr. Panzirer.

Mr. Panzirer left a career in commercial real estate to pursue his mission. Working side by side with Helmsley Charitable Trust staff and other trustees, he helps determine the best ways to use the trust’s substantial philanthropic resources. Among the other trustees is Sandor Frankel, who has helped develop the trust’s substantial funding for research in inflammatory bowel disease, especially Crohn’s Disease.

Mr. Panzirer’s and Mr. Frankel’s commitment to these diseases, coupled with the funding resources available through the trust, enables high-risk, high-reward research for innovative and collaborative programs designed to uncover the causes of and treatments for both diseases. Today, half of the trust’s funding is in areas of medical research, including significant programs that focus on Type 1 Diabetes and Crohn’s Disease. Research exploring the cause of both Type 1 Diabetes and Crohn’s is pursued at the Broad Institute with generous grant support from the trust.

Discoveries made in recent years at the Broad and around the world have revealed biological connections between Type 1 Diabetes and Crohn’s Disease, with genetic variations now known to be shared by the two immune-mediated diseases. Dana Ball, who directs the Type 1 Diabetes Program at the Helmsley Charitable Trust, had been watching the Broad since its inception, tracking its strategy of bringing experts together across different disciplines. The trust’s connection to the Broad Institute evolved from the trust’s medical research mission to accelerate the understanding of disease and, ultimately, create better diagnostic tools and uncover new treatments.

“We liked the Broad model because it had eliminated independent research silos, bringing investigators and bioinformatics together through partnerships with research institutes and hospitals in Boston. It’s really an end-to-end system because researchers have the access to patients, remarkable infrastructure, and technology – all of the resources of the 21st century and led by the people who really developed and expanded genomics,” Mr. Ball says. “Working with the Broad seemed to be the right solution. They have been successful in convening the brightest and best minds to study human disease in a whole new way. It is a very different approach to disease research that is based on a nonprofit model.”

Mr. Ball says it will take nothing less to match the challenge: “It would be hard to do this collaborative research project anywhere else.”
PROGRAMS

The Broad's programs bring together academic and staff scientists from across multiple institutions, working together to address major challenges in specific diseases or disciplines.

CURRENT PROGRAMS INCLUDE:

**Cancer Program**
Focuses on understanding the basic molecular mechanisms of cancer and applying this knowledge to transform the practice of cancer medicine.

**Cell Circuits Program**
Focuses on deciphering the functions and interactions of critical molecular components in cells.

**Chemical Biology Program**
Integrates chemical biology and genome biology to provide powerful new ways of creating therapies to treat human diseases.

**Epigenomics Program**
Involves the large-scale study of DNA and the protein scaffold that supports it, with a focus on how modifications to this structure can affect development and disease.

**Genome Sequencing and Analysis Program**
Uses sequencing and other genomic technologies to identify and understand the function, regulation, and evolution of elements encoded in the human and related genomes, including the vertebrate lineage. The program also studies a variety of pathogens that cause disease in humans and model organisms, including viruses, bacteria, fungi and parasites, as well as insect vectors of disease. The program also develops cutting-edge laboratory and computational methods to exploit the power of genomic technology in a wide range of biomedical research areas.

**Infectious Disease Program**
Focuses on using genomic tools to understand the mechanisms behind infectious diseases and applying this knowledge to transform the prevention, diagnosis, and treatment of these diseases.

**Metabolism Program**
Pioneers systematic approaches to understand both normal metabolism and disease, including diabetes, obesity, cardiovascular disease, and inborn errors of metabolism, with the goal of accelerating the development of new therapeutic and preventive strategies.

**Program in Medical and Population Genetics**
Focuses on understanding how genomic variation contributes to susceptibility to human disease and to an individual’s response to therapy.

**Psychiatric Disease Program**
Aims to unravel the molecular basis of psychiatric disease, with the ultimate aim of improving diagnosis, treatment, and, if possible, prevention.
PLATFOMS

The Broad's scientific platforms are teams of professional scientists who focus on the discovery, development, and optimization of the critical technological tools needed to obtain and analyze the massive amounts of genome-related data that are being generated by scientists at the Broad and around the world. Platform scientists have the expertise and organization to carry out major projects that could not be done within a single research laboratory, and work closely with the scientific programs and other collaborators to tackle critical questions in human biology and disease.

CURRENT PLATFORMS INCLUDE:

**Biological Samples Platform**
Combines expertise in advanced technologies for sample storage and processing, the appropriate procedures for collection and use of human samples in biomedical research, the analysis of normal and abnormal human tissues, and the development of laboratory information management systems for detailed sample tracking.

**Chemical Biology Platform**
Empowers researchers to discover chemical compounds known as small molecules that can be used to understand cell circuitry and disease biology, as well as in therapeutics.

**Genetic Analysis Platform**
Collaborates with scientists at the Broad and across the world to identify and characterize patterns of genetic variation and gene expression. These patterns can yield a deeper understanding of how genetic factors influence disease risk and treatment outcomes in a wide range of human diseases, including Type 2 Diabetes, Crohn's disease, schizophrenia, and cancer, among many others.

**Genome Sequencing Platform**
Designs and carries out large-scale genome sequencing projects, together with groups throughout the Broad community. Genomes of interest include human, mammals, fish, insects, fungi, plants, bacteria and viruses.

**Imaging Platform**
Develops advanced methods to quantify and mine the rich information present in cellular images to yield biological discoveries; develops open-source software tools and helps biologists apply them to significant questions in the life sciences.

**Metabolite Profiling Platform**
Collaborates with researchers across the Broad and other communities to study metabolism and elucidate metabolic signatures of both normal and pathological cellular processes.

**Proteomics Platform**
Develops and applies advanced methods of identifying and analyzing proteins and their modifications to further our understanding of human biology, disease, drug targets, and drug effects.

**RNAi Platform**
Empowers researchers to identify the genes underlying diseases and to elucidate biological pathways and mechanisms.
The Broad is dedicated to solving problems that can change the world. Sequencing the human genome, for example, made such a mark.

Another major challenge, says Bruce Birren, is engaging the full talents of our population in science – and especially the under-representation of many minorities in biomedical research.

“The Broad’s tremendous resources give us a responsibility to take on really important problems that truly have to be solved,” says Dr. Birren, co-director of the Broad’s Genetic Sequencing and Analysis Program and advisor to the institute’s Diversity Initiative in Scientific Research. “The Broad feels a strong obligation to change the future of science by expanding who participates in it.”

Since 2003, the Diversity Initiative’s mission has been to increase the number of under-represented minority members pursuing careers in genomics-related fields and becoming leaders in their career tracks. Two of its graduates, Jean Junior and Esther Uduehi, have reached one of the loftiest pinnacles of academic success by winning Rhodes scholarships.

Directed by Eboney Smith, the Diversity Initiative doesn’t merely teach participants about science; it encourages them to think boldly and become leaders. These young scholars also acquire the skills and career tools they need to fulfill their ambitions.

“The purpose of the program is to help them dream big and realize their full potential,” she says. “They experience a confidence boost, affirming what they can accomplish in science.”

Since its inception seven years ago, 158 students have worked side by side with leading scientists at the Broad, making important contributions to genomics projects while learning what it takes to have an impact in science. What makes the initiative different from other education programs at the Broad is its emphasis on also teaching the “unwritten rules” of science.

“Left to its own, a majority culture isn’t sensitive enough to the potential differences and needs of minority trainees,” Dr. Birren says, as was the case during the decades when there were few women in the field.

Students who are in the minority are more likely to feel isolated or feel the need to do more than others to prove themselves, research has shown. Other studies have correlated decisions to pursue science with the presence of minority mentors or professors who let students know, by their example, that this is a path they can follow.

“We have to work hard in the Diversity Initiative and elsewhere to recognize there can be people of tremendous capabilities who simply never had the same opportunities,” Dr. Birren says. “Being at the Broad and having that on your resumé is a great thing. But if we just did that, we would not have the success we do in really getting people to fly out of here with the momentum to succeed.”

Participants do rigorous work in their time at the Broad, whether they are high school students participating in Minority Introduction To Engineering and Science (MITES), college students gaining expertise in the Summer Research Program in Genomics (SRPG), or engineers, medical students, postdocs, or faculty members further along the leadership pipeline.

“Esther and Jean, like many others here, are unabashedly passionate about the contributions they will make to science and to the world,” Ms. Smith says about the two Rhodes Scholars. “The future is bright and I am thrilled to be a part of this initiative at the Broad.”

Dr. Birren is certain that somewhere in their youth, every scientist at the Broad had an opportunity to feel the addictive excitement of discovery in a way that not only helped them see themselves as scientists, but also taught them to persevere through the ups and downs of science.

“All of us got here because someone helped us.”
Profiles: From Broad scholars to Rhodes Scholars

Jean Junior: Big-picture thinking
When Jean Junior thinks of a child with HIV or tuberculosis, she sees more than infectious pathogens and clinical tests. She wonders whether that child has enough food to eat, what the family’s living conditions are like, and whether there’s enough money to pay for transportation to and from a clinic.

This 2010 Rhodes Scholar and Broad Diversity Initiative alumna sees the big picture as she explores what she calls holistic poverty alleviation. “I see my work in the lab, in the clinic, in the field, and at Oxford as simply different routes to the same end – making sure that the child with HIV or TB survives and thrives,” she says.

Ms. Junior traces her route to Oxford back to the summer of 2004, when she was enrolled in the Minority Introduction To Engineering and Science program. That experience helped encourage her to come back to Cambridge for college. Before studying at Harvard, she joined the Summer Research Program in Genomics, which later led her to the lab of HIV researcher and Broad associate member Dr. Bruce D. Walker. Through her work there, she found out about Integration of TB in Education and Care for HIV/AIDS, also known as iTEACH, a program in South Africa where she volunteered in the summer of 2007 as well as during her first year after graduating from college.

After completing her two years of study at Oxford, she will enter Harvard Medical School in the fall of 2012. Her dream is to weave together programs that alleviate poverty through strategies such as improving health care, income generation, water and sanitation, and education.

“If I hadn’t found out about iTEACH, I don’t think I would be where I am today,” she says. “I am so incredibly thankful for the life course-changing opportunities that I have been given by the Diversity Initiative and the Broad Institute!”

Esther Uduehi: Synthesizing opportunity
When Esther Uduehi was in high school, summer science camps were an all-expenses-paid way to spread her wings. After her freshman year, she landed at a NASA camp in Virginia, where she worked on nuclear fusion. Her project made a natural – and prize-winning – science-fair entry when she got back to school, one that propelled her further into science.

She didn’t fall in love with chemistry until her first year at Indiana University, when she dove into the research lab that would become her scientific home. Focused on organic chemistry, she became proficient at making compounds but seized the opportunity to study synthetic chemistry at the Broad’s Summer Research Program in Genomics. She will pursue that interest further at Oxford as a 2011 Rhodes Scholar.

“What attracted me to the Broad was I felt I could see more directly the applications of what chemistry is being used for,” she says. “I want to continue seeing that application of chemistry within medicine.”

Chemistry is just one of her passions. At Indiana, she co-founded the university’s Minority Association of Pre-Medical Students, which taught her about leadership. She already knew how few members of minority groups are represented in academia from her father, who is a professor of art.

“If I look at my university and at science, it is very discouraging, but I think it is changing,” she says.

In the fall, it will be a return to Oxford for Ms. Uduehi, who spent a semester there as a junior and hoped ever since to have the opportunity to go back.

“I really see the importance of science in the overall human condition and I want to be able to affect that,” she says. “I want to be able to have a lasting impact in science through chemistry.”
Arthur D. Levinson may not look like a rock star, but to the employees at Genentech and to the whole biotech industry, he’s got the same magnetic pull.

When word spread on Genentech’s South San Francisco campus that the 60-year-old chairman would be visiting a pilot laboratory for an interview and a photo shoot, workers of all stripes began filtering through the low-slung building’s corridors, sidling past the borrowed office where he was talking so they could peer through a window in the door. Farther down the hall, technicians in mandatory white coats were lining up outside sliding steel doors of a lab, ready for their chance to rub shoulders with the man who ran day-to-day operations for 15 years.

Can we get a picture with Art? Can he sign my badge?

Such is the affection inspired by Dr. Levinson, leader of pioneering biotech company Genentech and member of the Broad Institute’s Board of Directors. Down to earth and disarmingly self-effacing, he is both endlessly curious and driven, determined to conquer human disease. Although out of daily lab work for many years, he is still deeply involved in research at Genentech. He says he contributes strategic thinking to the board of the Broad, including the business acumen refined by his years at the helm of Genentech, nicknamed “DNA by the Bay.”

Genentech was the first company to create genetically engineered drugs. Since then its innovative products have included Avastin, which fights cancer by using specially engineered versions of the body’s own antibodies to choke off blood vessel development in tumors, and Xolair, which prevents asthma attacks with antibodies that short-circuit overactive immune responses.

Dr. Levinson stepped down from his role as CEO in 2009, when Genentech was acquired by Swiss pharmaceutical giant Roche. During that transition to chairman only, employees gathered in a spontaneous rally known ever since as “Hearts for Art” in the company’s collective memory (and a YouTube video) because of the handmade signs people brought or hung in windows.

He says Genentech is a different kind of company because of its insistence on giving scientists what they need to solve significant biomedical problems. Allow people the freedom to work hard, give them the technical and administrative support they need, bring them together across scientific disciplines, and the rewards will be great, he explains.

If that philosophy sounds a lot like the ethos espoused by the Broad, Dr. Levinson emphatically agrees.

“There are certain big questions in science that only get done with a highly interdisciplinary approach that requires tremendous partnerships, teamwork, integration, and a reliance on great technology and infrastructure. That’s exactly what the Broad does.”

He learned that lesson in 1980, when he first came to Genentech from the University of California at San Francisco. Intrigued by an invitation from Genentech cofounder Herbert W. Boyer to learn how to clone a gene, he settled in for what he thought would be a two-year tenure at most. What he saw within two weeks changed his mind.

As a postdoc, he had been spending most of his time pipetting buffers or running gels or injecting a mouse to make an antibody – all necessary but time-consuming chores of lab science. At Genentech, even when it was a young company with no more than 100 employees, there were many expert staff members. He soon realized that he could be more productive following this model of fully supported expert staff.

The scene hasn’t changed much in 30 years except at the Broad, Genentech, and a few other institutions.
“The single-lab model has worked quite well for a hundred years, but it can be a limited model if you have very ambitious goals, including trying to solve human disease,” he says.

He is convinced that science is closing in on understanding the genetics of cancer, perhaps within the next five years. It will likely take another 10 years or more to figure out the cascade of molecular events that a cancer gene sets in motion – commonly called a “pathway” – but he’s confident that cancer will be solved based on basic research.

“When we understand the genetics, the pathway biology, all the inter-connections, and we’re able to intervene therapeutically by simultaneously targeting three or four pathways that are aberrant at the same time, then boom! Goodbye, cancer,” he says. “It’s going to happen.”

He is known for taking the long view. In one of his first moves as CEO, he ratcheted up spending on research and development – an area he previously headed – to an unheard-of 50 percent of annual revenues.

Dr. Levinson’s father was a physician, but from an early age he found himself drawn more to the scientific side of medicine, where he could solve the puzzle of disease.

“I thought I would find it more fulfilling to be part of the discovery process than to be a physician treating patients. I was always more of a curious individual,” he says.

He serves on other boards, including Apple, Roche, and Amyris, and is a past member of the Google board. His other interests center on astronomy and his family.

“I have a terrific wife, I have two great kids,” he said. “I do little socializing, to my wife’s dismay, but she’s getting used to me after all these years. I’m kind of a hermit.”

He still thinks of himself as a scientist first. He attends research meetings on Wednesdays and stays fully immersed in the science.

“I’m pretty plugged in still,” he says.

And for the people working at Genentech and in the biotech industry, he’s still a rock star.
“Over my lifetime I’ve made a lot of different investments. Our investment in the Broad Institute has been the largest philanthropic investment we have made. It has without question yielded the greatest returns.” – Eli Broad

The ambitious projects undertaken by the Broad Institute would not be possible without the critical support and continued commitment of our donors, research sponsors, and friends. We would like to thank the following individuals and organizations for their investment in improving human health through their support of the Broad Institute:

Eli and Edythe L. Broad
Discussions among Los Angeles philanthropists Eli and Edythe L. Broad, MIT, Harvard, and the Harvard-affiliated teaching hospitals shaped the vision for a new kind of research organization and community. The visionary generosity of the Broads ($100 million over ten years, subsequently doubled to $200 million) made it possible to formally announce the Eli and Edythe L. Broad Institute of MIT and Harvard in June 2003 and to launch it in May 2004. In September 2008, the Broads, Harvard and MIT declared the new model a success. At the same time, the Broads announced that they would endow the institute with an additional $400 million, the largest single gift to a biomedical academic research center to date.

The Stanley Medical Research Institute
The Broad Institute's Stanley Center for Psychiatric Research was created in 2007 with the extraordinary support of a ten-year $100 million grant from the Stanley Medical Research Institute (SMRI). In April 2011, SMRI extended its support to fund the work of the Stanley Center through 2022. The mission of the Stanley Center is to discover the human genes that confer risk for bipolar disorder and schizophrenia and to use this information to develop new diagnostic tests and treatments for these illnesses.

Instituto Carlos Slim de la Salud
In 2010 Carlos Slim Helú announced the launch of a major research project in genomic medicine to help accelerate progress in public health in Mexico and around the world. The major goal of this project, called the Slim Initiative for Genomic Medicine, is to investigate the genomic basis of cancer in worldwide populations, and of Type 2 Diabetes in Mexican and Latin American populations. The Broad is collaborating in the $65 million project with the Carlos Slim Institute of Health and Mexico’s National Institute for Genomic Medicine.
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Financial Information for Fiscal 2010

The institute completed its first full year as a nonprofit 501(c)(3) research institute on June 30, 2010. The Broad Institute had a 16% increase in operating growth over fiscal 2009. The institute received $100 million of the $400 million founding endowment gift on July 1, 2009. The balance was recorded as a pledge receivable and is managed by the Broad Foundation.

Statement of Activities | July 1, 2009 through June 30, 2010 | (in thousands of dollars)

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<tr>
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| Total Operating Revenues            | $258,107 | $519,602 | $777,709 |
| Total Nonoperating Gains            | $37      | $11,967  | $12,004  |
| Total Revenues and Gains            | $258,144 | $531,569 | $789,713 |
| Total Operating Expenses            | $235,971 | –        | $235,971 |
| Increase in Net Assets              | $22,173  | $531,569 | $553,742 |

Balance Sheet | As of June 30, 2010 | (in thousands of dollars)

| Total Assets:                       | $738,818 |
| Total Liabilities:                  | $97,282  |
| Total Net Assets:                   | $641,536 |

Broad Institute Funding Sources FY2010

(in thousands of dollars)

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History of Operating Growth

Operating growth (FY2005-FY2010)