

BURROUGHS
WELLCOME
FUND 

2008 ANNUAL REPORT



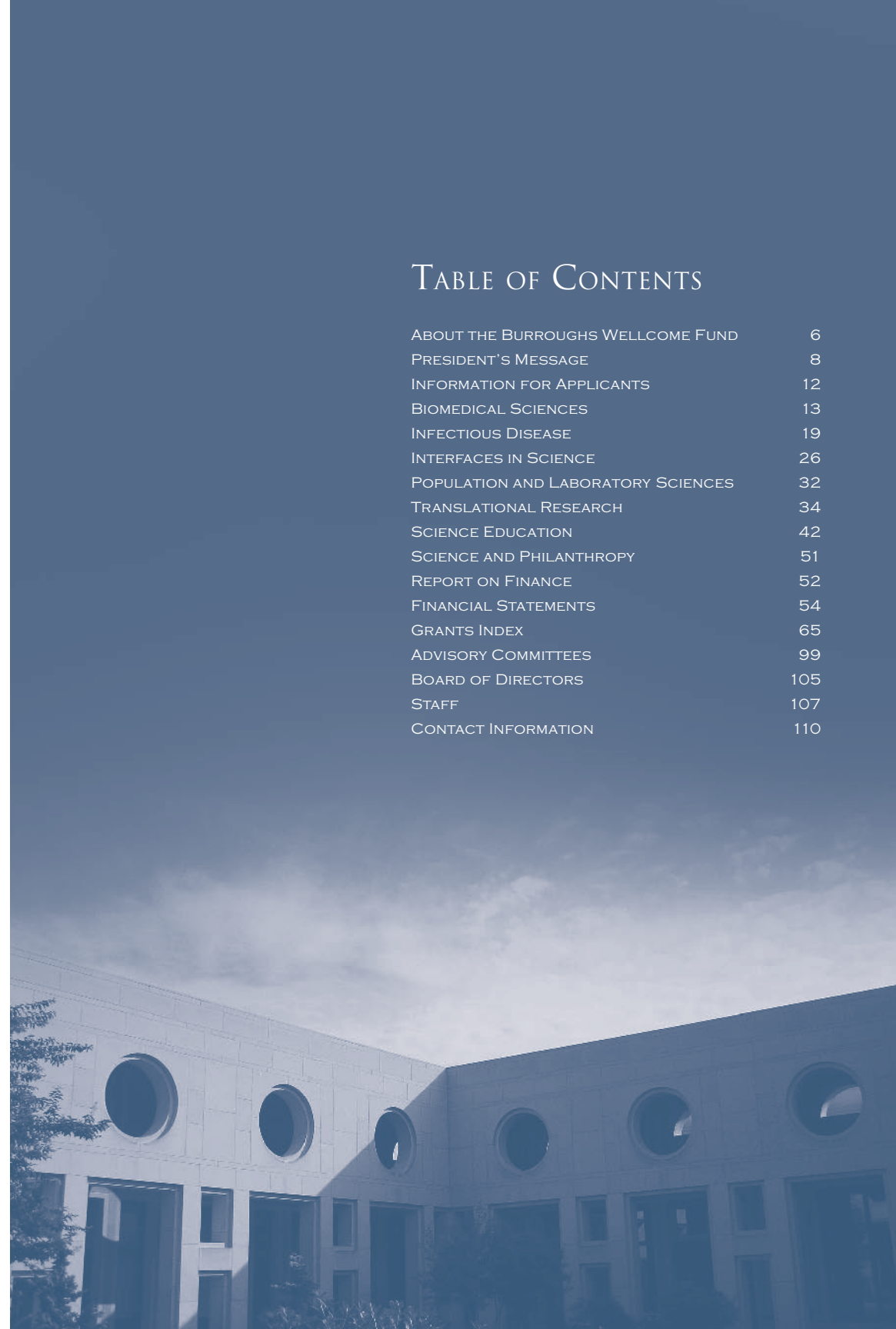
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2008 ANNUAL REPORT
RESEARCH TRIANGLE PARK, NORTH CAROLINA

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The Burroughs Wellcome Fund is an independent private foundation dedicated to advancing the biomedical sciences by supporting research and other scientific and educational activities. Within this broad mission, BWF seeks to accomplish two primary goals—to help scientists early in their careers develop as independent investigators, and to advance fields in the basic biomedical sciences that are undervalued or in need of particular encouragement.

Financial support is channeled primarily through competitive peer-reviewed award programs, which encompass six major categories—biomedical sciences, infectious diseases, interfaces in science, population and laboratory sciences, translational research, and science education. Grants are made primarily to degree-granting institutions on behalf of individual researchers, who must be nominated by their institutions. To complement these competitive award programs, grants are also made to nonprofit organizations conducting activities intended to improve the general environment for science.

BWF was founded in 1955 as the corporate foundation of Burroughs Wellcome Co., the U.S. branch of the Wellcome pharmaceutical enterprise, based in the United Kingdom. In 1993, BWF received a \$400 million gift from the Wellcome Trust, the main entity in the enterprise, to become a fully independent foundation.

LEGACY

The Wellcome enterprise was born in 1880 when two young American pharmacists, Henry Wellcome and Silas Burroughs, moved to London to manufacture and sell “compressed medicines”—that is, pills—which they believed could replace the potions and powders of the day.

The firm prospered. After Burroughs died in 1895, Wellcome directed the growth of the company into an international network with subsidiaries in numerous countries on several continents. As the business grew, Wellcome held firm to his belief that research was fundamental to the development of excellent pharmaceutical products and established the industry’s first research laboratories.

When Wellcome died in 1936, his will vested all of the corporate shares in a new organization—the Wellcome Trust—devoted to supporting research in medicine and allied sciences and to maintaining museums and libraries dedicated to these fields. The Trust grew to become the world’s largest charitable foundation devoted exclusively to the biomedical sciences.

The importance of curiosity-driven research, as endorsed by Henry Wellcome, guides the mission of the Burroughs Wellcome Fund and our commitment to the belief that fostering research by the best and brightest scientists offers the fullest promise for improving human health.



John E. Burris, Ph.D.

I tackle this annual message with a measure of caution, as my tenure is just approaching six months as president of the Burroughs Wellcome Fund. However, I am forging ahead with my initial thoughts using a free pen from an investment banker, a good reminder that while recounting the past is possible, predicting the future is a bit tougher.

Foundations provide only about 3 percent of total funding for biomedical and health-related research and development in the United States, but this is still a substantial amount of money—in the range of \$3 billion annually. Within this landscape, the Burroughs Wellcome Fund is a small, but important, participant.

A number of years ago, BWF's Board of Directors decided to concentrate on funding undervalued fields of research and education. This decision, coupled with the superb leadership of my predecessor, Dr. Enriqueta Bond, enabled BWF to establish a significant presence in these areas. Even with our currently reduced endowment, we remain a key funder in these areas.

It is essential that we continue our mission to advance the biomedical sciences by supporting research and other scientific and educational activities in this era of the life sciences. Many people have called the 21st century the biological century, and it is easy to understand the basis of this claim. The scientific community is poised to understand life in a way never before possible. The enormous amount of data from genomic sequencing and other large-scale projects, coupled with a much greater understanding of systems, will allow for the integration of all of the subdisciplines in biology to paint a far more complete understanding of living organisms and their interactions with the environment.

Interestingly, in this century of biology there is an increased need to integrate physics, mathematics, computation, and chemistry with biology in order to gain

a more complete understanding of life. Biologists will need to embrace these diverse disciplines—and to interact with their practitioners—to raise and answer the questions of the life sciences that seemed impossible to consider even several years ago. Successful interactions here will mean that these other disciplines also will grow and flourish. The Burroughs Wellcome Fund has recognized the need to involve scientists from other disciplines for a number of years, most prominently through our Career Awards at the Scientific Interfaces Program, in which we have asked physical scientists and mathematicians to tackle biological questions. This path-setting program is now being echoed by other foundations and the federal government.

The opportunities for life sciences in the 21st century to better understand life—and in so doing to improve the treatment and prevention of disease, increase crop yield, and reduce human impacts on the environment—are enormous. How are we at BWF doing our part to stimulate and expand the opportunities for understanding and application?

We primarily affect the world of biomedical research by providing support to early career scientists both in the clinic

and in the laboratory. Our programs in Career Awards for Medical Scientists, Clinical Scientist Awards in Translational Research, Career Awards at the Scientific Interfaces, and Investigators in the Pathogenesis of Infectious Disease are all examples of how we choose outstanding scientists and provide them the flexible support needed to build their careers and tackle interesting and innovative problems. In fiscal year 2008, BWF funded a record number of awardees through these programs.

During fiscal year 2008 BWF also developed initiatives in two new areas. We are excited about the possibilities presented as we bring together medical schools

“INTERESTINGLY, IN THIS CENTURY OF BIOLOGY THERE IS AN INCREASED NEED TO INTEGRATE PHYSICS, MATHEMATICS, COMPUTATION, AND CHEMISTRY WITH BIOLOGY IN ORDER TO GAIN A MORE COMPLETE UNDERSTANDING OF LIFE.”

and schools of public health to train a new generation of scientists working at the interfaces of biomedical research and population-based approaches to human health through our program in Population and Laboratory Sciences.

We are also extending our long-term commitment in the reproductive sciences through a new grants program to support research in the area of preterm birth. This program will accept its initial round of applications in June 2009. An estimated 12 percent of U.S. pregnancies end prematurely, at an estimated cost of care and other ancillary expenses of \$26 billion per year. In one catalytic effort in this area, we held a meeting in December 2008, jointly sponsored by the March of Dimes, to bring together scientists from a variety of disciplines to share their knowledge regarding this important area of human health.

BWF recognizes that we cannot stand still in these changing times, and we are thus beginning to plan strategically for our future, through a process we call terrain

mapping (which we undertake every five years). As we carry out our next round of terrain mapping in 2009, we will remain aware of the many issues, most of them nonscientific, that confront the research community.

“IT IS IN SUCH TIGHT TIMES THAT FOUNDATION SUPPORT, BY BWF AND OTHERS, BECOMES EVEN MORE VITAL.”

We share the concerns of many people regarding the lack of growth in the National Institutes of Health's budget (which in 2009 represents a decline, again, in purchasing power). We are also worried about the continuing increase in the age at which investigators receive their first NIH R01 grant (NIH's primary type of grant for principal investigators). In 1980, investigators received their first such grant at an average age of 37; it is now 42. For M.D.'s it is even higher, with 44 being the average age for their first R01. Initial academic appointments have also been delayed; today, the average age is 38.5, while in 1980 it was 34. The picture on applicant success rate is also not cause for celebration, with fewer than 20 percent of new R01's being successful. Nor are conditions much better for investigators seeking continuing R01 grants: the success rate was 35 percent in 2007 versus 50 percent in 2001.

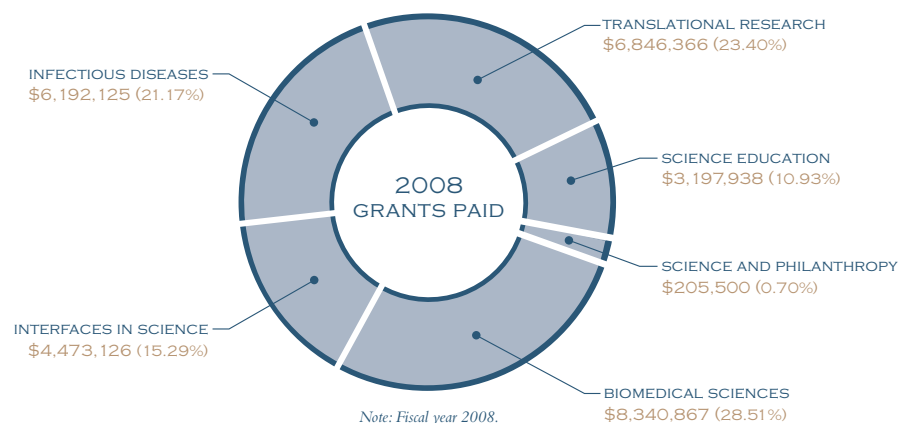
It is in such tight times that foundation support, by BWF and others, becomes even more vital. BWF's funding flexibility, targeted areas of support, and

nontraditional selection of research areas have helped us to maintain an important spot in the universe of funding for biomedical research. Our terrain mapping will be particularly helpful as we examine how to spend our limited dollars wisely.

Although most of our funds will continue to support biomedical research, we will continue our investment in precollege education. We have made important contributions in North Carolina, and we plan to continue to disseminate some of our exciting results to a broader national audience.

In addition to funding our Student Science Enrichment Program, we are initiating a Career Award for Science and Mathematics Teachers—a unique partnership between BWF and the North Carolina State Board of Education that will provide selected outstanding science and mathematics teachers in North Carolina with financial assistance and rewards to pursue opportunities for professional development, while remaining classroom teachers. Further information on this novel program is scheduled to be available in the coming year.

For more information about BWF's efforts in funding both research and education, please turn to the program descriptions in the following pages. These sections offer highlights from the past year and profiles of some of our outstanding award recipients that make all of us proud to continue the mission of the Burroughs Wellcome Fund.



The Burroughs Wellcome Fund makes approximately 90 percent of our grants through competitive award programs, which support investigators in targeted areas of basic biomedical research that have relevance to human health.

Most of BWF's award programs are open only to citizens or permanent residents of the United States and Canada. (Programs with different requirements are noted in the descriptions that follow.) Awards are made with the advice of our advisory committees, which comprise scientists and educators selected for their expertise in the program areas.

Most grants are made only to degree-granting institutions on behalf of individual researchers, who must be nominated by their institution. Institutions receiving grants must be tax-exempt 501(c)(3) organizations. Government agencies, such as the National Institutes of Health and the Centers for Disease Control and Prevention, generally are not eligible for grants.

Throughout the following program descriptions, references to M.D. and Ph.D. degrees include all types of medical and scientific doctoral degrees.

BWF does not support activities that are primarily related to health care and health care policy. We generally do not provide support for research projects or other activities outside our competitive programs, nor do we generally support endowments, development campaigns, ordinary operating expenses, capital facilities and equipment, or publications.

BWF believes that diversity within the scientific community enhances the well-being of the research enterprise; therefore, we encourage applications from women and from members of underrepresented minority groups.

Visit www.bwffund.org for current information.

The Burroughs Wellcome Fund's newest initiative is in reproductive science and is focused on preterm birth, an emerging public health burden. The issue was recently addressed in the National Academies report Preterm Birth: Causes, Consequences, and Prevention.

In the United States, preterm birth is the leading cause of neonatal morbidity and mortality in children without congenital anomalies, and the number of preterm births has increased almost 30 percent over the past two decades. Today, 12 percent of pregnancies end preterm. Despite this growing prevalence, little progress has been made in understanding the risk factors for preterm birth or the key physiological mechanisms leading to normal parturition. With our new initiative, BWF seeks to promote innovation and discovery regarding preterm birth and parturition by fostering new multidisciplinary interactions among talented investigators.

The initiative's initial phase is an international conference, Preventing Prematurity: Establishing a Network for Innovation and Discovery, jointly sponsored by BWF and the March of Dimes, which took place on December 1-3, 2008. The conference's goal is to promote and catalyze multidisciplinary efforts by bringing together 150 invited investigators already working in the area with others new to the field.

The conference served to announce BWF's commitment of \$3.5 million for grants to advance scientific issues related to preterm birth. The grants are intended to bring together an interdisciplinary group of researchers with expertise in such fields as genetics/genomics, immunology, microbiology, and proteomics, as well as in the more traditional areas of parturition research, such as maternal fetal medicine, obstetrics, and pediatrics. The key to success for this initiative will be forming new connections among reproductive scientists and investigators who are involved in other areas to give the problem a fresh look and to catalyze research at these interfaces. BWF expects to make a total of five full research grants under this initiative.

Regarding BWF's ongoing Career Awards for Medical Scientists program (which grew out of the Career Awards in the Biomedical Sciences program that ran from 1995 to 2006), two award cycles have been completed. Intended to increase the

number of physician-scientists and keep them in academic research, the grants provide \$700,000 over five years. The ideal candidate for these awards will be two years away from becoming an independent investigator.

A recent article in the *Journal of the American Medical Association* (Andriole, D, et al, Characteristics and career intentions of the emerging MD/PhD workforce, JAMA 300(10): 1165-73, 2008)

reinforces the importance of focusing on physician-scientists. The article reported the results of a survey to determine the career intentions of the M.D./Ph.D. workforce compared with the M.D. (only) workforce for the years 2000-2006. Of the 79,104 respondents, only 13 percent (9,972 respondents) planned to

“AS A MEASURE OF THE PROGRAM’S SUCCESS, 43 PERCENT OF THE AWARDEES ALREADY HAVE RECEIVED TENURE-TRACK FACULTY APPOINTMENTS AT SOME OF THE MOST PRESTIGIOUS INSTITUTIONS IN NORTH AMERICA.”

have substantial involvement in research. BWF is convinced that physician-scientists are critical to the success of the biomedical research enterprise, and we therefore believe it is imperative that these highly trained individuals be retained within the research enterprise—more specifically the academic research enterprise.

For the 2007 and 2008 award cycles, the Career Awards for Medical Scientists program received 277 proposals, and BWF made awards to 37 young physician-scientists representing 10 institutions. Eight of the awardees were women and six were underrepresented minorities. Seventy-six percent of the awards went to physician-scientists who hold M.D./Ph.D.s, and 22 percent went to M.D. (only) awardees. One award went to an investigator with a D.D.S./Ph.D.

As a measure of the program’s success, 43 percent of the awardees already have received tenure-track faculty appointments at some of the most prestigious institutions in North America. BWF feels that the \$25 million investment made to these young physician-scientists will move the biomedical academic research enterprise in a positive direction.

GRANT OPPORTUNITIES:

CAREER AWARDS IN THE MEDICAL SCIENCES

Awards foster the development and productivity of physician-scientists who are early in their careers and help them make the critical transition to becoming independent investigators. The award provides \$700,000 over five years to bridge advanced postdoctoral/fellowship training and the early years of faculty service. Candidates should have an M.D., D.D.S., D.V.M., or equivalent clinical degree. Proposals must be in the area of basic biomedical, disease-oriented, translational, or molecular, genetic, or pharmacological epidemiology research. Researchers who want to work in the area of epidemiology should contact BWF to determine the eligibility of the proposal. Proposals in health services research or involving large-scale clinical trials are ineligible. During the postdoctoral/fellowship period, awardees may train at degree-granting institutions in the United States or Canada. All faculty positions must be taken at U.S. or Canadian degree-granting institutions. During the award period, at least 75 percent of the awardee’s time must be devoted to research-related activities. Researchers who hold a faculty appointment as an assistant professor or the equivalent, or who know they will hold such an appointment within a year of the application deadline, are not eligible.

Please see www.bwffund.org for program information.

PRETERM BIRTH INITIATIVE

Awards will bring together a diverse interdisciplinary group with expertise in genetics/genomics, immunology, microbiology, and proteomics along with the more traditional areas of parturition research such as maternal fetal medicine, obstetrics, and pediatrics, to address the scientific issues related to preterm birth. The formation of new connections between reproductive scientists and investigators who are involved in other areas will give preterm birth research a fresh and unique look. Applicants must first apply for a planning grant by submitting a Letter of Intent. Only applicants whose letters are approved will be invited to apply for the full research grant. Full research grants will provide up to \$600,000 over a four-year period.

Letter of Intent/Planning Grant deadline: June 1, 2009



PROFILE: HEIDI A. TISSENBAUM CONNECTING THE DOMINOES

When Heidi A. Tissenbaum, Ph.D., chose to pursue a career in research, she never imagined that she would one day find herself conducting weekly laboratory meetings from a hospital bed. But that is exactly the situation she found herself in while recovering from a bleed in her brain stem, less than two years after starting a laboratory of her own.

Heidi A. Tissenbaum, Ph.D.

“I felt that I had a responsibility to make the best of the situation and push forward, because as hard as it was for me, it was also hard for everyone else—for my family, and for my lab,” said Dr. Tissenbaum, who received a Burroughs Wellcome Fund Career Award in the Biomedical Sciences in 2001. Although Dr. Tissenbaum describes her hospitalization as “terrible,” she also admits that it taught her something very important. “It told me how much I love to do science,” she said.

Dr. Tissenbaum, an associate professor in the programs of gene function and expression and of molecular medicine at the University of Massachusetts Medical School, has endured three separate brain bleeds, accompanied by lengthy hospitalizations, radiation treatments, and even brain surgery. The root of these medical maladies is an overgrowth of blood vessels in the brain—what doctors call a cavernous hemangioma. While most of the overgrowths have been removed, one remains, hidden away in a region too risky for surgery.

But Dr. Tissenbaum hasn’t turned from her dedication to research. Growing up in a medical family—her father was a physician and her mother a nurse—she had initially considered going to medical school. But because she believed that research was an important part of medicine, she opted to first enroll in a master’s degree program in physiology at the University of Ottawa. There she found her calling—and decided to forgo the medical degree, instead going on to earn her Ph.D. at Harvard Medical School.

Dr. Tissenbaum’s love of science began in a purely visual manner. Drawn to research she can see and touch, she prefers to conduct her experiments in a model organism rather than in a test tube. Because her organism of choice, a transparent

roundworm called *Caenorhabditis elegans*, lives for only two weeks, it can be used to find factors that significantly change lifespan. Dr. Tissenbaum began studying aging in *C. elegans* when she was in graduate school. “I sort of just stumbled into the field, and found the whole question of aging simply fascinating,” she said. Through her research, Dr. Tissenbaum has been instrumental in making key discoveries in the two main branches of the aging field: the insulin-signaling pathway and sirtuins.

The pathways that Dr. Tissenbaum studies can be thought of as a set of dominoes arranged in a pattern to target a final destination. In reality, biological pathways are a cascade of biological events that lead to a certain complex outcome, such as aging, a reaction to stress, or metabolism. Alterations in the spacing of the dominoes, or in the integrity of the genes in the pathway, can make the process go faster, or block it altogether.

A key role of the insulin-signaling pathway is to regulate blood glucose levels to prevent diabetes, but it also controls life span. Dr. Tissenbaum helped to identify several of the genes in this pathway, including *daf-2* (the receptor or molecular structure that binds insulin), *daf-16* (the target at the end of pathway), and *age-1* (the first gene shown to play a role in lifespan), all while working on her dissertation in the laboratory of Gary Ruvkun. Since then, researchers have shown that this same pathway exists in fruit flies and in mice, albeit in a slightly more complicated form.

“THE PATHWAYS THAT DR. TISSENBAUM STUDIES CAN BE THOUGHT OF AS A SET OF DOMINOES ARRANGED IN A PATTERN TO TARGET A FINAL DESTINATION.”

As a postdoctoral fellow, Dr. Tissenbaum worked at the Massachusetts Institute of Technology under the tutelage of Leonard Guarente. Dr. Guarente published some of the first papers on yeast lifespan, which was measured differently than in *C. elegans*. In yeast, the researchers measured the replicative lifespan or the number of progeny the yeast produce. Every time the yeast cell buds off to create a daughter cell, a lifespan is tallied. In *C. elegans*, as in humans, researchers instead measure what is called a chronological lifespan, or the number of days the animal lives. So when Dr. Tissenbaum discovered that altering yeast to have more of a particular gene product, a type of sirtuin protein called *sir-2*, extended longevity in worms as it had in yeast, it was a breakthrough for the field.

“The fact that changes in this gene give the same effect in two organisms where lifespan was measured so differently suggested that sirtuins really are important in regulating longevity across species,” Dr. Tissenbaum said. “Since I made this discovery, there has been an explosion of research into sirtuin biology across species, including mammals.” Sirtuins such as sir-2 are part of a group of proteins that control how tightly DNA is packaged in the cell. Sirtuins have been implicated in many processes, including aging, programmed cell death (apoptosis), and stress resistance.

Since starting her own laboratory at the University of Massachusetts Medical School, Dr. Tissenbaum has identified even more new genes and pathways involved in lifespan, along with gaining insight into the coupling of longevity and fat storage. But today she feels that it is not enough to study single genes or single pathways, and instead she is searching for interactions among all of the genes and pathways in all of the cells and organs of the worm. By integrating this information together into what is called a systems biology approach, she hopes to see how a change in longevity is brought about in the whole animal. “I am interested in determining how the various pathways, cues, and signals are coordinated in a three-dimensional context,” Dr. Tissenbaum said.

Dr. Tissenbaum first wants to figure out why worms have only one insulin receptor but 39 different insulin genes that may or may not bind to the receptor. To answer this question, she and her colleague Marian Walhout, a systems biologist, are systematically going through each of the 39 genes, one by one, to see where in the cell they are active and what exactly they are doing. They are also looking at the genes as a group to see how they interact—whether they form a simple line or a more complex pattern, for instance. In addition, Dr. Tissenbaum is performing genomewide studies to determine how *daf-16*, the gene she identified at the end of the insulin signaling pathway, ultimately performs the task of turning on or off hundreds of different target genes throughout the genome.

As a scientist whose work in the worm has taught her about reproduction, fat deposition, and systems biology, Dr. Tissenbaum says that these unexpected lessons come from dedicating her research to one model organism: “Because you see changes in so many different aspects of an organism, you never know where the science is going to lead—and that is exciting.”

—By *Marla Broadfoot*

The 14 Investigators in the Pathogenesis of Infectious Disease that the Burroughs Wellcome Fund named during the 2008 award cycle are taking a variety of scientific approaches with one broad aim: understanding the interactions between microbe and host and the critical transactions that lead toward coexistence or disease.

Their efforts focus on, among other things, probing the human immune system and deciphering social mechanisms and communications strategies that enable microbes to communicate with one another as they interact with their human host. Since the program's inception in 2001, BWF has made awards to a total of 72 researchers.

BWF also held in 2008 the latest in a series of periodic program gatherings, this time in Denver. A group of more than 100 past and present awardees, advisers, and others convened to consider the interactions that influence infection, commensalism, and cohabitation between microbes and man. Touching on evolutionary and population biology, the mechanics of damage, and the complexity of the conversations between human and microbial systems, the meeting illustrated the ideas that make BWF's award program about pathogenesis itself rather than about specific pathogens or human defenses against them.

On another front, BWF convened a meeting on next steps for postgenomic research in human malarias, the second community meeting on this topic since details of the *Plasmodium falciparum* genome were published in 2002. The meeting's focus was on how to apply currently available and future tools to get at two things: better insight into why children get sick and why they die, and better understanding of the biology of this resilient tripartite system.

Particularly valuable were discussions of endemic country contexts, in terms of both clinical observations and observations of changes in parasite populations, especially the alarming appearance and potential advance of resistance to the antimalarial drug artemisinin. The meeting highlighted areas where the malaria basic research community has much to gain by working together, especially in understanding the diversity of the malarial parasites in regions of the world where the disease is endemic.

BWF also launched new activities in 2008 focused on two underserved areas: molecular helminthology, and career development of veterinarian scientists working on problems relevant to human health.

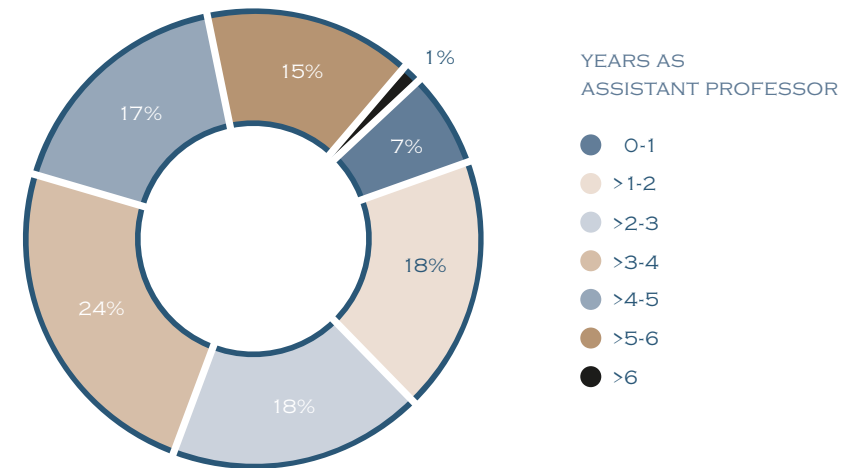
In 2007, BWF's Board of Directors set aside a modest sum for support of efforts to strengthen the parasitic helminth research community, attract new researchers to study the remarkable biology of the helminth human parasites, and accelerate tool development for work in these pathogens. This year, work in the helminths attracted BWF's favorite type of small grant: one that has an impact well beyond its cash value. The grant will support work at the University of Pittsburgh that will make possible the closure, assembly, and annotation of the *Brugia malayi* genome, which had been sequenced but unassemblable using older sequencing technologies. In other efforts slated for 2008–2009, BWF anticipates supporting and participating in a meeting that will bring together researchers from the worm parasite systems with researchers and trainees working in eukaryote models, especially the nematode *Caenorhabditis elegans*.

Work in the parasite worms, which are themselves multicellular animals, has lagged behind work in other human pathogens. The worms that live within and on humans are a diverse group, and generalities about their genetics and biochemistry do not get researchers far. But recent years have brought comparative genomics and better data across evolutionary biology, newly established genetic tools, and the clarity that is emerging with gene ontogeny efforts across species. Over the next year, BWF will be working toward understanding whether a revolution is on the horizon for the worm fields, and whether there is a role for BWF in bringing it to fruition more quickly.

Comparative science is important on the macro scale, too. The world teems with animals, and all animals—including humans—teem with things that bite, or enter cells, or dwell on their bodies. The insights of comparative medicine are important across human health, but perhaps nowhere more critical than in infectious diseases. Emerging pathogens most often come into the human population from animals. Domesticated food animals and pets, along with the uncounted wild creatures that live within inches, feet, yards, and miles of human populations, hold a potentially important role in the health of individuals and societies. So do the birds, domestic and wild, local or migratory.

Thus veterinarians, with a medical education that is both broad and deep, should be integrated into human health research, but all too often they are not. In 2008, BWF joined with the Howard Hughes Medical Institute to begin supporting veterinary students—as HHMI-BWF Fellows—who will spend a year doing research as part of HHMI's well-established Medical Fellows Program. In the upcoming year, BWF looks forward to career development efforts focused on early-career D.V.M./Ph.D.s.

CURRENT INVESTIGATOR SNAPSHOT



GRANT OPPORTUNITY:

INVESTIGATORS IN THE PATHOGENESIS OF INFECTIOUS DISEASE

Awards provide new opportunities for accomplished investigators at the assistant professor level to study pathogenesis, with a focus on the intersection of human and pathogen biology. The program is intended to shed light on the overarching issues of how human hosts handle infectious challenge. These five-year grants, which provide \$100,000 per year, are intended to give recipients the freedom and flexibility to pursue new avenues of inquiry and higher-risk research projects that hold potential for advancing significantly the biochemical, pharmacological, immunological, and molecular biological understanding of how infectious agents and the human body interact. BWF is particularly interested in work focused on the host, as well as host pathogen studies originating in viral, bacterial, fungal, or parasite systems. Studies in these areas may have their root in the pathogen, but the focus of the work should be on the effects on the host at the cellular and/or systemic levels. Excellent animal models of human disease are within the scope of the program. Candidates must have an established record of independent research and hold a tenure-track position as an assistant professor or equivalent at a degree-granting institution in the United States or Canada.

Please see www.bwfund.org for program information.



Britt Glaunsinger, Ph.D.

PROFILE: BRITT GLAUNSINGER
COMMANDEERING MOLECULAR PIRATES

Viruses are molecular pirates. They commandeer the cellular pathways and processes of organisms—including humans—and many have stolen human genes to help in the attack.

In fact, viruses are so skilled at co-opting human cellular machinery that they are fantastic tools for exploring the inner workings of cells, says Britt Glaunsinger, Ph.D., who received a Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Disease Award in 2007.

“They point you to what’s important,” said Dr. Glaunsinger, an assistant professor of virology at the University of California-Berkeley. “They’ve figured out how to best interface with nearly every cellular pathway.”

Dr. Glaunsinger hopes to reveal how human cells regulate gene expression by studying the herpesvirus that causes Kaposi’s sarcoma. When the virus replicates itself, gene expression in a cell grinds to a halt. Dr. Glaunsinger has discovered the culprit: a viral protein, called SOX, that destroys messenger RNA (mRNA), the couriers that transmit genetic blueprints from DNA to guide protein production within the cell. She’s pursuing several lines of evidence which suggest that SOX enables the virus to hijack the cell’s regulatory system for controlling mRNA.

“If we can pinpoint how it’s commandeering these regulators, it will give us a window into the focal points of messenger RNA stability,” she said.

Scientists don’t know how cells control the lifespan of an RNA message (that is, how mRNA remains stable), nor do they know how cells prevent garbled or out-of-date signals from reaching their cellular target. In fact, Dr. Glaunsinger said, all of the cellular processes that govern mRNA remain poorly understood, even though messenger RNA plays a critical role in turning genes on and off.

“When people think of changes in gene expression, they think of transcriptional changes or protein stability; but they don’t consider stability of a message itself. But that can play as huge a role in gene expression as transcription effects or protein stability,” Dr. Glaunsinger said.

Decoding how cells maintain or destroy mRNA is of keen interest to researchers. The messages go awry in many different medical disorders, including cancer, inflammation, and various inherited diseases such as cystic fibrosis.

Because the Kaposi's sarcoma herpesvirus exploits the same tumor pathways as other cancers, studying its effect on cells could provide new insight into cancer growth, Dr. Glaunsinger said. The potential for Dr. Glaunsinger's research to lead to new cancer therapeutics was recognized with a 2008 Distinguished Young Scholar in Medical Research award from the W. M. Keck Foundation.

Dr. Glaunsinger's results suggest that the Kaposi's sarcoma virus corrupts more than 90 percent of a cell's mRNA. Her most recent research indicates that the SOX protein shuts down mRNA communication by interfering with the molecular signals that protect mRNA from being destroyed. "An event that normally in human cells would guard messages against destruction is now being used to destroy them," Dr. Glaunsinger said.

With her BWF grant, Dr. Glaunsinger is trolling for genes affected by SOX. "This is one of my most exciting projects," she said. In collaboration with researchers at the Genomics Institute of the Novartis Research Foundation, Dr. Glaunsinger

has performed a whole genome screen to find out which pieces of cellular machinery the virus commandeers. Dr. Glaunsinger hopes this approach will help in elucidating how cells control messenger RNA.

"There's a mountain of data we're sorting through now, and there's

some pretty exciting things coming out of the initial filtering," she said. "It's taking us in an unexpected direction, one we wouldn't have anticipated if we hadn't taken this unbiased route."

Dr. Glaunsinger's interest in viruses came late in her undergraduate career at the University of Arizona. Though she is the daughter of a chemistry professor and a biology teacher, Dr. Glaunsinger intended to major in anything but science. But then she read *The Hot Zone*, a book by Richard Preston.

"That got me completely hooked on viruses," she said. "These minute agents aren't even considered living, but they've completely shaped evolution on the planet. Any life form has been shaped by a virus."

Dr. Glaunsinger received her Ph.D. in molecular virology and microbiology from Baylor College of Medicine in 2001, then completed a postdoctoral fellowship at the University of California-San Francisco before moving across the bay to UC-Berkeley. She joined its department of plant and microbial biology in 2006.

In addition to her work on the SOX protein, Dr. Glaunsinger is trying to solve another viral puzzle—the Kaposi's sarcoma virus can send its own RNA messages, which escape destruction even as the virus shuts down cellular communication.

"The issue of how viral messages are escaping is fascinating," Dr. Glaunsinger said. "They're escaping what we envision as a security system check. Somehow they have a get-out-of-jail-free card, and we don't know what that is yet."

—By *Becky Oskin*

“WHEN PEOPLE THINK OF CHANGES IN GENE EXPRESSION, THEY THINK OF TRANSCRIPTIONAL CHANGES OR PROTEIN STABILITY; BUT THEY DON'T CONSIDER STABILITY OF A MESSAGE ITSELF.”

When the Burroughs Wellcome Fund launched its Interfaces in Science program in 1996, the notion that the future of biology would be driven by physicists and mathematicians was not exactly mainstream. Since that time, BWF has invested more than \$63 million to draw the brightest young minds from physical, computational, and theoretical disciplines toward the increasingly data-rich frontiers of biology.

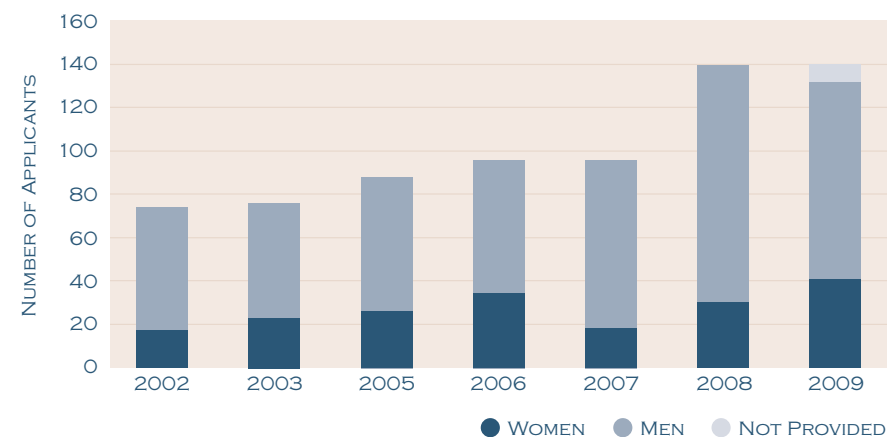
BWF's first strategy was to build habitats for multidisciplinary training, awarding funding for 10 programs between 1996 and 2000. These experimental programs were among the first of their kind, and BWF was well aware of the risk that these trainees would emerge as scientists with expertise that was broad but shallow. During 2008, BWF probed for early career outcomes among program alumni, and found that roughly half of those who responded had moved into tenure-track positions at research universities. A scan of the five most recent publications from this group indicates that the vast majority are persisting in interdisciplinary work. More importantly, 43 percent of them already have received funding from the National Institutes of Health, indicating that their work is not only biological but health-related. These early indications point to the success of the BWF experiment, in that cross-disciplinary training prepared these young investigators to make robust scientific contributions, measured by their academic success and productivity.

In 2002, BWF moved to a second strategy by launching the Career Awards at the Scientific Interface program, which targets individual investigators rather than institutional programs. Fiscal year 2008 marked a high point for the program, as BWF made 15 awards, the most ever in a single award cycle. The applicant pool has doubled since the program's inception, and the number of institutions submitting candidates has risen 39 percent since 2006, indicating that the habitats for these interdisciplinary scientists are becoming more plentiful. BWF encourages projects that meld together computational and theoretical with experimental approaches, and which have in view not just a narrow experimental system but the broader biological context. All 15 of the most recent awardees will be conducting experiments, many of them pioneering new technologies. Examples include using

in vivo cellular imaging of the retina to understand glaucoma, applying optical trapping to understand myosin force generation, and developing "bimodal nano-particle assemblies" for use in tumor imaging and therapy.

To date, the program has made 63 awards across 30 institutions. One important distinctive feature of these awards is the hands-on approach that BWF takes to the postdoc-to-faculty transition. BWF reviews each offer letter and provides a context in which the awardee can evaluate it. Thus far, 46 awardees have transitioned to tenure-track positions. Roughly half of them are in physical science or engineering departments, providing further evidence that the environment is changing and that traditional boundaries between disciplines are no longer obstacles to great science.

YEARLY PROGRAM AWARD SNAPSHOT



Note: No awards were made in 2004. Years are Fiscal.

GRANT OPPORTUNITY:

CAREER AWARDS AT THE SCIENTIFIC INTERFACE

Awards foster the early career development of researchers with backgrounds in the physical/computational sciences whose work addresses biological questions and who are dedicated to pursuing a career in academic research. Candidates are expected to draw from their training in a scientific field other than biology to propose innovative approaches to answer important questions in the biological sciences. The grants provide up to \$500,000 over five years to support up to two years of advanced postdoctoral training and the first three years of a faculty appointment. Candidates must have a Ph.D. degree in physics, chemistry (physical, theoretical, or computational), mathematics, computer science, statistics, or engineering. Exceptions will be made only if the candidate can demonstrate significant expertise in one of these areas, evidenced by publications or advanced course work. This program is open to U.S. and Canadian citizens and permanent residents as well as U.S. temporary residents.

Please see www.bwfund.org for program information.



Daniel Goldman, Ph.D.

PROFILE: DANIEL GOLDMAN NAVIGATING CHALLENGING TERRAINS

Few people can say their lives have not changed much since they were a kid. But Daniel Goldman, Ph.D., still spends his days picking up little creatures—bugs and lizards and the like—and placing them in his sandbox to see how they behave, just as he did when he was eight years old.

Dr. Goldman, who received a Burroughs Wellcome Fund Career Award at the Scientific Interface in 2006, is interested in how animals move about in their environment, particularly how they have adapted to navigate such challenging terrains as sand, bark, leaves, and grass. By changing the type of ground that experimental animals must traverse, Dr. Goldman is straying from the approach employed by most biomechanics researchers, who typically study movement on flat, rigid, nonskid surfaces.

“If you look in the real world, you will rarely find an organism that moves in an environment with those features,” he said. “Typically, environments can have irregular footholds, they can be at steep angles, and they can slip and flow in response to a foot impact.” In order to truly understand how an animal moves around in the wild, Dr. Goldman feels it is necessary to look at the biophysical interaction of the organism and its environment.

Although his early childhood interests lay in biology, as he grew older he became more and more fascinated with the physical aspects of the world. He majored in physics at the Massachusetts Institute of Technology, and then earned a doctorate in the same discipline at the University of Texas–Austin, where he first began his investigation of the unique features of granular materials such as sand. Sand is a particularly challenging terrain because though it is normally acts like a solid, under certain circumstances it can shift and move like a fluid.

Through the mentorship of Robert J. Full, his postdoctoral adviser at the University of California–Berkeley, Dr. Goldman became interested in how animals tackle the challenge of moving around on sand and other complex surfaces. “At one moment a lizard may be resting on the surface of the sand, which in turn is supporting its whole weight just like a solid, but as soon as it pushes off the material fluidizes, and the animal is now thrusting against material that has fluidlike properties,” Dr. Goldman said.

To further study this phenomenon in the laboratory, Dr. Goldman developed miniature sandboxes, or “fluidized” beds, where he could control the conditions that lizards, crabs, and other creatures travel on. Instead of using actual grains of sand, which can vary in size and shape depending on their origin, Dr. Goldman filled his beds with smooth glass beads of sizes comparable to those of desert or beach sand. Underneath the beads he placed a rigid porous membrane, which enabled him to control the packed state of the “sand” using an upward flow of air. When he turned the air flow on, the entire collection of sand grains would become fluidized, and when he turned it off, the grains would settle into a packed state of material.

Dr. Goldman is looking not just at how organisms respond when the packing of the sand has changed, but also at how models of these organisms—specifically, robots—can be adapted to respond as well. He began his work on robots while in the Director of Central Intelligence Postdoctoral Research Program, which the

federal government established to fund postdocs conducting projects of interest to the intelligence community. At the time, his mentor's research was focused on studying how the principles of organism locomotion can be translated into building devices with similar capabilities as organisms.

Together, Drs. Goldman and Full videotaped ghost crabs, geckos, and zebra-tailed lizards as they scampered, trudged, or darted across a sand bed. They discovered that the animals ran equally fast on hard-packed sand. However, as the material weakened, the crab and the gecko became bogged down, while the zebra-tailed lizard continued on, undeterred. The results of this research have much larger implications than which creature got the gold medal: the lessons learned from studying differences in locomotion can be applied to design better robots.

For instance, when Dr. Goldman tested the ability of funnel weaver spiders to traverse a wire mesh surface—used to simulate broken terrain, such as ground covered in debris—he found that their movement was facilitated by the presence of specialized spines along the length of their legs. The spines, essentially large hairs, flex as the spider moves, maximizing the contact of its legs with the surface. He then glued artificial spines onto the legs of ghost crabs—which normally don't possess them—and showed that the spines increased the mobility of the crabs on the wire mesh. The addition of steel spines to a six-legged robot had a similar effect—a finding that could lead to development of rescue robots that are better equipped to cross a range of environments.

Now an assistant professor of physics at the Georgia Institute of Technology, Dr. Goldman is continuing his work on robots as he puts one called SandBot through the rigors of travel on his fluidized sand beds. Unlike his experiments with animals, in this case he can carefully control the robot's motion and check how different movement patterns must be modified to keep the robot moving smoothly on the sand as it weakens. His experiments with robots make it possible to test hypotheses generated from similar studies in animals.

Dr. Goldman has developed a variety of methods to help him generate these hypotheses on how organisms move around their environment. "We can measure forces generated when an animal pushes or drags sand, how much an animal wobbles as it climbs up an incline, and how much stress is on particular limb as it impacts ground," he said.

Not only does he use these methods to interrogate animals in his laboratory, but he also takes them out into the field. He is now examining the challenges faced by hatchling sea turtles as they spend their first hour of life scurrying across sand to reach their ultimate home in the ocean. It is part of a larger project studying how various organisms, including spiders and cockroaches, climb sandy hills.

Working with wild animals, whether in the laboratory or the field, takes technical prowess and more than a little patience on the part of Dr. Goldman and

the "terrific" grad and undergrad students in his laboratory. To discover how ghost crabs deal with the stress on their limbs as they move around, Dr. Goldman attaches strain gauges onto the exoskeletons of his subjects. He then outfits the crabs with tiny wireless backpacks to record the signals from the gauges. Altogether, the process takes four hours, and doesn't always produce the intended results.

"The worst is when you are done, put the crab on the ground, yell 'Go!' and, rather than running as you wanted, it lunges at you, tries to bite you, and strips off the equipment," Dr. Goldman said. "But that is what I like about this research. At times it can seem completely insane, but there are usually good reasons for doing it."

—By Marla Broadfoot

“THE WORST IS WHEN YOU ARE DONE, PUT THE CRAB ON THE GROUND, YELL ‘GO!’ AND, RATHER THAN RUNNING AS YOU WANTED, IT LUNGES AT YOU, TRIES TO BITE YOU, AND STRIPS OFF THE EQUIPMENT.”

The Burroughs Wellcome Fund launched a new program in fiscal 2008 to train researchers to use both population science and traditional bench-based approaches to get at difficult problems in human health. The first awards in the Program Unifying Population and Laboratory-Based Sciences will be made early in the 2008-2009 cycle.

The program will support institutional partnerships that will establish training programs that will develop young researchers who are equally at home with the ideas, approaches, and insights generated at both the molecular scale and the population scale. The hope is that participating graduate students will build careers by bringing new approaches to combining genomics with the study of phenotype characterizations, or phenomics, and addressing questions of population genetics as well as a range of other problems that reflect a new understanding of human health and its disruptors.

In the first round of applications, BWF received proposals that can be sorted roughly into six topic areas: proposals covering infectious disease/cancer; proposals focused on complex diseases such as asthma, diabetes, and obesity; proposals focused on environmental factors; proposals growing out of human genetics; proposals that are not centered around a particular scientific theme; and proposals that draw heavily on clinical translation of bench science for use in human patients.

The goal is to enable institutions to develop new graduate programs that will bring together ways of thinking that have historically been housed in separate departments and often in separate colleges within universities. The program is expected to run for a limited period. BWF will make 10 awards over three to five years, for a total investment of \$25 million.

As these training programs are established, BWF will work with the funded institutions to develop evaluation tools that we can use to understand the origins and destinations of students who are drawn to problems that fall between fields.

GRANT OPPORTUNITY:

INSTITUTIONAL PROGRAM UNIFYING POPULATION AND LABORATORY BASED SCIENCES

Awards provide \$500,000 a year for five years in order to stimulate institutional training programs that partner researchers working in schools of medicine and schools (or academic divisions) of public health. Our hope is to develop a new cadre of scientists working at the connections between population approaches to human health and basic biomedical research. Understanding human health will be a focal priority for the programs that are funded. There is ample room for building on institutional strengths to achieve this focus. Examples include: building on institutional interests in chronic diseases, autoimmune diseases, infectious diseases, genetic diseases, toxicology, reproductive health, and other areas where questions relating to human health are ripe for exploration at both the population and molecular scales. Likewise, institutional strengths in applied mathematics and modeling, statistics, genomics, bioinformatics and other informatics and data-driven sciences including geography and demographics, and phenomic approaches could provide excellent foundations for programs that encourage such work.

Please see www.bwfund.org for program information.

The Burroughs Wellcome Fund's Clinical Scientist Awards in Translational Research program hit a high-water mark in fiscal year 2008, with 13 new awards made—the highest number in the program's 11-year history. BWF has now provided support for 93 clinical scientists at 41 institutions across the United States and Canada.

The new awardees are focusing on a range of disorders, including cancer, diabetes, HIV/AIDS, affective disorders, and autoimmune diseases. One theme runs through many of their projects: improving the prediction and prevention of disease. One awardee is identifying biomarkers that may identify individuals at risk for colon cancer, another aims to identify pregnant women who are at risk for preeclampsia, and another seeks to unravel the effects of maternal nutrition on childhood obesity.

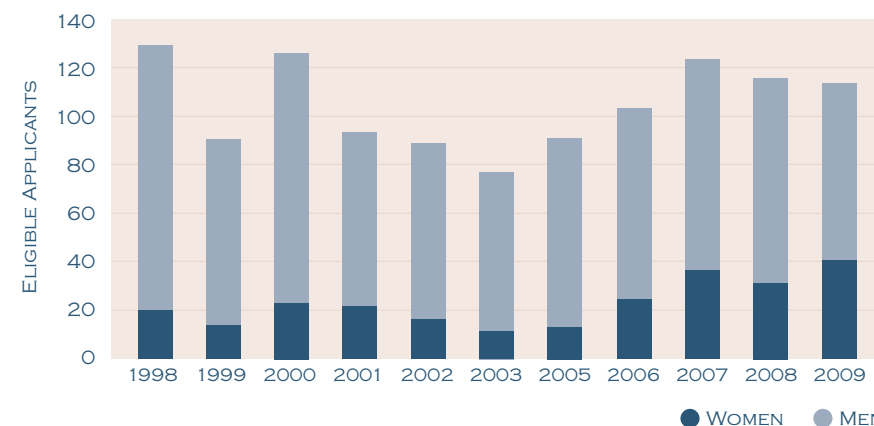
Among the program's goals, one key aim is to encourage outstanding physician-scientists to move their most significant discoveries from the laboratory into the clinic. BWF recognizes that there are many barriers to translational research that go beyond the availability of research dollars and talented trainees. The current consensus among BWF's awardees is that the overall environment for translational research has improved in the past couple of years, but that major obstacles still remain. Chief among them are the regulatory burden for research involving human subjects, the apparent flat future of funding from the National Institutes of Health, the need for infrastructure that supports clinical studies, and the need for a clearer path to commercialization of potential therapies.

Because this environment has a direct effect on BWF's awardees' ability to launch clinical studies, we are centrally engaged in the consideration of these issues, through involvement in efforts such as the Institute of Medicine's Forum on Drug Discovery, Development, and Translation, as well as through support for convening events that bring leaders in this field together. Perhaps most importantly, BWF has sustained our leadership role in the Health Research Alliance, a growing consortium of foundations and voluntary health agencies with a shared interest in fostering the movement of discoveries into therapeutic application and ultimately better health.

In a similar vein, BWF has long paid close attention to the career path of clinical investigators, and for years the community has indicated that a central, freely available career development resource for physician-scientists and clinical investigators is needed. In response to this need, during 2008 BWF began working with the American Association for the Advancement of Science to develop the Center for Careers in Clinical and Translational Science. Targeted at prospective and current trainees, the web portal will assemble articles addressing all aspects of building a career, including topics such as finding the right mentor and training program, navigating human subjects regulations, and managing conflict of interest when working with industry. The site will be officially launched in early 2009, and will be shaped with the input of leaders from a broad range of professional societies as well as NIH.

BWF is pleased that our pioneering investment in translational research of nearly \$73 million over 11 years has been followed by a significant effort in this area by federal funding agencies. Notably, NIH has developed 38 Clinical and Translational Science Award programs that provide integrated infrastructure, training, and research resources. These programs also should facilitate the work of BWF's awardees, many of whom have leadership roles within these institutions.

YEARLY PROGRAM AWARD SNAPSHOT



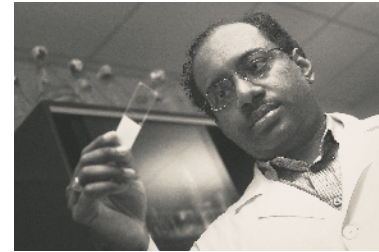
Note: No awards were made in 2004. Years are Fiscal.

GRANT OPPORTUNITY:

CLINICAL SCIENTIST AWARDS IN TRANSLATIONAL RESEARCH

Awards foster the development and productivity of established independent physician-scientists who will strengthen translational research, the two-way transfer between work at the laboratory bench and clinical medicine. The grants provide \$750,000 over five years (\$150,000 per year). We are interested particularly in supporting investigators who will bring novel ideas and new approaches to translational research and who will mentor the next generation of physician-scientists. Proposed activities may draw on the many recent advances in the basic biomedical sciences—including such fields as biochemistry, cell biology, genetics, immunology, molecular biology, and pharmacology—that provide a wealth of opportunities for studying and alleviating human disease. Candidates generally must be affiliated with a medical school; candidates at other types of degree-granting institutions (including schools of veterinary medicine, public health, and pharmacy) will be considered only if they can demonstrate a plan for coordinating with institutions that provide the patient connection essential for translational research. Candidates must have an M.D. or M.D.-Ph.D. degree and hold an appointment or joint appointment in a subspecialty of clinical medicine. Candidates must hold a current medical license to practice medicine in the United States or Canada. Candidates must be tenure-track investigators at the late assistant professor level or the early associate professor level, or hold an equivalent tenure-track position, at the time of application. Candidates must present evidence of already having established an independent research career, as this is not a “new investigator” award. Individuals holding the rank of professor are ineligible.

Please see www.bwfund.org for program information.



Jayakrishna Ambati, Ph.D.

PROFILE: JAYAKRISHNA AMBATI
GAINING INSIGHT INTO A DISEASE

If asked to list a few of the most prevalent diseases in the United States, many people would likely place cancer at or near the top. Few people realize that age-related macular degeneration (AMD), a disease that results in the gradual loss of sight, affects more people than all cancers combined.

Jayakrishna Ambati, M.D., who received a Burroughs Wellcome Fund Clinical Scientist Award in Translational Research in 2007, knows well the tremendous impact of AMD on public health, and he has spent the past decade studying the disease. Dr. Ambati's interest in AMD began during his residency in ophthalmology at the University of Rochester and subsequent fellowship at Harvard Medical School. He now is a professor and vice chair of ophthalmology and visual sciences at the University of Kentucky.

When Dr. Ambati first turned his attention to AMD, little was known about what actually caused the disease at a molecular level. This gap, he says, fueled his desire to develop a fundamental understanding of the processes that drive macular degeneration in an effort to devise new treatment strategies.

“I think most people who go into basic research want to solve puzzles, want to solve problems, want to gain new knowledge and advance the field,” Dr. Ambati said. “A physician-scientist has something more at stake—to see a smile on your patient's face when you've done something for them that basically no one else can do.” He quickly notes that providing medicine or surgical skills can certainly make a difference one person at a time, and he still sees patients approximately once a week. “But doing basic research and translational research has the potential to put smiles on the faces of thousands and millions of people,” he said.

AMD can occur in two forms: dry or wet. Dry AMD, the most common form, results in the breakdown of cells within the retina. The advanced form of dry AMD is called geographic atrophy, because “when you look at the eye, it looks as though someone has taken an eraser and wiped out various parts of the retina,” Dr. Ambati explained.

The remaining minority of AMD patients have the wet form of the disease, in which blood vessels grow abnormally and invade the retina. Wet AMD results in a dramatic,

almost instantaneous loss of vision. Over the past several years, there has been a sea change in how physicians treat wet AMD. “There are drugs now that actually block the growth of these blood vessels and their leakage and offer the hope of improved vision for the first time,” Dr. Ambati said.

Unfortunately, in the case of geographic atrophy, there is no good treatment. In an effort to address this void, Dr. Ambati and colleagues embarked on a research project that led to a paradigm-shifting discovery, recently published in the *New England Journal of Medicine*, about the role of a certain class of genetic molecules, called small interfering RNAs, in AMD.

These molecules are members of a larger class of genetic molecules, called double-stranded RNA (dsRNA), that are most notably known for their involvement in a newly discovered genetic process called RNA interference, which is a mechanism that inhibits gene expression in several ways. In one case, dsRNA works by activating another protein called TLR3, a type of cell receptor in the immune system that mediates apoptosis, or programmed cell death.

The results of Dr. Ambati’s research suggest that viral dsRNA may play a role in the development of geographic atrophy. This discovery began as an extension of earlier research which suggested that small interfering RNAs appear to activate TLR3 and may be involved in wet AMD. “So I contacted another researcher, Kang Zhang, to see if there was a TLR3 mutation in macular degeneration,” Dr. Ambati said.

Dr. Zhang, a professor of ophthalmology at the University of California-San Diego, is also a retina specialist, as well as a 2008 recipient of a BWF Clinical Scientist Award in Translational Research. Dr. Zhang “has a tremendous resource in terms of a large library of serum samples from patients with and without macular degeneration,” Dr. Ambati said.

Together, the researchers tested for an association between AMD and a particular mutant form of the TLR3 gene—a polymorphism in which the amino acid phenylalanine is substituted for leucine at a particular location. This variant had been identified as a possible culprit in the previous study. Dr. Ambati’s group also examined the effect of two other variants of TLR3 on the viability of human retinal pigment epithelial cell in vitro, as well as on apoptosis, in retinal pigment epithelial cells from wild and genetically engineered strains of mice.

“These experiments showed that activating TLR3 can cause geographic atrophy in mice and that the disease doesn’t happen in mice that lack TLR3. That makes the

genetic association functionally relevant; people who have a dysfunctional form of TLR3 are protected against this disease,” Dr. Ambati explained.

Through this study, Dr. Ambati and colleagues found that one particular TLR3 variant, called 412Phe, protects against geographic atrophy, likely by suppressing retinal pigment epithelial cell death. They also found that activation of TLR3, which is enhanced by another variant, called 412Leu, appears to promote progression to the geographic atrophy phenotype.

“If activation of TLR3 contributes to this progressive process, intercellular transmission of viral intermediates or transcripts that activate TLR3 could mediate the pathogenesis of geographic atrophy in some patients,” Dr. Ambati said. “Given our findings, it is important to search for the existence and nature of this type of RNA (viral or otherwise) in eyes affected with geographic atrophy.”

“WHAT GREATER ACCOMPLISHMENT
COULD A PHYSICIAN-SCIENTIST HAVE
THAN TO ACTUALLY TRANSFORM THE
NATURAL HISTORY OF A DISEASE?”

In this way, Dr. Ambati added, this discovery may prove important both in understanding the AMD pathogenesis and, even more importantly, in helping develop agents that can block TLR3 activation.

Dr. Ambati now is developing new TLR3 antagonists and is in the process of publishing data that show these molecules actually protect against macular degeneration in animals.

Over the next year, Dr. Ambati plans to begin a preliminary clinical trial using these TLR3 antagonists to initially show their safety, with a view to advancing them as a new therapeutic modality for the dry form of macular degeneration.

“Beyond that, I’d like to discover more of the truth that’s out there. In my view, biology is just a big jigsaw puzzle where all the pieces have been randomly thrown about, and it’s our job, collectively, to put the pieces back in order,” Dr. Ambati said. “The more sections of that puzzle we can help put together, I think we’ve fulfilled our desires. What greater accomplishment could a physician-scientist have than to actually transform the natural history of a disease?”

—By Rachel Ahmed



Kate Ahlport
Executive Director
Health Research Alliance

CATALYTIC PROGRAM IN TRANSLATIONAL RESEARCH: HEALTH RESEARCH ALLIANCE

Shortly after the Burroughs Wellcome Fund became an independent private foundation, BWF assumed a collaborative leadership role in the community of private funders. Slowly and deliberately over the next decade, this community expanded—and a robust network of staff in foundations and voluntary health agencies began to form, largely due to the initiative and vision of then-BWF President Enriqueta Bond, Ph.D. In 2004, BWF’s Board of Directors recognized that significant momentum was gathering, and that there was a need for a professional organization where foundation leaders could share best practices, learn from each others’ experiments, and consider together the landscape for biomedical research. Thus they agreed to “incubate” the Health Research Alliance (HRA). The HRA’s mission is to work together to optimize investment in health research and training. Its vision is to become the leading resource in health research philanthropy.

As of 2008, HRA has 35 organizational members, whose collective annual investment in biomedical and health research exceeds \$1.6 billion and reaches over 6,000 investigators. The alliance developed a formal membership structure in 2006, and members pay dues annually. BWF continues to provide leadership to the alliance. Nancy Sung, Ph.D., a BWF senior program officer, chairs HRA’s 12-member Board of Directors, which comprises representatives from member organizations, and she also works closely with HRA Executive Director Kate Ahlport. In January 2007, HRA became financially independent from BWF.

Highlights of the 2008 fiscal year include HRA’s biennial national conference, Accelerating Medical Discovery through Strategic Philanthropy, which attracted approximately 150 participants representing 65 funding organizations.

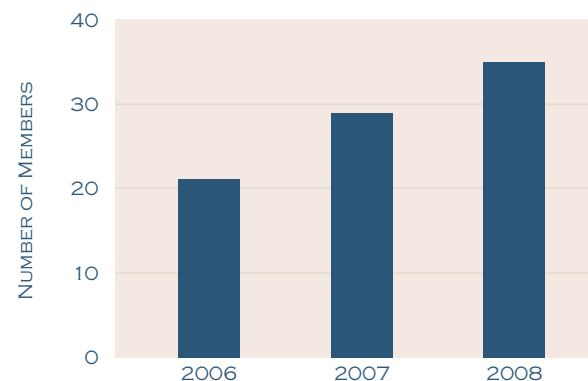
HRA recognizes that in an era of constrained federal funding, the contribution of the nonprofit, nongovernmental sector to the research enterprise is more critical than ever, and yet there is no reliable data on their collective contribution. HRA is in a unique position to assemble this data, and in 2008 completed the preparation

of its “gHRAsp” database: Grants in the Health Research Alliance Shared Portfolio. The database will be implemented in 2009, when HRA will issue a public report on the scope its members’ grantmaking.

Other HRA working groups are focusing on issues in grants administration and program evaluation, as well as on “translational philanthropy” by which foundations can accelerate the development of therapies from basic science discoveries.

More information about the Health Research Alliance can be found at www.healthra.org.

YEARLY MEMBERSHIP GROWTH



The Burroughs Wellcome Fund believes that all Americans deserve to be scientifically literate and share in the excitement that comes from learning about the natural world. In helping to reach this goal, BWF focuses on working in our home state of North Carolina, where we collaborate with educators, policymakers, and other stakeholders to improve the pipeline of young people choosing to pursue careers in science and science-related fields.

Scientific literacy is increasingly important in the global workforce that requires people to think critically, solve problems, use technology, and participate meaningfully in society's decisions. BWF is committed to inspiring primary and secondary students by exposing them to the wonders of science through hands-on enrichment programs, educating policymakers who are responsible for what is taught in classrooms, fostering cohorts of master science and mathematics teachers to populate schools, and building the capacity of organizations to advance science and mathematics education.

In fiscal 2008, BWF received the largest number of applications in the history of our Student Science Enrichment Program (SSEP), and also convened the largest group of enrichment-activity providers involved in SSEP. This competitive institutional award program is the cornerstone of our work in this area. BWF has invested more than \$40 million in science education through SSEP since 1996. The majority of these funds (\$18.3 million) supports programs offered through schools, universities, colleges, museums, and other nonprofit organizations, which can receive grants of up to \$180,000 over three years to reach students from kindergarten through twelfth grade. BWF has made a total of 128 SSEP awards, and the programs, offered by 64 organizations, have reached nearly 27,000 students statewide. For 2008, BWF made 20 awards to 17 organizations.

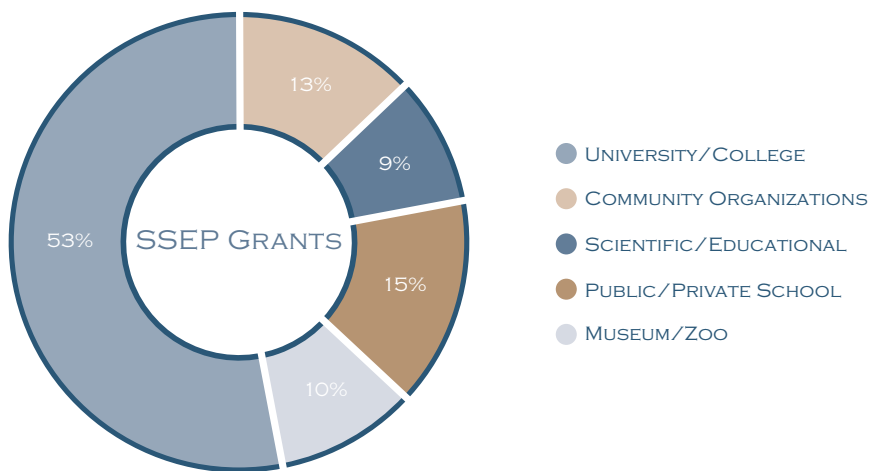
The goals of SSEP are to nurture students' enthusiasm for science, improve their competence in science, and encourage them to pursue careers in research or other science-related areas. SSEP provides students with science-rich activities outside the traditional classroom environment, although we encourage a connection to classroom learning. We further require the programs to align with the North Carolina

Standard Course of Study. BWF has evaluated SSEP from the beginning. In one finding, more than 50 percent of student participants have gone on to pursue science-related careers. Directly or indirectly, SSEP activities have reached more than 95 percent of North Carolina's counties.

In the area of public policy, BWF funds the North Carolina Institute for Education Policymakers, established in 1996 in partnership with the Kenan Trust. Among its activities, the institute took a delegation of 29 key legislators, other policymakers, education association leaders, academicians, K-12 educators, and nonprofit representatives to Singapore in January 2008. The purpose was to investigate their school system and bring back best practices to North Carolina. Participants learned about how Singapore's government, businesses, and educators effectively coordinate efforts to project and meet workforce needs, as well as about how Singapore systematically targets and trains teachers and principals for its schools. One key contributor to Singapore's success is the National Institute for Education, a research center that brings together multi-disciplinary teams of scientists and educators to develop new approaches for teaching science and mathematics and also uses the school system as a laboratory to continuously improve the quality of teaching. On their return home, members of the delegation published a report on their findings. The report, which includes recommendations for North Carolina, was distributed to state legislators.

As another part of BWF's activities to help the state's K-12 schools, we are working with the University of North Carolina system (comprising 16 university campuses) and the North Carolina School of Science and Mathematics to support a pilot program to produce more undergraduates with degrees in the sciences and mathematics who have interests in teaching. Known as FastTrack, this program involves the efforts of four universities—the University of North Carolina-Chapel Hill, the University of North Carolina-Asheville, North Carolina Central University, and North Carolina State University. Our goals are to produce 120 new teachers with strong content knowledge in science and mathematics and to enrich the environments in which they will work.

In addition, BWF has worked with the North Carolina Network of Grantmakers to better coordinate and leverage education funding in the state. A number of foundation representatives have collaboratively developed a report that addresses a range of critical issues. In its entirety, the report is intended to bring a sense of urgency to policymakers, funders, and the general public on the importance of having high-quality leadership for North Carolina schools, strengthening standards and accountability for school performance, increasing support for children and families, aligning governance and funding for 21st century results, and engaging communities in supporting education. The report is scheduled for publication in February 2009.



GRANT OPPORTUNITY:

STUDENT SCIENCE ENRICHMENT PROGRAM

Awards are limited to nonprofit organizations in BWF's home state of North Carolina and provide up to \$60,000 per year for three years. The program's goals include improving students' competence in science and mathematics, nurturing their enthusiasm for science mathematics, and interesting them in pursuing careers in research or other science-related areas. The awards are intended to support projects that provide creative science enrichment activities for elementary and secondary students who have shown exceptional skills and interest in science, as well as those who may not have had an opportunity to demonstrate conventional "giftedness" in science but are perceived to have high potential. The projects must enable students to participate in hands-on scientific activities and pursue inquiry-based avenues of exploration—an educational approach that has proven to be an effective way to increase students' understanding and appreciation of the scientific process. Project activities must take place outside of the usual school environment, such as after school, on weekends, or during vacation periods. Projects may be conducted all year, during the school year, or during the summer. Eligible organizations include colleges and universities, community groups, museums and zoos, public and private schools, scientific groups, and others that can provide experiential activities for middle school and high school students. We encourage partnerships—for example, between scientific groups and school systems or between universities and community groups. Industries may participate in collaboration with nonprofit organizations that assume the lead role.

Please see www.bwfund.org for program information.



Student displaying an insect.

PROFILE: BUG CAMP EXPLORING THE WORLD OF INSECTS

Thirteen-year-old Thomas Ohmen can tell you all about the horned passalus, a kind of beetle, or the club-tailed dragonhunter dragonfly. And it's safe to say he knows more about the tobacco hornworm than most other eighth graders at his Valley Springs middle school in the mountain city of Asheville, North Carolina.

Thanks to a program at the University of North Carolina-Asheville, this growing bug enthusiast has been able to learn more about them as a participant in Bug Camp. With financial support from the Burroughs Wellcome Fund, the overnight summer camp is a weeklong opportunity for middle school students to learn about biological science by exploring the world of insects in a hands-on manner. The program, which was conceived as a day camp in 2001 and has grown into a full week of residential learning for students on a university campus, was perfect for Mr. Ohmen.

"I like touching bugs, and that's mostly what we did, study them," said Mr. Ohmen, who attended the camp during summer 2008 for a second year.

Camp organizers say the objective is to expose middle school students to science and help them become critical observers of the natural world—while having fun as well. The camp also seeks to encourage girls and minority students to explore the world of science.

Camp founder and codirector Timothy Forrest, Ph.D., an assistant professor of biology at the university, said some of the students are pretty apprehensive about the camp when they first arrive. Some have never even held an insect before.

"Many of them have no idea what Bug Camp is all about," he said.

To introduce the students to what they'll be studying, Bug Camp organizers set up stations to display different insects to the new arrivals. One of the most notable creatures is the hissing cockroach, which gets its name for the noise it makes when it expels air from its trachea system. Dr. Forrest said there are always students who would never think of touching the inch-long roaches, but once he finds one or

two brave souls to take the plunge, a little friendly peer pressure is all it takes to get the rest of the students on board. By the end of the week, Dr. Forrest said, the students are just "asking to go to the roach cage."

That sort of experimentation and discovery, Dr. Forrest said, is an integral part of the camp, which encourages students who historically have been under-represented in the mathematics and science disciplines to try their hands at science.

"When you start looking at who the scientists are, it turns out there aren't many women in the sciences and even fewer minorities," Dr. Forrest said. "If we can start at the middle school age and get them excited about science and build an enthusiasm that will carry them through high school and college, hopefully they will become scientists."

To recruit campers, Dr. Forrest and camp codirector Herb Pomfrey, a lecturer in the university biology department, target area science teachers with e-mails. For the most recent camp, 40 middle school students from 16 schools in seven North Carolina counties were accepted, and more than 50 percent of the participants were minorities.

Mr. Pomfrey said BWF's financial support has enabled camp organizers to reach out to students who might not be able to attend the camp if they had to pay tuition (the weeklong camp, including room and board, is free.)

"Our population of students who attend the camp has changed dramatically," Mr. Pomfrey said. "When it was a tuition-based camp, when we started, we tried to keep costs low, but there were certain students who were eliminated when it came to costs. With BWF's grant, it just opened it up to a whole new population. We could target all income groups."

BWF provided Bug Camp with a three-year, \$90,000 grant in 2005, and the grant was renewed in 2008 for three more years. The organizers say the support not only has enabled expanded student outreach, but also has made it possible to provide campers with cutting-edge equipment. This year, the campers used portable data acquisition computers, which enable them to gather and analyze data in real time.



“That’s been fantastic, it’s just opened their eyes to a whole different side of science,” Mr. Pomfrey said.

Students currently use the equipment in the lab, Dr. Forrest said, but the computers may be used in the future to assist students on the insect-collecting field trips that are a part of the camp. Dr. Forrest said the excursions, in which students trap and identify insects, are crucial for getting students interested in science through hands-on activities.

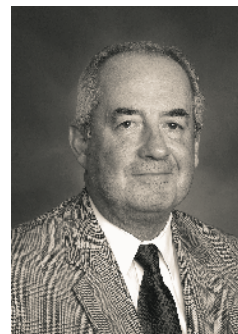
“Any time you can get out into the field, you just never know what you’re going to find,” he said. “We’ve found some insects that are very uncommon. These are just special experiences that these kids get.”

Using exit surveys, camp organizers are learning that the hands-on activities are having an impact on students’ enthusiasm for science. In the most recent camp, 91 percent of the students said they were more interested in science because they attended the camp. This is a positive sign for educators like Dr. Forrest and Mr. Pomfrey who see the importance in improving the performance of U.S. students in science and mathematics in the face of a global economy that relies on them.

“When you look at where the country is at the moment and where it seems to be headed in terms of science and math education, I think we’re headed in the wrong direction compared to other countries,” Dr. Forrest said. “We should be increasing the number of students who are going into these disciplines. We don’t seem to be keeping pace.”

For his part, Thomas Ohmen, the eighth grader at Valley Springs, says he wants to pursue science as a career. His goal? He wants to be an entomologist—just like Dr. Forrest.

—By *Jim Walsh*



*Sam Houston, Ed.D.
President and
Chief Executive Officer
SMT Center*

CATALYTIC PROGRAM IN SCIENCE EDUCATION: NORTH CAROLINA SCIENCE, MATHEMATICS, AND TECHNOLOGY EDUCATION CENTER

The North Carolina Science, Mathematics, and Technology Education Center (SMT Center), through a variety of activities in fiscal year 2008, significantly increased the capacity of educators to improve science, mathematics, and technology education in North Carolina. Using proven methods and working in conjunction with other organizations, the SMT Center helped educators deepen their understanding of content, pedagogy, and the structures necessary to support student learning.

The SMT Center (which the Burroughs Wellcome Fund founded in 2002 and continues to support) and the Public School Forum of North Carolina were selected by the N.C. Senate to administer the Collaborative Project—an effort to raise the level of student performance, especially in mathematics and science, in five low-performing, rural, and poor counties in various regions of the state. Drawing on the expertise of nationally recognized mathematics educators, the SMT Center offered intensive, five-day institutes for kindergarten through eighth-grade teachers to help them better use algebraic reasoning in their classrooms. The teachers come away with an increased understanding and a stronger disposition to teach the concepts.

The SMT Center continued its partnership with the National Science Resources Center to provide LASER Institute training for school districts in North Carolina. In these LASER (Leadership and Assistance for Science Education Reform) sessions, participants work alongside experts to develop plans that address a range of key issues, including curriculum, professional development, student assessment, materials support, community involvement, and administrative support. In this way, teams from the districts developed strategic plans for their K-8 science programs. Fourteen districts attended the institute, which was held June 15-20,

2008, in Asheville, N.C. These districts join the 17 districts that attended the 2007 institute. From this effort, the districts are building a network of schools that are increasingly giving students opportunities to actively engage in science investigations.

To further increase the opportunities for students to engage in science investigations, the SMT Center, with support from the North Carolina General Assembly, is creating the North Carolina Science Competitions Program

Center. Through the efforts of the SMT Center, statewide science competitions have seen a significant increase in coverage of their competitions in local and statewide newspapers, as well as on television and radio. Additionally, the SMT Center has worked closely with the

“FROM THIS EFFORT, THE DISTRICTS ARE BUILDING A NETWORK OF SCHOOLS THAT ARE INCREASINGLY GIVING STUDENTS OPPORTUNITIES TO ACTIVELY ENGAGE IN SCIENCE INVESTIGATIONS.”

North Carolina Science Fair and the North Carolina Science Olympiad to support teachers as they align student research opportunities with the standard course of study, in an effort to better encourage students to compete in science competitions. Work is under way on designing a web portal that will serve as a one-stop clearinghouse for all administration, registrations, and information on science competitions.

For more information on the SMT Center, visit www.ncsmt.org.

SCIENCE AND PHILANTHROPY

The Burroughs Wellcome Fund makes noncompetitive grants for activities and career development opportunities for scientists that fall outside of our competitive award programs but are closely related to our targeted areas.

We place special priority on working with nonprofit organizations, including government agencies, to leverage financial support for our targeted areas of research, and on encouraging other foundations to support biomedical research. Proposals should be submitted to BWF in the form of a letter, which should be no more than five pages.

Applicants should describe the focus of the activity, the expected outcomes, and the qualifications of the organization or individuals involved; provide certification of the sponsor's Internal Revenue Service tax-exempt status; and give the total budget for the activity, including any financial support obtained or promised. Proposals are given careful preliminary review, and those deemed appropriate are presented for consideration by BWF's Board of Directors.

Applications are accepted throughout the year.

The Burroughs Wellcome Fund's investments totaled \$693.2 million at August 31, 2008, the end of our fiscal year. BWF's primary financial goal is to pursue an investment strategy that will support annual spending needs and maintain a constant real level of assets over the long term. To achieve this goal, a high percentage of our investments are placed in strategies that derive the bulk of their returns from exposure to U.S. and international capital markets. Hence, fluctuations in BWF's investment results will be due largely to variability in capital market returns.

BWF's investment policies are developed with the recommendations and review of the Investment Committee, which is appointed by and reports to BWF's Board of Directors. The committee, which meets three times a year, has seven voting members, including four representatives from outside BWF and three representatives of our board. The board's chair, BWF's president, and BWF's vice president for finance also serve on the committee as nonvoting members.

As part of BWF's investment strategy, we have established "allocation targets"—that is, percentages of our total assets to be invested in particular asset classes. Investment managers hired by BWF pursue more focused mandates within each sector. As of the end of the fiscal year, BWF's asset mix and market values were:

- U.S. large capitalization equity assets had a market value of \$141.9 million. The sector's target allocation was 25 percent, and actual holdings stood at 20.5 percent.
- U.S. small capitalization equity assets had a market value of \$100.6 million. The sector's target allocation was 18 percent, and actual holdings stood at 14.5 percent.
- International equity assets had a market value of \$173.4 million. The sector's target allocation was 32 percent, and actual holdings stood at 25 percent.
- Fixed income assets had a market value of \$119.1 million. The sector's target allocation was 22 percent, and actual holdings stood at 17.2 percent.
- Cash equivalent assets had a market value of \$15 million. The sector's target allocation was 3 percent, and actual holdings stood at 2.2 percent.

- Alternative assets had a market value of \$143.2 million. The sector did not have a target allocation, and actual holdings stood at 20.6 percent. The maximum permitted allocation to alternative assets stood at 20 percent.

The total market value of BWF's investments decreased by \$98.0 million, or 12.4 percent, from the end of the previous fiscal year. This decrease in assets was due primarily to declines in global equity markets in 2008. Bonds had low positive returns for the 12 month period. BWF's total investment return before investment management fees for the fiscal year was -7.7 percent. Returns in all three equity sectors were negative for the fiscal year, while bonds posted a positive result. The U.S. large capitalization equity sector returned -12.5 percent, the U.S. small capitalization equity sector had a -10.9 percent result, the international equity sector posted a return of -12.3 percent, and fixed income produced a +4.9 percent result.

As of August 31, 2008, BWF employed 11 marketable securities investment managers. In the U.S. large capitalization equity sector, the managers were Independence Investment Associates, LSV Asset Management, and Enhanced Investment Technologies. A.G. Asset Management, Kenwood Capital Management, and FAF Advisors managed U.S. small capitalization equities. Pacific Investment Management Company and Smith Breeden Associates were the fixed income managers. Capital Guardian Trust Company, Northern Cross, and Hansberger Global Investors managed international equities.

BWF also held investments in seven venture capital funds: Intersouth Partners IV; V and VI; Spray Venture Funds I and II; Mission Ventures II, and A. M. Pappas Life Science Ventures II. Barlow Partners and Winston Partners managed funds of equity-oriented hedge funds. Blackrock Alternative Advisors and Franklin Street Partners managed funds of absolute return strategies. Hamilton Lane Advisors managed a fund of private equity strategies. Finally, Mellon Capital Management managed a global macro strategy.

REPORT OF INDEPENDENT AUDITORS

To the Board of Directors of The Burroughs Wellcome Fund:

In our opinion, the accompanying statements of financial position and the related statements of activities and of cash flows present fairly, in all material respects, the financial position of The Burroughs Wellcome Fund (the "Fund") at August 31, 2008 and 2007, and the changes in its net assets and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Fund's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

Our 2008 audit was conducted for the purpose of forming an opinion on the basic financial statements taken as a whole. The information in Schedules I and II is presented for purposes of additional analysis and is not a required part of the basic financial statements. Such information has been subjected to the auditing procedures applied in the audit of the basic financial statements and, in our opinion, is fairly stated in all material respects in relation to the basic financial statements taken as a whole.

PricewaterhouseCoopers LLP

Raleigh, North Carolina
December 15, 2008

STATEMENTS OF FINANCIAL POSITION
AUGUST 31, 2008 AND 2007

(All dollar amounts presented in thousands)

	2008	2007
ASSETS		
Cash and cash equivalents	\$ 23,508	\$ 36,738
Marketable securities	695,415	798,970
Accrued interest and dividends receivable	1,867	1,709
Federal excise tax receivable	–	243
Other assets	44	41
Property and equipment, net	10,761	11,209
Total assets	\$ 731,595	\$ 848,910
LIABILITIES AND NET ASSETS		
Transactions payable, net	\$ 27,200	\$ 45,390
Accounts payable and other liabilities	1,389	1,406
Federal excise tax payable	180	–
Deferred federal excise taxes	11	1,855
Unpaid awards	104,133	90,697
Total liabilities	132,913	139,348
Unrestricted net assets	598,682	709,562
Total liabilities and net assets	\$ 731,595	\$ 848,910

The accompanying notes are in integral part of these financial statements.

STATEMENTS OF ACTIVITIES

YEARS ENDED AUGUST 31, 2008 AND 2007

(All dollar amounts presented in thousands)

	2008	2007
REVENUES		
Interest and dividends, less investment expenses of \$4,676 and \$4,765 in 2008 and 2007, respectively	\$ 12,412	\$ 12,215
Net realized gain on sales of marketable securities	16,673	71,056
Total revenues	29,085	83,271
EXPENSES		
Program services	42,803	47,620
Management and general	6,796	8,244
Total expenses before net unrealized appreciation and deferred federal excise tax	49,599	55,864
Net unrealized appreciation (depreciation) of marketable securities, net of provision for (benefit from) deferred federal excise taxes of \$(1,844) and \$381 in 2008 and 2007, respectively	(90,366)	19,451
Change in net assets	(110,880)	46,858
Net assets at beginning of year	709,562	662,704
Net assets at end of year	\$ 598,682	\$ 709,562

The accompanying notes are in integral part of these financial statements.

STATEMENTS OF CASH FLOWS

YEARS ENDED AUGUST 31, 2008 AND 2007

(All dollar amounts presented in thousands)

	2008	2007
CASH FLOWS FROM OPERATING ACTIVITIES		
Change in net assets	\$(110,880)	\$ 46,858
<i>Adjustments to reconcile change in net assets to net cash provided by operating activities:</i>		
Depreciation	512	613
Net realized gain on sales of marketable securities	(16,673)	(71,056)
Net unrealized depreciation (appreciation) of marketable securities	92,210	(19,832)
Provision for (benefit from) deferred federal excise taxes	(1,844)	381
Awards granted, net of cancellations and change in unamortized discount	42,692	47,585
Award payments made	(29,256)	(29,445)
<i>Changes in operating assets and liabilities:</i>		
Accrued interest and dividends receivable	(158)	161
Other assets	420	(245)
Transactions payable, net	(18,190)	6,377
Accounts payable and other liabilities	(17)	(465)
Net cash used in operating activities	(41,184)	(19,068)
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchases of marketable securities	(1,399,824)	(1,172,799)
Proceeds from sales of marketable securities	1,427,842	1,198,672
Purchase of property and equipment	(64)	(127)
Net cash provided by investing activities	27,954	25,746
Net (decrease) increase in cash and cash equivalents	(13,230)	6,678
Cash and cash equivalents at beginning of year	36,738	30,060
Cash and cash equivalents at end of year	23,508	36,738
<i>Supplemental disclosure of cash flow information:</i>		
Cash paid during the year for federal excise taxes	\$ 257	\$ 2,779

The accompanying notes are in integral part of these financial statements.

NOTES TO FINANCIAL STATEMENTS

AUGUST 31, 2008 AND 2007

*(All dollar amounts presented in thousands)**1. Organization and Summary of Significant Accounting Policies*

The Burroughs Wellcome Fund (the “Fund”) is a private foundation established to advance the medical sciences by supporting research and other scientific and educational activities.

Cash equivalents

Cash equivalents are short-term, highly liquid investments that are readily convertible to known amounts of cash and have maturity of three months or less at the time of purchase.

Forward currency contracts

The Fund enters into financial instruments with off-balance sheet risk in the normal course of its investment activity. The instruments are primarily forward contracts to reduce the Fund’s exposure to fluctuations in foreign currency exchange rates. These contracts are for delivery or sale of a specified amount of foreign currency at a fixed future date and a fixed exchange rate. Gains or losses on these contracts occur due to fluctuations in exchange rates between the commencement date and the settlement date. Gains and losses on settled contracts are included within “net realized gain (loss) on sales of marketable securities,” and the changes in market value of open contracts is included within “net unrealized appreciation (depreciation) of marketable securities” in the accompanying statements of activities. It is the Fund’s policy to utilize forward contracts to reduce foreign exchange rate risk when foreign-based investment purchases or sales are anticipated.

The contract amount of open forward currency contracts totaled \$85,117 and \$135,272 at August 31, 2008 and 2007, respectively. Realized losses on forward currency contracts totaled \$(1,928) and \$(260) in 2008 and 2007, respectively. The market value of open forward currency contracts at August 31, 2008 and 2007 was \$(135) and \$(67), respectively. The market value is recorded as an asset (liability) in the Fund’s financial statements. The average market value of open foreign currency contracts totaled \$(338) and \$(147) during the years ending August 31, 2008 and 2007, respectively.

Futures contracts

The Fund enters into futures contracts in the normal course of its investment activity to manage the exposure to interest rate risk associated with bonds and mortgage backed securities. The Fund is required to pledge collateral to enter into these contracts. The amounts pledged for futures contracts at August 31, 2008 and 2007 were \$3,768 and \$18,279, respectively. It is the Fund’s intention to terminate these contracts prior to final settlement. Gains and losses on the contracts are settled on a daily basis. Included in transactions payable at August 31, 2008 and 2007 is the net settlement relating to these contracts of \$642 and \$(308), respectively.

Options

The Fund utilizes options to manage the exposure to interest rate risk associated with mortgage backed securities. The market value of these options totaled \$(31) and \$241 at August 31, 2008 and 2007, respectively, which is recorded as an asset (liability) in the Fund’s financial statements. The average fair value of open contracts totaled \$78 and \$220 for the years ending August 31, 2008 and 2007, respectively. Realized gains and losses on options totaled \$(292) and \$(111) for the years ending August 31, 2008 and 2007, respectively.

Marketable securities

Marketable securities are carried at estimated market values based on quoted prices. Gains and losses from sales of securities are determined on an average cost basis and are recognized when realized. Changes in the estimated market value of securities are reflected as unrealized appreciation (depreciation) in the accompanying statements of activities. The Fund has engaged investment advisors to manage the portfolio of marketable securities. The Fund’s management critically evaluates investment advisor performance and compliance with established diversification and investment policies.

Property and equipment

Property and equipment is primarily comprised of a building, furniture, and computer equipment, which are stated at cost less accumulated depreciation and are being depreciated over their estimated useful lives using the straight-line method. Ordinary maintenance and repair costs are expensed as incurred.

Building	40 years
Furniture and fixtures	7 years
Computer equipment	3 years

Transactions receivable and transactions payable, net

These amounts represent the net receivable or payable resulting from investment transactions with trade dates prior to August 31 and settlement dates subsequent to August 31.

Awards granted and unpaid awards

Grants are recorded at their fair value in the initial award year. Grants payable over several years are immediately expensed, and carried on the statements of financial position at the present value of their estimated future cash flows, using a risk free discount rate determined at the time the award is granted.

Functional allocation of expenses

Costs related to the Fund's operations and activities have been summarized on a functional basis in the statements of activities.

Estimated fair value of financial instruments

Financial instruments include cash and cash equivalents, marketable securities, accrued interest and dividends receivable, and accounts payable. All financial instruments are reported at their estimated fair value. The carrying values of accrued interest and dividends receivable, and accounts payable approximate fair values based upon the timing of future expected cash flows. The estimated fair value of marketable securities is determined based upon the latest quoted sales price for such securities as of the balance sheet date. The Fund's remaining assets and liabilities are not considered financial instruments.

Use of estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Market risk

Market risk represents the risk of changes in value of a financial instrument, derivative or non-derivative, caused by fluctuations in interest rates, foreign exchange rates and equity prices. The Fund manages these risks by using derivative financial instruments in accordance with established policies and procedures.

2. Property and Equipment

The Fund's property and equipment as of August 31 consisted of the following:

	2008	2007
Building	\$ 13,451	\$ 13,451
Furniture and fixtures	2,016	1,964
Computer equipment	1,099	1,087
	16,566	16,502
Less: accumulated depreciation	(5,805)	(5,293)
	\$ 10,761	\$ 11,209

Furniture and fixtures includes non-depreciated art work, as defined by the provisions of Statement of Financial Accounting Standards No. 93 "Recognition of Depreciation by Not-for-Profit Organizations", of \$78 and \$77 at August 31, 2008 and 2007, respectively.

3. Federal Excise Taxes

The Fund is exempt from federal income taxes under Section 501(c)(3) of the Internal Revenue Code. However, since the Fund meets the definition of a private foundation under the Internal Revenue Code, it is subject to federal excise tax on its annual net investment income.

Deferred federal excise taxes represent the estimated tax liability on unrealized appreciation of marketable securities. At August 31, 2008 and 2007, the Fund was in a net unrealized appreciation position; therefore, a deferred federal excise tax liability of \$11 and \$1,855, respectively, was recorded.

4. Qualified Distributions

The Fund is required to distribute 5% of the excess of the aggregate fair market value of the assets over the acquisition indebtedness with respect to such assets. Failure to distribute according to Section 4942(e)(1) results in a tax equal to 15% of the undistributed income of the Fund.

5. Unpaid Awards

Unpaid awards as of August 31 are scheduled for payment as follows:

	2008	2007
Payable in less than one year	\$ 30,879	\$ 28,264
Payable in one to five years	76,938	66,846
	107,817	95,110
Unamortized discount	(3,684)	(4,413)
Total	\$ 104,133	\$ 90,697

The expected future liability to the Fund has been calculated based on discount rates ranging from 1.94% to 3.34%, determined at the separate grant dates.

6. Marketable Securities

The cost and estimated market values of marketable securities at August 31 are as follows:

	2008		2007	
	Cost	Estimated market value	Cost	Estimated market value
U.S. and Foreign				
governmental obligations	\$ 91,658	\$ 92,356	\$ 104,426	\$ 104,412
Corporate bonds	54,096	49,584	43,422	42,039
Common and preferred stocks	244,272	242,136	267,976	291,531
Foreign stocks and foreign				
equity funds	170,441	172,730	168,461	233,522
Option and forward foreign				
currency investments	–	(31)	317	241
Venture capital investments	33,845	23,139	27,507	17,024
Mutual funds	100,396	115,501	94,068	110,201
	\$ 694,708	\$ 695,415	\$ 706,177	\$ 798,970

7. Employee Benefit and Retirement Plans

The Fund provides medical insurance to all employees working at least 30 hours per week. The Fund also pays 80% of the cost to cover each employee's spouse and dependent children, if applicable. The expense for this employee benefit was \$222 and \$188 during fiscal 2008 and 2007, respectively.

The Fund has a defined-contribution retirement plan. Under the terms of the plan, the Fund matches 50% of all employees' contributions up to 6% of the employee's annual compensation. Employees are 100% vested in employee and employer contributions immediately. The Fund also has a defined-contribution

retirement plan funded solely through employer contributions. Under the terms of the plan, the Fund contributes 10% of the employee's annual compensation. This plan covers all employees and vesting in contributions is immediate. The expense for these retirement plans was \$53 and \$216 in fiscal 2008, and \$47 and \$199 in fiscal 2007, respectively.

8. Classification of Expenses

During the years ended August 31, expenses were classified as follows:

	2008		2007	
	Program Services	Management and General	Program Services	Management and General
Awards granted, net of cancellations and refunds of \$3,421 and \$5,904 in 2008 and 2007, respectively	\$ 42,200	–	\$ 47,025	–
Federal excise tax	–	681	–	2,536
Salaries and other employee expenses	279	2,841	301	2,556
Depreciation expense	–	512	–	613
Travel and entertainment	163	850	101	903
Maintenance and supplies	10	804	6	715
Honoraria	9	419	–	416
Professional fees	118	348	166	182
Printing and design costs	20	140	19	148
Miscellaneous	4	201	2	175
Total Expenses	\$ 42,803	\$ 6,796	\$ 47,620	\$ 8,244

9. Related Parties

The North Carolina Science, Mathematics and Technology Education Center, Inc. (the "Center") was formed on April 24, 2002. This not-for-profit corporation solicits grants for the purpose of providing funding to improve the performance of students in science, mathematics, and technology. The Fund paid \$582 and \$529 of expenses on behalf of the Center during 2008 and 2007, respectively. Expenses included salaries, travel, entertainment, maintenance, supplies, professional fees, printing cost, and other miscellaneous items. These expenses are included within "program services" for the respective years.

The Health Research Alliance ("HRA") was formed in November 2005. HRA is a public charity focusing on improving and building strategic partnerships

to advance health research. The Fund paid \$21 and \$65 of expenses on behalf of HRA during 2008 and 2007, respectively. Expenses included salaries, travel, entertainment, maintenance, supplies, professional fees, printing cost, and other miscellaneous items. These expenses are included within “program services” for the respective years.

The financial statements of the Fund, the Center, and HRA are not presented on a combined basis, as the Fund is not the legal owner of the Center or HRA, does not have controlling interest of the Center’s or HRA’s financial transactions, and does not have considerable representation on the board of the Center or HRA.

10. Subsequent Events

With the recent turmoil in the stock market, the Fund’s marketable securities have declined in value by approximately \$188,000 during the period from September 1, 2008 to December 15, 2008.

SCHEDULE I: STATEMENT OF AWARD TRANSACTIONS
YEAR ENDED AUGUST 31, 2008

(All dollar amounts presented in thousands)

Unpaid awards, beginning of year	\$ 90,697
Add – Awards granted (Schedule II)	44,891
Less – Award payments made	(29,256)
Award cancellations (excluding refunds)	(2,928)
Net increase in unamortized discount	729
Unpaid awards, end of year	\$ 104,133

SCHEDULE II: STATEMENT OF AWARD TRANSACTIONS
YEAR ENDED AUGUST 31, 2008

Schedule II information is included in the “Grants Index” beginning on the opposite page. The dollar amounts listed in the schedule reflect the actual dollar amounts (not rounded to thousands) approved and paid to awardees.

GRANTS INDEX 

PROGRAM SUMMARY
YEAR ENDED AUGUST 31, 2008

	<i>Approved</i>	<i>Paid</i>	<i>Transferred/ Cancelled*</i>
BIOMEDICAL SCIENCES			
Career Awards in the			
Biomedical Sciences	\$ 537,021.32	\$ 5,671,717.69	\$ 1,384,475.00
Career Awards in the			
Medical Sciences	11,200,000.00	1,865,000.00	0.00
Hitchings–Elion Fellowship	0.00	0.00	168,000.00
Other Grants (Ad Hoc)	188,500.00	804,150.00	0.00
Total	\$ 11,925,521.32	\$ 8,340,867.69	\$ 1,552,475.00

INFECTIOUS DISEASE

Investigators in Pathogenesis			
of Infectious Disease	\$ 7,061,447.06	\$ 5,131,447.06	\$ 0.00
Other Grants (Ad Hoc)	1,110,678.00	1,060,678.00	0.00
Total	\$ 8,172,125.06	\$ 6,192,125.06	\$ 0.00

INTERFACES IN SCIENCE

Career Awards at the			
Scientific Interface	\$ 7,985,788.47	\$ 4,221,126.96	\$ 643,600.00
Other Grants (Ad Hoc)	446,000.00	252,000.00	0.00
Total	\$ 8,431,788.47	\$ 4,473,126.96	\$ 643,600.00

SCIENCE AND PHILANTHROPY

Science and Philanthropy	\$ 195,500.00	\$ 205,500.00	\$ 0.00
Total	\$ 195,500.00	\$ 205,500.00	\$ 0.00

	<i>Approved</i>	<i>Paid</i>	<i>Transferred/ Cancelled*</i>
SCIENCE EDUCATION			
Student Science			
Enrichment Program	\$ 3,259,772.00	\$ 2,257,810.12	\$ 56,869.00
Other Grants (Ad Hoc)	1,136,935.00	940,128.00	0.00
Total	\$ 4,396,707.00	\$ 3,197,938.12	\$ 56,869.00
TRANSLATIONAL RESEARCH			
Clinical Scientist Award in			
Translational Research	\$ 10,425,000.00	\$ 6,075,000.00	\$ 675,000.00
Other Grants (Ad Hoc)	1,344,700.00	771,366.67	0.00
Total	\$ 11,769,700.00	\$ 6,846,366.67	\$ 675,000.00
GRAND TOTAL†	\$ 44,891,341.85	\$ 29,255,924.50	\$ 2,927,944.00

*The “Transferred/Cancelled” totals reflect grants made to award recipients who changed institutions, modified the terms of their grant at their current institution, or both changed institutions and modified their grant. In these cases, BWF’s policy has been to cancel the remaining portion of the original grant and, as necessary, approve a new grant, which is why in the following index an approved amount has been noted, but the recipient is not a new awardee. When the award recipient has changed institutions, the new grant is made to the new institution; when the award recipient has not moved but has modified the terms, the new grant is made to the current institution.

†To more accurately reflect the total amount that BWF approved in actual “new” dollars during this fiscal year, the “Transferred/Cancelled” total must be deducted from the “Approved” total.

Key to Grants Index

BWF makes all grants to nonprofit organizations. For most of the programs the name of the individual on whose behalf the grant is made is listed first, the title of the award recipient’s project is listed second, and the name of the organization that received the money is listed third. In the competitive grant sections, new awardees for FY 2008 are noted by an asterisk (*).

For programs that may have coaward recipients, the award recipients and their organizations are listed first, followed by the project title. For grants made directly to organizations and not on behalf of an individual, the name of the organization is listed first, followed by the title of the project or a brief description of the activity being supported.

In addition to making competitive awards, BWF makes noncompetitive grants—Other Grants (Ad Hoc)—for activities that are closely related to our major focus areas. These grants are intended to enhance the general environment for research in the targeted areas.

BIOMEDICAL SCIENCES

CAREER AWARDS IN THE BIOMEDICAL SCIENCES

Derek W. Abbott, M.D., Ph.D.

Regulation of innate immunity via non-traditional ubiquitin linkages
Case Western Reserve University
School of Medicine

Suzanne J. Admiraal, Ph.D.

University of Michigan Medical School

Geoffrey K. Aguirre, M.D., Ph.D.

fMRI studies of the process architecture of face perception
University of Pennsylvania
School of Medicine

Karl Mark Ansel, Ph.D.

Endogenous RNA interference and gene silencing in T cell differentiation
University of California-San Francisco

Aaron P. Batista, Ph.D.

Neural gating within the cerebral cortex during sensory-motor behavior
University of Pittsburgh

Diana M. Bautista, Ph.D.

Molecular and cellular mechanisms of mechanotransduction in mammalian sensory neurons
University of California-San Francisco

Thomas G. Bernhardt, Ph.D.

Coordinating cell division and chromosome segregation in *Escherichia coli*
Harvard Medical School

Bradley E. Bernstein, M.D., Ph.D.

Proteomic studies of post-translational histone modifications
Harvard Medical School

Ben E. Black, Ph.D.

Epigenetic mechanisms for centromere specification
University of Pennsylvania
School of Medicine

Michael D. Blower, Ph.D.

Analysis of the role of RNA in spindle assembly
Harvard Medical School

David L. Brody, M.D., Ph.D.

Amyloid-beta and apolipoprotein E in traumatic brain injury
Washington University
School of Medicine

Mark M. Churchland, Ph.D.

Experimental study of settling neural processes in the primate brain
Stanford University
Approved: \$58,000

William (Bil) M. Clemons, Ph.D.

Structural studies of complexes involved in protein translocation and synthesis
California Institute of Technology

Leah E. Cowen, Ph.D.

Hsp90 and the evolution of pathogens and their hosts
University of Toronto Faculty of Medicine

Jeremy S. Dasen, Ph.D.

Role of Hox proteins in sensory-motor neuronal connectivity and identity
New York University School of Medicine

Daniela M. Dinulescu, Ph.D.

Role of endometriosis in fertility and ovarian cancer pathogenesis
Harvard Medical School

Justin L. Gardner, Ph.D.

Flexible sensory representations in human visual cortex
New York University Faculty of Arts and Science

Levi A. Garraway, M.D., Ph.D.

Linking genetic alterations to tumor dependencies in human melanoma
Dana-Farber Cancer Institute

Ruben L. Gonzalez Jr., Ph.D.

Single-molecule fluorescence studies of eukaryotic translation initiation and regulation
Columbia University

Or P. Gozani, M.D., Ph.D.

Regulation of chromatin remodeling events by nuclear phosphoinositides
Stanford University

Ira M. Hall, Ph.D.

Investigation of DNA copy-number fluctuation and epigenetic inheritance using genomic microarrays
University of Virginia School of Medicine
Approved: \$58,000

Victoria G. Herman, Ph.D.

Defining the molecular code for synaptic target selection
University of Oregon

Chyi-Song Hsieh, M.D., Ph.D.

Determining the antigen specificity of CD25+ CD4+ regulatory T cells
Washington University School of Medicine

James D. Jontes, Ph.D.

Role of protocadherins in neural development studied in living zebrafish embryos
Ohio State University

Susan M. Kaeck, Ph.D.

Investigation of the mechanisms that regulate memory CD8 T cell development
Yale University School of Medicine

Alla Y. Karpova, Ph.D.

Using molecular inactivators of synaptic transmission to study cortical function and its modulation by subcortical systems in health and disease
Approved: \$16,828

Leslie S. Kean, M.D., Ph.D.

Innate immunity and transplantation tolerance: Defining the role of natural killer (NK) cells in allograft rejection
Emory University School of Medicine

Dennis H. Kim, M.D., Ph.D.

Genetic analysis of innate immunity in *Caenorhabditis elegans*
Massachusetts Institute of Technology

Steven T. Kosak, Ph.D.

Genomic organization of hematopoietic differentiation
University of Washington
Approved: \$58,000

Cheng-Yu Lee, Ph.D.

Genetic regulation of neural stem cell self-renewal
University of Michigan-Ann Arbor

Anthony Leonardo, Ph.D.

Neuronal population dynamics underlying the retinal code for motion
Harvard University
Approved: \$6,329

Yaping Joyce Liao, M.D., Ph.D.

Neurophysiological dysfunction in calcium channelopathies
Stanford University School of Medicine
Approved: \$58,000

Ania K. Majewska, Ph.D.

Imaging rapid plasticity in the visual cortex
University of Rochester

Marc D. Meneghini, Ph.D.

Regulating chromatin domains in yeast and during animal development
University of Toronto Faculty of Medicine

Kakoli Mitra, Ph.D.

Probing the dynamics of protein integration into and translocation across membranes using fluorescence spectroscopy and cryo-electron microscopy
New York University School of Medicine
Approved: \$46,984

Vamsi K. Mootha, M.D.

Genomic approaches to mitochondrial biogenesis
Harvard Medical School

Suzanne M. Noble, M.D., Ph.D.

Identification of virulence genes in *Candida albicans*, a diploid, commensal human fungal pathogen
University of California-San Francisco School of Medicine

Stephanie A. Pangas, Ph.D.

Defining the role of TGF β superfamily in ovarian cancer through mouse models
Baylor College of Medicine

Catherine L. Peichel, Ph.D.

Genetic and molecular basis of reproductive isolation of threespine sticklebacks
Fred Hutchinson Cancer Research Center

Bijan Pesaran, Ph.D.

Cortical mechanisms for hand-eye coordination
New York University

Michael G. Poirier, Ph.D.

Study of DNA accessibility within nucleosome arrays
Ohio State University

Margot E. Quinlan, Ph.D.

Collaboration between two actin nucleators—Spir and Capu
University of California-Los Angeles
Approved: \$58,000

Oliver J. Rando, M.D., Ph.D.

Time scales of epigenetic inheritance: How and why
University of Massachusetts Medical School

David E. Reich, Ph.D.

Applying population genetics to find genes for common diseases
Harvard Medical School

Jeremy F. Reiter, M.D., Ph.D.

Tectonic: discovery of novel signal directing mammalian development
University of California-San Francisco

Noah A. Rosenberg, Ph.D.

Efficient genome-based inference of ancestry for use in genetic association studies
University of Michigan Medical School

Pardis C. Sabeti, M.D., D.Phil.

Evolutionary genomics and its applications to human disease
Harvard University
Approved: \$29,000

Alan Saghatelian, Ph.D.

Identifying functional connections between the proteome and metabolome by global metabolite profiling
Harvard University

Annette E. Salmeen, D.Phil.

Reactive oxygen species as temporal coordinators of cell signaling pathways
Stanford University School of Medicine
Approved: \$39,000

Sara L. Sawyer, Ph.D.

Using rapid evolution to identify intracellular proteins interacting with retrotransposons in yeast
University of Texas-Austin
Approved: \$34,799

Bradley L. Schlaggar, M.D., Ph.D.

Development of cognition: fMRI studies
Washington University
School of Medicine

Kristin E. Scott, Ph.D.

Taste representation in *Drosophila* brain
University of California-Berkeley

Shu-ou Shan, Ph.D.

Mechanism of signal recognition particle-mediated protein targeting
California Institute of Technology

Michael D. Shapiro, Ph.D.

Genetic and developmental basis of skeletal diversity in ninespine sticklebacks
University of Utah

Collin M. Stultz, M.D., Ph.D.

Conformational free energy landscape of collagen and its relationship to atherosclerotic plaque rupture
Massachusetts Institute of Technology

Sinisa Urban, Ph.D.

Exploring the role of rhomboid signalling in development and disease
Johns Hopkins University
School of Medicine

Kevin B. Urdahl, M.D., Ph.D.

Role of MHC class I molecules against tuberculosis
University of Washington
School of Medicine

Amy J. Wagers, Ph.D.

Dynamic circulation of hematopoietic stem cells: implications for stem cell function
Joslin Diabetes Center

Loren D. Walensky, M.D., Ph.D.

Targeting protein interactions in vivo using chemically reinforced helical peptides
Harvard Medical School

David M. Weinstock, M.D.

Defining individual DNA double-strand break repair capacity using zinc-finger nucleases
Harvard Medical School
Approved: \$74,082

Karen M. Zito, Ph.D.

Regulation of synapse formation in the mammalian cortex
University of California-Davis

CAREER AWARDS IN THE MEDICAL SCIENCES

*New Recipient

Jonathan Paul Alexander, M.D., Ph.D.

Isolation of a putative alveolar stem cell population and analysis of its role in development, maintenance, and repair of the lung epithelium
University of California-San Francisco

Antonios O. Aliprantis, M.D., Ph.D.*

Novel regulators of the osteoclast differentiation program
Harvard School of Public Health
Approved: \$700,000

Robert Baloh, M.D., Ph.D.

Mechanism of peripheral neuropathy from Mitofusin 2 mutations
Washington University

James Elliott Bradner, M.D.

Design and characterization of highly potent inhibitors of HDAC6
Harvard University

Kathleen H. Burns, M.D., Ph.D.*

Investigating the role of retrotransposons in hematopoietic neoplasias
Johns Hopkins University
Approved: \$700,000

Daniel Cahill, M.D., Ph.D.*

Translational molecular genetic analyses of chemotherapeutic resistance in human brain tumors
Approved: \$700,000

Clark C. Chen, M.D., Ph.D.

Molecular basis and therapeutic implications of genome instability during brain tumor progression
Harvard Medical School

Alice Siau-In Chen-Plotkin, M.D.*

Genomic approaches to frontotemporal dementia
University of Pennsylvania School of Medicine
Approved: \$700,000

Sandeep Robert Datta, M.D., Ph.D.*

Characterization of neural circuits that drive innate behaviors
Columbia University
Approved: \$700,000

Arlene Dent, M.D., Ph.D.

Acquisition of immunity to blood stage *Falciparum* malaria in infants
Case Western Reserve University

Mahalia Sabrina Desruisseaux, M.D.

Neuroparasitology: neurological complications of cerebral malaria
Albert Einstein College of Medicine of Yeshiva University

Jay F. Dorsey, M.D., Ph.D.

Identification of mSin3b and Mad4 as novel p53 target genes directing p53-mediated transcriptional repression
University of Pennsylvania

Joseph Alexander Duncan, M.D., Ph.D. *

Dissecting cryopyrin-mediated inflammatory signaling and its role in the pathogenesis of infectious diseases
University of North Carolina-Chapel Hill
Approved: \$700,000

Benjamin Levine Ebert, M.D., Ph.D.

Genomic approaches to disorders of erythroid differentiation
Harvard Medical School

Brian Todd Edelson, M.D., Ph.D.

Macrophage and dendritic cell development
Washington University

Rene L. Galindo, M.D., Ph.D.

Genetic dissection of the Rhabdomyosarcoma initiator PAX-FKHR and PAX-related signaling in skeletal muscle development
University of Texas Southwestern Medical Center-Dallas

Wendy Sarah Garrett, M.D., Ph.D. *

Novel effectors and regulators of inflammation, chronic infection, and carcinogenesis in the colon
Harvard School of Public Health
Approved: \$700,000

Jeffrey Parker Henderson, M.D., Ph.D. *

Iron acquisition by bacterial siderophores as a pathogenic determinant in urinary tract infections
Washington University School of Medicine
Approved: \$700,000

Darnell Kaigler, D.D.S., Ph.D.

Cell therapy for the treatment of alveolar bone defects
University of Michigan-Ann Arbor

Lu Quang Le, M.D., Ph.D. *

Cell of origin and tumor micro-environment in NF1-associated neurofibroma development
University of Texas Southwestern Medical Center-Dallas
Approved: \$700,000

Michael Z. Lin, M.D., Ph.D.

Elucidating mechanisms of synaptic plasticity and learning by visualizing and controlling local protein turnover
University of California-San Diego

Roger Lo, M.D., Ph.D.

Melanoma in the skin: initiation, progression, and crosstalk with dermal fibroblasts
University of California-Los Angeles

Ravindra Majeti, M.D., Ph.D. *

Identification and targeting of human acute myeloid leukemia stem cell-specific cell surface molecules
Stanford University
Approved: \$700,000

Emanuel Maverakis, M.D.

gC399tr an inhibitor of autoimmunity
University of California-Davis

Heather Christy Mefford, M.D., Ph.D. *

Novel genomic rearrangements in developmental pediatric disorders
Approved: \$700,000

Ken Nakamura, M.D., Ph.D. *

Physiologic and pathologic interactions of alpha-synuclein with mitochondria in Parkinson's disease
University of California-San Francisco
Approved: \$700,000

Christopher Newton-Cheh, M.D.

Genomic dissection of QT interval duration and sudden death
Harvard Medical School

Dao Nguyen, M.D.

Stringent response in *Pseudomonas aeruginosa* biofilm formation and antibiotic tolerance
University of Washington

Robert M. Plenge, M.D., Ph.D. *

Genotype-phenotype studies of rheumatoid arthritis susceptibility genes
Harvard Medical School
Approved: \$700,000

Anil Potti, M.D.

Gene expression patterns coupled with signatures of oncogenic pathway deregulation provide a novel approach to targeted therapeutics in non-small cell lung carcinoma
Duke University Medical Center

David Tevis Pride, M.D., Ph.D. *

Bacteriophage communities in oral health and disease
Stanford University
Approved: \$700,000

Frank J. Probst, M.D., Ph.D.

Generation of mouse models for X-linked diseases
Baylor College of Medicine

Miguel Nicolas Rivera, M.D. *

Characterization of a novel X-linked tumor suppressor, WTX, in pediatric cancer
Harvard Medical School
Approved: \$700,000

Agata Smogorzewska, M.D., Ph.D. *

Role of the Fanconi Anemia and other DNA crosslink repair pathways in genome maintenance and cancer prevention
Harvard Medical School
Approved: \$700,000

Joseph C. Wu, M.D., Ph.D.

Molecular and cellular mechanisms of cardiac regeneration
Stanford University

Mark Nan Wu, M.D., Ph.D.

Identification of novel genes that regulate sleep in *Drosophila melanogaster*
University of Pennsylvania

OTHER GRANTS (AD HOC)**American Society for Cell Biology**

Support for Minorities Affairs Committee activities at the annual meeting

Approved: \$15,000

American Society for Cell Biology

Support for Women in Cell Biology activities at the annual meeting

Approved: \$5,000

American Society for Cell Biology

Support for the annual meeting

Approved: \$15,000

American Society for Microbiology

Support for training programs on presentation skills and career planning for graduate students in the microbiological sciences

Approved: \$16,000

Benemerita Universidad Autonoma de Puebla Instituto de Ciencias

Support for a project to characterize strains of *Streptococcus mutans*

Approved: \$5,000

Burnham Institute for Medical Research

Support for a laboratory management training course

Approved: \$6,000

California State University-East Bay

Support for the 2008 College of Science Scholarship Fund

Approved: \$1,500

Commission on Professionals in Science and Technology

Support for 2008

Approved: \$5,000

Federation of American Societies for Experimental Biology

Support for FASEB Diversity Award

Approved: \$5,000

Gairdner Foundation

Support for three major symposiums to bring internationally recognized biomedical scientists (Gairdner awardees) to Canada

Gairdner Foundation

Support for the Gairdner Foundation's 50th anniversary celebration

Approved: \$10,000

Gordon Research Conferences

Support for the 2008 Reproductive Tract Biology Gordon Research Conference

Approved: \$5,000

Hospital for Sick Children

Support for the first annual Canadian Human Genetics Conference

Approved: \$20,000

Marine Biological Laboratory

Support for the 2007, 2008, and 2009 sessions of the Frontiers in Reproductive course

Marine Biological Laboratory

Support for the 2008 Frontiers in Reproductive Symposium

Approved: \$6,000

National Postdoctoral Association

Support for the 2008 National Institute of Environmental Health Sciences/NTA Biomedical Career Fair

Approved: \$2,000

Rosalind Franklin Society

Support for women scientists in the life sciences

Approved: \$10,000

Society for Neuroscience

Support for postdoctoral travel to the annual meeting

Approved: \$15,000

Society for the Study of Reproduction

Support for 2008 activities of the Minority Affairs Committee

Approved: \$15,000

Thomas Jefferson University

Support for the Philadelphia Regional Postdoc Symposium

Approved: \$6,000

University of California-San Francisco

Support for the 2008 Reproductive Scientist Development Program scholar's annual research conference/retreat

Approved: \$6,000

University of California-San Francisco School of Medicine

Support for a Reproductive Scientist Development Program junior faculty scholar

University of Texas Southwestern Medical Center-Dallas

Support to initiate a pilot study on the role of poly (ADP-ribose) polymerases in the function of the androgen receptor

Approved: \$20,000

Washington University School of Medicine

Support for a BWF research consortium on preterm birth

INFECTIOUS DISEASE

INVESTIGATORS IN THE PATHOGENESIS OF INFECTIOUS DISEASE

*New Recipient

David Artis, Ph.D. *

Tracking helminth-specific immune responses in vivo
University of Pennsylvania
Approved: \$500,000

Jody L. Baron, M.D., Ph.D.

Understanding immunopathogenesis of Hepatitis B virus
University of California-San Francisco School of Medicine

Choukri Ben Mamoun, Ph.D.

Function and regulation of host and parasite nutrient transporters during malaria infection
University of Connecticut Health Center

Richard J. Bennett, Ph.D. *

Phenotypic variation and host adaptation by the human fungal pathogen *Candida albicans*
Brown University
Approved: \$500,000

Helen E. Blackwell, Ph.D.

Interception of bacterial quorum sensing with synthetic ligands
University of Wisconsin-Madison

David C. Bloom, Ph.D.

Identification of neuron-specific factors that regulate HSV-1 chromatin structure and transcription during latency
University of Florida College of Medicine

Matthew S. Bogyo, Ph.D.

Chemical mapping of proteolytic networks involved in *Toxoplasma gondii* pathogenesis
Stanford University School of Medicine

Miriam Braunstein, Ph.D. *

Identification of in vivo-secreted proteins of Mycobacterium tuberculosis with roles in host-pathogen interactions
University of North Carolina-Chapel Hill
Approved: \$500,000

John H. Brummell, Ph.D.

Recognition of bacteria in the cytosol of mammalian cells by protein conjugation systems
University of Toronto

James R. Carlyle, Ph.D. *

MHC-independent recognition of infected cells by natural killer cells of the innate immune system
University of Toronto
Approved: \$500,000

Benjamin K. Chen, M.D., Ph.D.

Dissemination of HIV through virological synapses
Mount Sinai School of Medicine

Blossom Damania, Ph.D.

Role of viral signaling proteins in the pathogenesis of Kaposi's sarcoma-associated herpes virus (KSHV)
University of North Carolina-Chapel Hill

Andrew Darwin, Ph.D.

Mechanisms of *Pseudomonas aeruginosa* tolerance to secretin-induced stress during host infection
New York University School of Medicine

Dana A. Davis, Ph.D.

Control of phenotypic switching and pathogenesis by the Mds3 protein
University of Minnesota-Twin Cities

Tatjana Dragic, Ph.D.

Entry and intracellular trafficking of Hepatitis C virus
Albert Einstein College of Medicine of Yeshiva University

Manoj T Duraisingh, Ph.D.

Epigenetic control of virulence gene expression in *Plasmodium falciparum*
Harvard School of Public Health

Peter J. Espenshade, Ph.D.

Oxygen-sensing and adaptation to host tissue hypoxia in the human fungal pathogen *Cryptococcus neoformans*
Johns Hopkins University

Michael R. Farzan, Ph.D.

Parallel identification of obligate viral receptors
Harvard Medical School

David A. Fidock, Ph.D.

Plasmodium falciparum transmembrane proteins and their role in parasite susceptibility to heme-binding antimalarials
Columbia University Medical Center
Approved: \$61,447

Michael J. Gale, Jr., Ph.D.

Control of hepatitis C virus replication
University of Washington

Stephen Girardin, Ph.D. *

Nod-like receptor Nod9 links mitochondrial dynamics and innate immunity to bacterial pathogens
University of Toronto
Approved: \$500,000

Britt Glaunsinger, Ph.D.

Global modulation of cellular gene expression by an oncogenic human herpesvirus
University of California-Berkeley

Michael S. Glickman, M.D.

Role of regulated intramembrane proteolysis in controlling *Mycobacterium tuberculosis* virulence and cell envelope composition
Memorial Sloan-Kettering Cancer Center

Karen J. Guillemin, Ph.D.

Regulation of gut epithelial cell homeostasis by the microbiota
University of Oregon

Chuan He, Ph.D. *

How *Staphylococcus aureus* senses host immune defenses
University of Chicago
Approved: \$500,000

Kent L. Hill, Ph.D. *

Cell-cell communication and social motility in pathogenesis and development of African trypanosomes
University of California-Los Angeles
Approved: \$500,000

Lora V. Hooper, Ph.D.

Innate immune responses to commensal bacteria at gut epithelial surfaces
University of Texas Southwestern
Medical Center-Dallas

Akiko Iwasaki, Ph.D.

Stromal cell contributions in innate and adaptive immune responses to mucosal viral infection
Yale University

Eckhard Jankowsky, Ph.D.

Molecular mechanisms of pathogen identification by the pattern recognition receptors RIG-I and MDA5
Case Western Reserve University

Robert F. Kalejta, Ph.D.

Cellular and viral determinants of human cytomegalovirus lytic and latent replication cycles
University of Wisconsin-Madison

Barbara I. Kazmierczak, M.D., Ph.D.

Role of injury in *Pseudomonas aeruginosa* pulmonary infection
Yale University

Margarethe (Meta) J. Kuehn, Ph.D.

Toxin trafficking via vesicles
Duke University Medical Center

D. Borden Lacy, Ph.D. *

Structural mechanisms of *Helicobacter pylori* pathogenesis
Vanderbilt University Medical Center
Approved: \$500,000

Manuel Llinas, Ph.D.

Global analysis of the *Plasmodium falciparum* metabolome
Princeton University

John D. MacMicking, Ph.D. *

Immune control of human phagosomal pathogens by a novel GTPase superfamily
Yale University School of Medicine
Approved: \$500,000

Harmit S. Malik, Ph.D.

Evolution-based identification and functional study of intracellular host-virus interactions
University of Washington

Dorian B. McGavern, Ph.D.

Chemical and molecular approaches to probe viral pathogenesis in real time
Scripps Research Institute

Yorgo Modis, Ph.D.

Cell entry and innate immune recognition of flaviviruses
Yale University

Christian Munz, Ph.D.

Regulation of macroautophagy by viral infection
Rockefeller University

Andrew S. Neish, M.D.

Transgenic analysis of prokaryotic effector proteins in the eukaryote *Drosophila melanogaster*
Emory University School of Medicine

Kim Orth, Ph.D.

VopL, a *Vibrio* effector that nucleates actin
University of Texas Southwestern
Medical Center-Dallas

John S. Parker, BVMS., Ph.D.

Reovirus-induced apoptosis: the role of the viral outer-capsid protein mu1
Cornell University College
of Veterinary Medicine

Lalita Ramakrishnan, M.D., Ph.D.

Forward genetic screens in the zebrafish to identify host determinants of susceptibility to tuberculosis
University of Washington School
of Medicine

Ana Rodriguez, Ph.D.

Role of hypoxanthine degradation in malaria-induced pathogenesis
New York University School
of Medicine

Eric J. Rubin, M.D., Ph.D.

Cell signaling by bacterial cytokines in *Mycobacterium tuberculosis*
Harvard School of Public Health

Karla Fullner Satchell, Ph.D.

Mouse model for the role of toxins in cholera pathogenesis
Northwestern University

Luis M Schang, D.V.M., Ph.D.

Silencing and antisilencing in the regulation of viral gene expression
University of Alberta

Neal Silverman, Ph.D.

Intracellular bacterial recognition in the *Drosophila* innate immune response
University of Massachusetts
Medical School

Eric Skaar, Ph.D.

In vivo identification of *Staphylococcus aureus* proteins that defend against host neutrophils.
Vanderbilt University Medical Center

Gregory A. Smith, Ph.D.

Coordination of herpesvirus assembly and transport in axons of sensory neurons
Northwestern University Feinberg
School of Medicine

Vanessa Sperandio, Ph.D.

Interkingdom signaling in bacterial pathogenesis
University of Texas Southwestern
Medical Center-Dallas

Adrie J.C. Steyn, Ph.D. *

Carbon monoxide and *Mycobacterium tuberculosis* persistence.
University of Alabama-Birmingham
Approved: \$500,000

Timothy L. Tellinghuisen, Ph.D. *

Subversion of a host kinase and vesicle trafficking components for the production of infectious hepatitis C virus
Scripps Research Institute
Approved: \$500,000

Chloe L. Thio, M.D.

Identification of human genes associated with hepatitis B virus outcomes
Johns Hopkins University School
of Medicine

Billy Tsai, Ph.D.

How cholera toxin hijacks cellular machineries to transport across the ER membrane
University of Michigan Medical School

Raphael H. Valdivia, Ph.D.

Role of secreted bacterial proteases
in chlamydial pathogenesis
Duke University

Linda F. van Dyk, Ph.D.

Analyzing the role of tumor suppressors
in the control of virus infection and
inflammation
University of Colorado Health
Sciences Center

Andres Vazquez-Torres, D.V.M., Ph.D.

Effects of nitrosative stress on bacterial
two component regulatory systems
in innate host defense
University of Colorado at Denver
and Health Sciences Center-
Fitzsimons Campus

David Wang, Ph.D. *

Genomics-based approach to novel viral
etiologies of diarrhea
Washington University School
of Medicine
Approved: \$500,000

Sean P. Whelan, Ph.D.

Exploration of the interaction of RNA
viruses with their host cells
Harvard Medical School

Marvin Whiteley, Ph.D. *

Mechanistic insight into host modulation
of bacterial group activities
University of Texas-Austin
Approved: \$500,000

Wenqing Xu, Ph.D.

Innate immunity: how do toll-like
receptors recognize microbial
pathogens?
University of Washington School
of Medicine

Dong Yu, Ph.D. *

Modulation of the DNA damage
response by human cytomegalovirus
Washington University School
of Medicine
Approved: \$500,000

Thomas C. Zahrt, Ph.D.

Mycobacterium tuberculosis regulators
modulating reactivation
Medical College of Wisconsin

Ning Zheng, Ph.D.

Viral hijacking of host ubiquitin
ligase machinery
University of Washington

OTHER GRANTS (AD HOC)**Albert Einstein College of Medicine
of Yeshiva University**

Support for awardee to give a seminar
Approved: \$1,000

American Society for Microbiology

Support for travel awards for graduate
students and postdoctoral fellows
in parasitology to attend the
general meeting
Approved: \$9,000

American Society for Microbiology

Support for conference on Candida
and Candidiasis
Approved: \$15,000

American Society for Microbiology

Support for the Beneficial Microbes
Conference
Approved: \$12,000

**American Society of Tropical Medicine
and Hygiene**

Support for the annual meeting
Approved: \$30,000

**American Society of Tropical Medicine
and Hygiene**

Support for the American Committee
of Molecular, Cellular and
Immunoparasitology's scientific
program at the annual meeting
Approved: \$18,000

**American Society of Tropical Medicine
and Hygiene**

Support for the annual meeting
Approved: \$30,000

**American Society of Tropical Medicine
and Hygiene**

Support for the scientific program of the
American Committee of Molecular,
Cellular and Immunoparasitology at
the annual meeting
Approved: \$18,000

Baylor College of Medicine

Support for awardee to give a seminar
Approved: \$1,000

Boston University

Support for *Institutions for closing the
knowledge-action gap in global health*
conference
Approved: \$6,000

Duke University Medical Center

Support for the Triangle Malaria
Consortium symposium
Approved: \$6,000

**Foundation for the National Institutes
of Health**

Support for travel of graduate students
to attend the Ecology and Evolution
of Infectious Disease meeting
Approved: \$6,000

**Foundation for the National Institutes
of Health**

Support for awardee to give a seminar
at the National Institute of Allergy
and Infectious Diseases
Approved: \$1,000

Genome Research Ltd

Support for travel to attend a workshop
for re-annotating the *Plasmodium
falciparum* genome
Approved: \$20,000

Gordon Research Conferences

Support for the Environmental
Endocrine Disruptors conference
Approved: \$6,000

Gordon Research Conferences

Support for the Cellular and Molecular
Fungal Biology conference
Approved: \$6,000

Gordon Research Conferences

Support for the Biology of Host-Parasite
Interactions conference
Approved: \$12,000

Institute of Medicine

Support for the activities of the Forum on Microbial Threats for 2006–2008
Approved: \$25,000

International Conference on Cryptococcus and Cryptococcosis

Support for young investigators to attend the 7th International Conference on Cryptococcus and Cryptococcosis
Approved: \$25,000

Johns Hopkins University

Support for the conference *Infectious diseases of the nervous system: pathogenesis and worldwide impact*
Approved: \$6,000

Keystone Symposia

Support for the 2008 Keystone Symposium meetings
Approved: \$24,000

Marine Biological Laboratory

Support for the Molecular Mycology: Current Approaches to Fungal Pathogenesis course for three years 2006–2008

Marine Biological Laboratory

Support for the Biology of Parasitism Course 2007–2011

Marine Biological Laboratory

Support for the Molecular Mycology course 2009–2011
Approved: \$325,000

Massachusetts Institute of Technology

Support for the design, validation, and pursuing of initial discoveries in vector genetics with a newly developed genotyping tool, the *Anopheles gambiae* single nucleotide polymorphism (AGSNP) array
Approved: \$50,000

MR4–American Type Culture Collection

Support for matching funds to the American Type Culture Collection for the purchase of Affymetrix arrays to enable a number of research project proposals to be performed from MR4 (Malaria Research and Reference Reagent Resource Center) users
Approved: \$51,678

National Postdoctoral Association

Support for the National Postdoctoral Association's Leadership Capacity-Building Project
Approved: \$25,750

New York University School of Medicine

Support for *Frontiers in the Molecular Understandings of the Complement System, Parasite Immunology and Vaccine Development* symposium
Approved: \$1,000

Oklahoma City University

Support for clean up and revamping of the Buchanan laboratory from hurricane Katrina
Approved: \$25,000

Society of Toxicology

Support for student travel to the annual meeting
Approved: \$6,000

State University of New York–Buffalo

Support for a second Infectious Disease Ontology Workshop
Approved: \$24,000

University of Cincinnati

Support for the 10th International Workshops on Opportunistic Protists
Approved: \$6,000

University of Georgia

Support for *Global infectious disease research: modern approaches to ancient diseases* symposium
Approved: \$6,000

University of Georgia College of Veterinary Medicine

Support for the development of a registry for research projects in Chagas disease
Approved: \$25,000

University of Massachusetts Medical School

Support for students and postdocs to attend a *Toll2008* conference
Approved: \$6,000

University of Pennsylvania

Support for the Molecular Approaches to Malaria meeting
Approved: \$30,000

University of Pennsylvania

Support for the parasitic helminth community

University of Pennsylvania School of Veterinary Medicine

Support for two meetings of the heads of Parasitology Training grants to discuss evaluation and success of the programs
Approved: \$25,000

University of Pittsburgh

Support for the cloning of the *Brugia malayi* genome
Approved: \$180,000

University of Wisconsin–Madison

Support for the Midwest Microbial Pathogenesis Conference
Approved: \$8,000

Vanderbilt University Medical Center

Support for awardee to give a seminar
Approved: \$1,000

Wadsworth Center

Support for the Biodefense–Emerging Infectious Diseases symposium
Approved: \$6,000

Walter and Eliza Hall Institute of Medical Research

Support for a workshop on the Plasmodium Genome Database
Approved: \$12,250

Wellcome Trust Sanger Institute

Support for a workshop to complete the assembly and annotation of *Schistoma mansoni* genome
Approved: \$20,000

INTERFACES IN SCIENCE

CAREER AWARD AT THE SCIENTIFIC INTERFACE

*New Recipient

Emre Aksay, Ph.D.

Neural mechanisms for control
of eye position
Weill Medical College
of Cornell University

Dirk R. Albrecht, Ph.D.*

Investigating neural circuits governing
chemotaxis using microtechnology
Rockefeller University
Approved: \$500,000

David Biron, Ph.D.*

Understanding small neural circuits
Brandeis University
Approved: \$500,000

Rachel Brem, Ph.D.

The genetics of transcription in
budding yeast
University of California-Berkeley

Jasna Brujic, Ph.D.

Mechanical networks in biology:
from proteins to cells
New York University

Lynette Cegelski, Ph.D.*

Mapping the structural and functional
landscape of the microbial
extracellular matrix
Stanford University
Approved: \$560,000

Yann R. Chemla, Ph.D.

Single-molecule study of bacteriophage
DNA packaging and mitochondrial
protein import
University of Illinois-Urbana-Champaign

Derek Cummings, Ph.D.

Natural and vaccine-induced immunity
and spatiotemporal dynamics
of epidemic dengue
Johns Hopkins University

Rhiju Das, Ph.D.*

High resolution prediction of new
RNA folds
University of Washington
Approved: \$500,000

Alfredo Dubra-Suarez, Ph.D.*

Understanding glaucoma through
structural and functional in vivo
cellular imaging of the retina
University of Rochester
Approved: \$500,000

Alexander Dunn, Ph.D.*

Single molecule characterization of
the energetic landscape underlying
myosin force generation
Stanford University
Approved: \$500,000

Margaret L. Gardel, Ph.D.

Dynamic force generation in cell migration
University of Chicago
Approved: \$108,478

Timothy J. Gardner, Ph.D.

Tracking neural programs for song
Massachusetts Institute of Technology

Maria Neimark Geffen, Ph.D.*

Perception and neural encoding
of textured sounds
Rockefeller University
Approved: \$500,000

Andrea Mitchell Goforth, Ph.D.*

Bimodal, luminescent/magnetic
nanoparticle assemblies targeted to
alpha-4-beta-1 integrin for tumor
imaging and therapy
Portland State University
Approved: \$600,000

Daniel I. Goldman, Ph.D.

Dynamic locomotion on challenging
substrates
Georgia Institute of Technology

Ming Hammond, Ph.D.*

Large-scale discovery and analysis of
regulatory RNAs using computational
and chemical approaches
Yale University
Approved: \$500,000

Christine E. Heitsch, Ph.D.

Combinatorial and computational
approach to deciphering the
biological information encoded by
single-stranded nucleotide sequences
Georgia Institute of Technology

Ajit P. Joglekar, Ph.D.

Building a mechanistic model of the
structure and function of a
kinetochore-microtubule attachment
University of North Carolina-Chapel Hill

Harold D. Kim, Ph.D.

Understanding the mechanisms of
sensitivity in gene expression
Harvard University

Gavin McLean King, Ph.D.

Dynamic structural biology of ion
channel proteins: an ultra-stable
atomic force microscope study
University of Colorado-Boulder

Mary L. Kraft, Ph.D.

Composition analysis of the influenza
virus pre-envelope by multiple isotope
imaging mass spectrometry (MIMS)
University of Illinois-Urbana-Champaign
Approved: \$12,184

Jeffrey R. Kuhn, Ph.D.

Total internal reflection fluorescence
microscopy of actin branching
dynamics in vivo
Virginia Polytechnic Institute and
State University

Edo L. Kussell, Ph.D.

Evolution of microbial physiologies
New York University

Alison L. Marsden, Ph.D.

Engineering new treatments for
cardiovascular disease via optimal
design and physiologic simulation
University of California-San Diego
Approved: \$40,000

Laura A. Miller, Ph.D.

Developmental and evolutionary biofluid
dynamics: case studies in locomotion
and heart development
University of North Carolina-Chapel Hill

Celeste M. Nelson, Ph.D.

Biophysical dynamics in the regulation
of tissue morphogenesis
Princeton University

Dana Pe'er, Ph.D.

Systems approach to elucidate integration of signal and decision in cells
Columbia University

Joshua B. Plotkin, Ph.D.

Novel methods to compute selection pressures on proteins at the genome-wide scale
University of Pennsylvania

Astrid A. Prinz, Ph.D.

Models of activity-dependent homeostatic regulation in neural networks on the basis of brute force exploration of high-dimensional parameter spaces
Emory University

Arjun Raj, Ph.D.*

Stochastic gene expression in development: from phenomena to function
Massachusetts Institute of Technology
Approved: \$500,000

Benjamin J. Raphael, Ph.D.

High-resolution analysis of tumor genome architectures
Brown University

Aviv Regev, Ph.D.

From modules to mechanisms: the function and evolution of molecular networks
Massachusetts Institute of Technology

Erin C. Rericha, Ph.D.

Fluid flows in cell mechanosensitivity and cell motion
University of Maryland-College Park

Jason T. Ritt, Ph.D.

Active sensing in natural and robotic organisms
Massachusetts Institute of Technology

Sridevi Vedula Sarma, Ph.D.*

Improved therapies for Parkinson's disease using advanced engineering methods
Massachusetts Institute of Technology
Approved: \$500,000

Georg Seelig, Ph.D.*

Nucleic acid logic circuits for conditional gene regulation
California Institute of Technology
Approved: \$500,000

Jason K. Sello, Ph.D.

Taking a chemical genetic scalpel to a streptomyces colony
Brown University

Eric T. Shea-Brown, Ph.D.

Neurobiological dynamics of timing and decisions
University of Washington

Alexander Sher, Ph.D.

Investigation of retinal processing through large-scale multielectrode recordings
University of California-Santa Cruz

Hadley D. Sikes, Ph.D.

Well-defined, supramolecular assemblies of redox enzymes via templated self-assembly for use in mechanistic electron transport studies and targeted apoptosis
California Institute of Technology
Approved: \$25,127

Jan Skotheim, Ph.D.*

Systems level approach to cell cycle control: from molecules to motifs to physiology
Rockefeller University
Approved: \$500,000

Megan T. Valentine, Ph.D.

Establishing the mechanism of kinesin processivity
University of California-Santa Barbara

Joshua Vaughan, Ph.D.*

Discovery of new motility mechanism and high speed, in vivo imaging of motor protein dynamics
Harvard University
Approved: \$500,000

Lauren J. Webb, Ph.D.*

Electrostatic fields at the protein-protein interface
University of Texas-Austin
Approved: \$640,000

Joshua S. Weitz, Ph.D.

Evolutionary ecology of bacterial viruses
Georgia Institute of Technology

Ryohei Yasuda, Ph.D.

Visualization of biochemical signaling in single dendritic spines
Duke University

Ahmet Yildiz, Ph.D.

Molecular mechanism of dynein in vitro and in living cells
University of California-San Francisco

Muhammad N. Yousaf, Ph.D.

Surface chemistry and materials approach to develop model substrates to study PI(4,5)P2 lipid raft dependent actin polymerization
University of North Carolina-Chapel Hill

OTHER GRANTS (AD HOC)

Biophysical Society

Support for two career development sessions and the child care program at the annual meeting
Approved: \$15,000

Georgia Institute of Technology

Support for a workshop on viral paradigms
Approved: \$15,000

Hamner Institutes for Health Sciences

Support for the Institute for Alternative Futures proposal for developing a strategic plan for the training and education of regulatory scientists in emerging areas of biology relevant to safety assessment decision making
Approved: \$75,000

Marine Biological Laboratory

Support for the Physiology: Modern Cell Biology Using Microscopic, Biochemical and Computational Approaches course, 2008-2010
Approved: \$291,000

National Academies

Support for study on research at the intersection of the physical and life sciences
Approved: \$50,000

SCIENCE AND PHILANTHROPY

American Association for the Advancement of Science

Support for the 2008 Mass Media Fellows Program

Approved: \$25,500

Association for Women in Science

Support for 2008 Internship Program

Approved: \$10,500

Council for the Advancement of Science Writing

Support for the 2008 New Horizons Briefing and the New Horizons

Traveling Fellowship Program

Approved: \$30,000

Council on Foundations

Support for 2008

Approved: \$39,500

Emory University

Support for the publication and distribution of the Blue Ridge Academic

Health Group report *Health Care Quality and Safety in the Academic Health Center*

Approved: \$10,000

Foundation Center

Support for 2007 and support for the Anniversary Campaign

Approved: \$27,500

Friends of the National Library of Medicine

General support for 2008

Approved: \$5,000

Friends of the National Library of Medicine

Supplemental support for 2008

Approved: \$20,000

Grants Managers Network

Support for providing members with opportunities for professional

development and a forum for learning best practices

Approved: \$2,000

Grants Managers Network

Support for providing members with opportunities for professional

development and a forum for learning best practices

Approved: \$2,500

Health Affairs

Support for the Health Policy Summit

Approved: \$5,000

Health Research Alliance, Inc.

Support for 2008

Approved: \$8,000

McGill University Faculty of Medicine

Support for the McGill Journal of Medicine

Approved: \$10,000

University of North Carolina-Chapel Hill

Support for the 2008 North Carolina Science Blogging Conference

SCIENCE EDUCATION

STUDENT SCIENCE ENRICHMENT PROGRAM

**New Recipient*

Appalachian State University*

Appalachian: Merging Math and Science in Intentional Natural Gains (AMMASING)

Approved: \$180,000

Appalachian State University*

Appalachian student experience-based education (AppalSEED) academy: Integrating science across the high school curriculum

Approved: \$179,000

Bladen County Schools

Excite Sci Summer Science Epic

Approved: \$180,000

Campbell University*

HISS – High School Science Seminars

Approved: \$126,290

Cherokee Middle School*

CSI: Cherokee Science Investigation

Approved: \$130,570

Contemporary Science Center*

Contemporary Science Center at the Museum of Life and Science Field Studies Program

Approved: \$180,000

Duke University*

LASST: Leadership Academy for

Students in Science and Technology

Approved: \$179,974

Duke University*

RoboCupJunior: Exhibitions of problem solving, teamwork, and creativity

Approved: \$180,000

Duke University Comprehensive Cancer Center

Summer on the Edge

Duke University Medical Center

LEAP – Launch into Education About Pharmacology

Durham Academy

Mars Outreach for NC Students (MONS)

East Carolina University*

Partnering with Industrial and Regional Assets for Teaching and Enrichment in Science (PIRATES) Summer Camp

Approved: \$176,740

Elizabeth City State University

Increasing student interest in Earth science through Problem Based Learning, use of geospatial technology, and field experience

Evergreen Community Charter School

Girls in Research, Invention, Technology and Science (GRITS)

Friday Institute for Educational Innovation

Geosciences in Middle Schools

Friends of Great Smoky Mountains National Park

Smoky Mountain Heights:
Science Education in Western
North Carolina

Lenoir-Rhyne College*

North Carolina Stream
Investigation Project
Approved: \$178,327

Meredith College*

Meredith College STEM Experience
for Middle School Students
Approved: \$180,000

Montreat College*

Center for Learning and Investigation
in Backcountry Ecosystems: Climate
Education and Research Program
Approved: \$180,000

North Carolina A&T State University*

Science and Technology
Enrichment Program
Approved: \$180,000

North Carolina A&T State University*

Students Hots On The Sciences
Approved: \$180,000

North Carolina Agricultural Foundation, Inc.

It's about T.I.M.E. to do Real Science

North Carolina Central University

Students Making Another Science
Success Story

North Carolina Mathematics and Science Education Network

Pre-College Experiences for Reaching
Students Interested in Science
Teaching (PERSIST)

North Carolina Science Olympiad

Science Olympiad Student
Enrichment Program

North Carolina Society of Hispanic Professionals

Good Stewards of Our Environment
Approved: \$60,000

North Carolina State University

Summer College in Biotechnology
and Life Sciences (SCIBLS)

North Carolina State University

Photonics Xplorers

North Carolina State University

College of Engineering
Engineering Reaches Out

Orange County Schools*

iWalk on the Eno
Approved: \$141,024

Pfeiffer University

Intersections: Land, Water, Life

Pisgah Astronomical Research Institute

The space science lab at the Pisgah
Astronomical Research Institute

Sampson Early College High School*

Inspiring Science
Approved: \$81,137

Schiele Museum of Natural History and Planetarium, Inc.*

Environmental Science Partnership
Approved: \$179,975

Shodor Education Foundation Inc.

Mentor Center @ Shodor

Swain County Schools

Project EXPLORE

University of North Carolina-Asheville*

Bug Camp: A Summer Experience
in Science Investigation
Approved: \$160,766

University of North Carolina-Greensboro

Slip Slidin' Away: Monitoring Local
Reptile and Amphibian Populations

University of North Carolina-Wilmington*

Camp Bones: A science enrichment
program for diverse middle school
students that provides a foundation
for careers in nursing
Approved: \$112,231

Wingate University*

Technological Advances in
Reproductive Biology Summer
Science Program
Approved: \$113,738

OTHER GRANTS (AD HOC)

Alpha Kappa Alpha Sorority Educational Advancement Foundation

Support for the Educational
Advancement Foundation, in lieu
of honorarium for SSEP Advisory
Committee Member, Dr. Julia Clark
Approved: \$5,000

Center for Inquiry-Based Learning

Support for the Science Master
Teachers Program
Approved: \$52,560

DonorsChoose

Support for 2008-09
Approved: \$25,000

Grantmakers for Education

Support for 2008
Approved: \$3,000

Health Research and Education Foundation

Project SEED

James B. Hunt Jr. Institute for Educational Leadership and Policy

Support for a State of Science
Education Survey and Report, as
well as another North Carolina
Science Summit
Approved: \$25,000

National Association of Academies of Science

Support for the “Breakfast with Scientists” at the annual National Association of Academies of Science Meeting

Approved: \$2,500

North Carolina Association of School Administrators

Support for the annual conference

Approved: \$10,000

North Carolina Center for International Understanding Council

General support for 2008

Approved: \$1,500

North Carolina Community Foundation/North Carolina Network of Grantmakers

Support for the North Carolina Network of Grantmakers’ Education Funders’ Initiative

Approved: \$75,000

North Carolina Community Foundation/North Carolina Network of Grantmakers

Support for 2008–2009

Approved: \$3,000

North Carolina New Schools Project

Support for the 2008 North Carolina School Innovation Leadership Retreat

Approved: \$10,000

North Carolina School of Science and Math

Support for travel of North Carolina Student Academy of Science (student members to national conferences of the American Junior Academy of Sciences and the American Association for the Advancement of Science

Approved: \$10,000

North Carolina Science Leadership Association

Support for the Summer Leadership Institute

Approved: \$10,000

Public School Forum of North Carolina

Support for the Institute for the Educational Policymakers and International Travel Program

Approved: \$537,875

Public School Forum of North Carolina

Support for the International Studies Program and the Institute for Educational Policymakers

Public School Forum of North Carolina

Support for the production of a series on the trip to Singapore

Approved: \$7,000

Southern Illinois University Foundation

Support for the Dr. Willie Pearson, Jr. Academic Excellence Fund, in lieu of honoarium

Approved: \$5,000

University of California–San Francisco

Support for the Scientist and Health Education Partnership programs that promote partnerships between scientists and educators in support of high quality science education for K–12 students, directed by BWF Board Member J. Michael Bishop, M.D.

Approved: \$20,000

University of North Carolina–Chapel Hill

Support for the 2008 North Carolina Alliance to Create Opportunity through Education Alliance Day Conference

Approved: \$15,000

University of North Carolina–Charlotte

Support for the travel of five teams to the Singapore Math Contest

Approved: \$30,000

University of Washington

Support for the research project on developing effective evaluation instruments to assess learning through hand-on, inquiry-based activities

Approved: \$59,500

University of Washington

Support for the research project on developing effective evaluation instruments to assess learning through hand-on, inquiry-based activities

Approved: \$230,000

TRANSLATIONAL RESEARCH

CLINICAL SCIENTIST AWARD
IN TRANSLATIONAL RESEARCH

*New Recipient

Jayakrishna Ambati, M.D.Target-independent suppression
of angiogenesis by siRNAs
University of Kentucky**Mark Stuart Anderson, M.D., Ph.D.***Translating AIRE-control of immune
tolerance to human autoimmunity
University of California-San Francisco
*Approved: \$750,000***Richard J. Auchus, M.D., Ph.D.**Pharmacogenomics of hypertension
University of Texas Southwestern
Medical Center-Dallas**Andrew D. Badley, M.D., F.R.C.P.**Novel antiapoptotic therapies for sepsis
Mayo Clinic-Rochester**Arul M. Chinnaiyan, M.D., Ph.D.**Autoantibody profiles for cancer
diagnosis, prognosis, and therapy
University of Michigan-Ann Arbor**Bruce E. Clurman, M.D., Ph.D.**Diagnostic and therapeutic approaches
to cell cycle-associated cancer
University of Washington**Kathleen Loretta Collins, M.D., Ph.D.***Viral mechanisms of persistence
in HIV infected people
University of Michigan-Ann Arbor
*Approved: \$750,000***Kenneth R. Cooke, M.D.**Acute lung injury after SCT: from
laboratory insights to novel strategies
for diagnosis and treatment
Case Western Reserve University
School of Medicine**Laurence Cooper, M.D., Ph.D.***Tumor-specific alloantigen-nergic
donor-derived T-cell therapy
after hematopoietic stem-cell
transplantation
University of Texas M.D. Anderson
Cancer Center
*Approved: \$750,000***James E. Crowe, Jr., M.D.**Immunology and cell biology of
human metapneumovirus infections
Vanderbilt University School
of Medicine**Kenneth Cusi, M.D.**Non-alcoholic fatty liver disease in
type 2 diabetes: a novel intervention
strategy targeting metabolic &
molecular defects
University of Texas Health Science
Center-San Antonio**George Q. Daley, M.D., Ph.D.**Chemotherapy and stem cell
transplantation in leukemia
Harvard Medical School**Michael R. DeBaun, M.D.**Cysteinyl leukotriene receptor inhibitors:
a target for decreasing sickle cell
disease-related morbidity
Washington University**Michael S. Diamond, M.D., Ph.D.**Epitope-based immunogens and
diagnostics for dengue virus
Washington University**Dean W. Felsher, M.D., Ph.D.**Pre-clinical validation of g-quadruplex
drugs that target MYC to treat cancer
Stanford University School of Medicine**Joseph G. Gleason, M.D.**Causes and pathogenesis of cerebellar
malformation syndromes in humans:
bedside to bench
University of California-San Diego
School of Medicine**Jeffrey S. Glenn, M.D., Ph.D.**Hepatitis C virus: from molecular
virology to effective pharmacologic
eradication
Stanford University School of Medicine**William M. Grady, M.D.***Novel biomarkers for the prevention
and treatment of colon cancer
University of Washington
*Approved: \$750,000***Anna Huttenlocher, M.D.**Diagnosis and treatment of
autoinflammatory disease
University of Wisconsin-Madison**S. Ananth Karumanchi, M.D.***Soluble endoglin in the pathogenesis
and prediction of preeclampsia
Harvard Medical School
*Approved: \$750,000***Jane E. Koehler, M.D., M.A.**Genomic and clinical correlates of
human *Bartonella quintana* infection
University of California-San Francisco
School of Medicine**Francis Lee, M.D., Ph.D.***Role of BDNF in therapeutic
strategies for affective disorders
Weill Medical College
of Cornell University
*Approved: \$750,000***Ernst Robert Lengyel, M.D., Ph.D.***Development of novel therapeutic
and diagnostic strategies for
ovarian cancer
University of Chicago
*Approved: \$750,000***Dean Y. Li, M.D., Ph.D.**Therapeutic potential of vascular
guidance cues
University of Utah**Ali J. Marian, M.D.**Molecular genetics and pathogenesis
of human arrhythmogenic right
ventricular cardiomyopathy/dysplasia
University of Texas Health Science
Center-Houston

David M. Markovitz, M.D.

New approaches to inhibiting
HIV replication
University of Michigan-Ann Arbor

Daniel L. Marks, M.D., Ph.D. *

Maternal nutrition and fetal
metabolic programming
Oregon Health and Science University
Approved: \$750,000

Sofia D. Merajver, M.D., Ph.D.

Genetic determinants of aggressive
breast cancer phenotypes: translation
to the clinic
University of Michigan-Ann Arbor

Branch Moody, M.D.

Human T-cell responses to CD1 and
lipid antigens from M. tuberculosis
Harvard Medical School

Richard J. O'Brien, M.D., Ph.D.

Alzheimers disease and synaptic
transmission
Johns Hopkins University School
of Medicine

W. Cam Patterson, M.D.

Oxidative profiles in cardiovascular
diseases
University of North Carolina-Chapel Hill
School of Medicine

Jonathan R. Pollack, M.D., Ph.D. *

Pathogenesis and diagnosis of
clinically-indolent prostate cancer
Stanford University
Approved: \$750,000

Kerry J. Ressler, M.D., Ph.D.

Neurobiology of fear, neuroplasticity
and posttraumatic stress disorder
Emory University

Annabelle Rodriguez, M.D.

Deficiency of the lipoprotein receptor,
scavenger receptor class B type I,
in women with infertility
Johns Hopkins University
School of Medicine

Theodora S. Ross, M.D., Ph.D. *

Abnormal HIP1 and cancer biology
University of Michigan-Ann Arbor
Approved: \$750,000

Charles M. Rudin, M.D., Ph.D.

Novel therapeutic strategies for small
cell lung cancer
Johns Hopkins University

Jean E. Schaffer, M.D.

Lipotoxic cardiomyopathy: from
molecular mechanisms to human
disease
Washington University

Norman E. Sharpless, M.D.

Tumor suppressor p16INK4 in stem cell
aging
University of North Carolina-Chapel Hill

Warren D. Shlomchik, M.D.

Memory T cells for improved immune
reconstitution and GVL in
allogeneic hematopoietic stem
cell transplantation
Yale University

Pradeep Singh, M.D.

Gallium as an antimicrobial and
anti-bio film agent: a trojan horse
strategy that disrupts bacterial
iron metabolism
University of Washington

Donald Small, M.D., Ph.D.

Translating FLT3 inhibition into
improved therapy for pediatric AML
and infant ALL
Johns Hopkins University
School of Medicine

Jeffrey A. Toretsky, M.D. *

Novel cancer therapeutics based
upon oncogenic fusion-protein
transcription factors
Georgetown University
Approved: \$750,000

Russell Van Gelder, M.D., Ph.D.

Pathogenesis of inflammatory eye disease
University of Washington
Approved: \$675,000

Edus Houston Warren, M.D., Ph.D. *

Toward immune therapy for colon
cancer: identification of antigens
recognized by CD8+ T lymphocytes
on colon cancer stem cells
University of Washington
Approved: \$750,000

William Weiss, M.D., Ph.D.

Combination therapy against EGFR
and PI3-kinase in glioma
University of California-San Francisco

Cassian Yee, M.D.

Adoptive therapy of cancer: strategies
to augment the antigen-specific
T cell response
University of Washington

Kang Zhang, M.D., Ph.D.

Define novel genes for diabetic
microvascular complications
University of California-San Diego
Approved: \$750,000

OTHER GRANTS (AD HOC)

**American Association for the Advancement
of Science**

Support for the development of an online
career development portal for clinical
investigators
Approved: \$1,180,000

American Medical Informatics Association

Support for Summit on
Translational Bioinformatics
Approved: \$7,200

American Medical Informatics Association

Support for the annual meeting
Approved: \$15,000

American Medical Informatics Association

Support for the redesign of the
organization website
Approved: \$25,000

Association for Clinical Research Training

Support for trainees attending the annual meeting and a professional society summit

Approved: \$15,000

Clinical Research Forum

Support for the annual meeting

Approved: \$40,000

Health Research Alliance, Inc.

Support for the national conference

Approved: \$15,000

Institute of Medicine

Support for the Roundtable on Evidence-Based Medicine, 2006–2009

Institute of Medicine

Support for the Forum on Drug Discovery, Development, and Translation

Approved: \$40,000

University of North Carolina–Chapel Hill**Lineberger Comprehensive Cancer Center**

Support for the annual symposium

Approved: \$1,500

University of South Dakota**School of Medicine**

Support for regional conference

Approved: \$6,000

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The Burroughs Wellcome Fund uses advisory committees for each competitive award program to review grant applications and make recommendations to BWF's Board of Directors, which makes the final decisions. We select members of these committees for their scientific and educational expertise in the program areas. In addition, BWF uses a financial advisory committee to help in developing and reviewing the BWF's investment policies. This committee is appointed by and reports to the Board of Directors.

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Sciences – 1995*)

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Professor of Microbial Pathogenesis
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(*Cochair*)

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Canadian Institutes of Health Research

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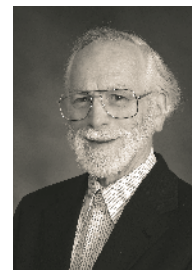
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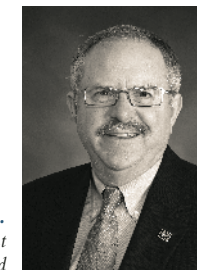
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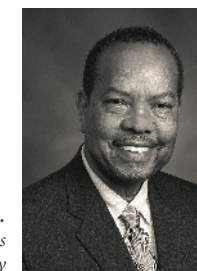
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