BURROUGHS WELLCOME FUND

2004 Annual Report

Depicted in BWF's logo,
the eye of the ancient Egyptian god Horus
is considered a symbol of health.

The Burroughs Wellcome Fund

is an Independent Private Foundation

Dedicated to Advancing the Biomedical Sciences

by Supporting Research and other Scientific

and Educational Activities.

2004 Annual Report

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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, we seek 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.

BWF has an endowment of about $600 million, and we award approximately $25 million in grants annually in the United States and Canada. We channel our financial support primarily through competitive peer-reviewed award programs, which encompass five major categories—basic biomedical sciences, infectious diseases, interfaces in science, translational research, and science education. BWF makes grants primarily to degree-granting institutions on behalf of individual researchers, who must be nominated by their institutions. To complement these competitive award programs, we also make grants to nonprofit organizations conducting activities intended to improve the general environment for science.

The Burroughs Wellcome Fund 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. The Wellcome enterprise was started in 1880 by two young American pharmacists, Henry Wellcome and Silas Burroughs, who had moved to London to manufacture and sell "compressed medicines"—that is, pills—which the pair believed could replace the potions and powders of the day.

Their firm prospered. After Silas Burroughs died in 1895, Henry Wellcome directed the growth of the company into an international network with subsidiaries in numerous countries on several continents. As the business grew, Henry Wellcome held firm to his strong belief that research was fundamental to the development of excellent pharmaceutical products—a belief he put into practice by establishing the industry's first research laboratories.

When Henry 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. Over the decades, the Trust grew to become the world's largest charitable foundation devoted exclusively to the biomedical sciences.

In 1955, leaders at the Wellcome Trust and Burroughs Wellcome Co.-USA envisioned an extension of this effort in

the United States—and so was born the Burroughs Wellcome Fund. After nearly four decades as a corporate foundation, BWF in 1993 received from the Trust a $400 million gift that enabled us to become a foundation fully independent of the Wellcome Trust and the Burroughs Wellcome Co. Though we are today an independent philanthropy, our history and joint program activities allow us to maintain productive ties with the Wellcome Trust.

With this increase in assets resulting from the Wellcome Trust endowment, BWF has been able to play a larger role in funding biomedical research, including extending our support into Canada. In carrying out this work, BWF is governed by a Board of Directors composed of distinguished scientists and business leaders, and our competitive award programs are guided by advisory committees composed of leading researchers and educators.

The importance of curiosity-driven research, as endorsed by Henry Wellcome, continues to be our guide. Thus, more than

a century after two enterprising American pharmacists set in motion their pioneering partnership, the Burroughs Wellcome Fund remains committed to the belief that fostering research by the best and brightest scientists offers the fullest promise for improving human health.

Enriqueta C. Bond, Ph.D.

Surveying the Science Landscape, Building Alliances, and Convening Awardees

On May 25, 2005, the Burroughs Wellcome Fund turns 50. Over the past half century, the Fund has shifted priorities to keep pace with the evolving nature of the research enterprise, though our mission—to advance the biomedical sciences through support of research and education—has stayed constant. So has our commitment to investing in the career development of young scientists and supporting investigators in underfunded or undervalued areas of science.

Every five years, BWF's Board of Directors and staff (with input from outside specialists) step back from day to day operations to reconsider the Fund's mission and strategies for implementing our programs—an exercise we call "terrain mapping." With the accelerating pace of scientific discovery, it makes sense to regularly scan advances in science, analyze government and industry funding gaps in science, benchmark our efforts against those of other science funders, and refine and update our programs. I will describe below some of the trends and issues that we think might affect our program plans for 2005-2006.

Scanning the Science Environment

These are exciting times. An unprecedented array of research opportunities challenges scientists to push the boundaries of science. Consequently, to guide our terrain mapping efforts, our board tracks changes in biomedical research and in the preparation and support of the science and engineering (S&E) workforce, as well as trends affecting our current programs. At present, our programs support scientific work at the interface between the physical, chemical, and computational sciences and biology; physician-scientists who work on translating basic knowledge from bench to bedside; scientists who advance understanding of the host-pathogen interface in infectious diseases; and grants encouraging earlier independence and risky science by young scientists. BWF also promotes K-12 science education in North Carolina so that there will be more students coming through the pipeline to fill tomorrow's S&E workforce.

The board also considers undervalued or underfunded areas of science in which a private funder can make a difference. Such areas include work on translational science and research at the interface of scientific disciplines, as well as work in reproductive science and prevention of premature birth where political concerns about abortion, malpractice liability, and complex science may slow research.

Congress has reacted to 9/11 and anthrax terrorism by increasing funding for research on infectious diseases and for producing new vaccines and therapeutics, especially those with potential to fight bioterrorism. These investments bring welcome new attention to the study of several specific infectious diseases, but in this funding climate, BWF's flexible support of work on pathogenesis—especially in underserved and undervalued systems—is more important than ever to young researchers working on basic problems.

The NIH Roadmap

Efforts by the National Institutes of Health (NIH) and other health funders reinforce our current investments and raise questions about how to reshape our funding for 2005-2006. This past year, both the NIH and the Food and Drug Administration (FDA) have issued strategic plans to guide government and industry investments in science. Recognizing that the five-year doubling of the NIH budget (completed in 2003) both picked up the pace of discovery and raised public expectations of better health, NIH director Dr. Elias Zerhouni led a process that culminated in the "NIH Roadmap" to guide future progress in science. (Elias Zerhouni. "The NIH Roadmap." *Science* Vol. 302, 3 October 2003 p63.) The first theme of the roadmap—New Pathways to Discovery—recognizes the need to understand complex biological systems and to reunite molecular biology and physiology in a new approach often called systems biology. The roadmap calls for investing in a better "toolbox" to provide scientists access to technologies, databases, and other scientific resources, such as molecular libraries, bioinformatics and computational biology, nanomedicine, and structural biology. BWF's Interfaces program, which draws scientists from other disciplines to biology, develops the kinds of scientists uniquely positioned to conduct such work.

"With the accelerating pace of scientific discovery, it makes sense to regularly scan advances in science, analyze government and industry funding gaps in science, benchmark our efforts against those of other science funders, and refine and update our programs."

The second roadmap theme—Research Teams of the Future—recognizes that the scale and complexity of biomedical research increasingly requires interdisciplinary and multidisciplinary research teams and urges scientists to find new ways to combine skills and disciplines in the physical and biological sciences as well as the social and behavioral sciences and biology. A National Academies report (*Large-Scale Biomedical Science—Exploring Strategies for Future Research.* National Academies Press. Washington D.C. 2003) noted that historically, most biomedical research has been conducted through small, independent projects initiated by individual investigators, although many future projects are likely to involve larger teams of scientists working on complex problems that cannot be addressed by single researchers. Since life scientists are concerned that such large projects might reduce the pool of money available for smaller studies, the Institute of Medicine called for the NIH to establish guidelines supporting both types of projects. Again, both our Interfaces and Career Awards programs develop independent scientists who can become tomorrow's knowledge and team leaders. In addition to continuing to invest in individual awards, the BWF board is discussing whether we have a role in supporting team science efforts and, if so, what that role might be.

Acknowledging that basic science discoveries must be translated into interventions that promote health and treat disease, the NIH developed its third roadmap theme—Re-engineering the Clinical Enterprise. To that end, the NIH will work on simplifying regulatory requirements, boosting clinical workface training, fostering development of informatics and electronic networking, providing core services to clinical investigators, funding translational research centers, and developing technologies for improved assessment of clinical outcomes. BWF applauds this renewed commitment to supporting clinical research and pushing for scientific discoveries to more quickly move from the bench to better patient health.

Mirroring the NIH effort, the Food and Drug Administration recognized that as the pace of new research findings has accelerated, there has been a slowdown in innovative medical therapies reaching patients, as well as escalating research costs for every drug approved. (*Innovation/Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products.* U.S. Department of Health and Human Services, Food and Drug Administration. March 2004). In the FDA's view, the applied sciences needed for developing medical products have not kept pace with the tremendous advances in the basic sciences, and there is a dearth of scientific work on creating new tools to get quicker and cheaper answers about the safety and effectiveness of new products.

The report calls for "a new product development toolkit —containing powerful new scientific and technical methods such as animal or computer-based predictive models, biomarkers for safety and effectiveness, and new clinical evaluation techniques…to improve predictability and efficiency along the critical path from laboratory concept to commercial product." The report also calls for identifying and prioritizing areas for attention and working with stakeholders to develop new breakthrough tools for creating new treatments. BWF Investigators in Translational Research may be well positioned to contribute to such new knowledge.

Both the NIH Roadmap and the FDA Critical Path note the need to continue to invest in clinical research. Given substantial NIH investments in clinical research, development of the series of awards for clinical investigators (K awards), and loan repayment programs, our board is looking at our Translational Research focus area to make sure our investments complement these new initiatives.

Workforce Issues

As I have written in many of our past annual reports, workforce issues are a primary concern of BWF. The National Science Board (NSB) supervises the collection of a broad set of data trends, including workforce trends, which it publishes as *Science and Engineering Indicators* (www.nsf.gov). In *Indicators 2004*, the NSB has continued to raise concerns about the composition of the science and engineering workforce. The NSB believes that if current trends continue, then three things will happen: 1) the number of jobs in the U.S. economy that require science and engineering training will grow; 2) the number of U.S. citizens prepared to fill those jobs will be, at best, level with current numbers; and 3) the availability of people from other countries who have science and engineering training will decline, either because of limits to entry imposed by U.S. national security restrictions or because of intense global competition for people with these skills.

"One of the biggest challenges facing the nation is how to create a better pipeline into the sciences, especially for underrepresented minorities and women. Science education is one of BWF's five program areas."

As noted by the National Science Foundation, one of the biggest challenges facing the nation is how to create a better pipeline into the sciences, especially for underrepresented minorities and women. Science education is one of BWF's five program areas. We have provided ongoing support for the Student Science Enrichment Program (SSEP) that makes awards to nonprofit organizations serving North Carolina middle- and high school students. The SSEP targets underrepresented minorities and females and provides them with hands-on, minds-on science enrichment experiences that will hopefully draw these students into science.

In conjunction with investing in SSEP, BWF also has been busy building the state's capacity to improve preK-12 education by establishing a new center—the North Carolina Science, Mathematics, and Technology Education Center (SMT Center)—to champion the importance of strong education for all children, to improve teacher preparation in science, mathematics, and technology, and to identify model teachers, schools, and successful N.C. programs.

Pipeline preparation and the need to nurture young scientists garner considerable attention. For example, NIH's Dr. Zerhouni has raised concerns about finding ways to make young scientists independent earlier in their careers, and he has asked Dr. Ruth Kirschstein, former acting director of the NIH, to explore approaches to address the problem. The National Academies of Sciences has established a committee, chaired by Dr. Thomas Cech, president of the Howard Hughes Medical Institute (HHMI), to prepare a report on support of young scientists and the S&E workforce. To help these efforts, BWF has provided data collected on our programs and will continue to champion earlier independence for young scientists. In an editorial in *Science* (vol. 304, 18 June 2004), Dr. Cech and I noted that young scientists also need laboratory management training. Reflecting on a successful lab management course that HHMI and BWF jointly offered our awardees (*Making the Right Moves: A Practical Guide to Scientific Management for Postdocs and New Faculty,* at www.hhmi.org/labmanagement), we call for professional societies and universities to provide such training on a much wider scale.

Building Alliances

BWF has consistently sought to make connections with other organizations that fund biomedical research, believing that by learning from them and collaborating with them, we will have a greater impact on the environment in which our awardees work. Making these connections has resulted in several significant collaborations. The most noteworthy are three private funder meetings held in 1998, 2000, and 2004. This series of meetings has created a forum for biomedical research funders that did not previously exist, and the participating funders have tackled a variety of issues, such as how to foster work at the interface of the biological and behavioral sciences and how to create better training programs for basic and clinical researchers.

The success of the international effort to sequence the genome of *Plasmodium falciparum*, the major parasite that causes malaria, was the result of a collaboration supported by BWF, the Wellcome Trust, the National Institute of Allergy

and Infectious Diseases, the Department of Defense, and the World Health Organization. This community of funders and researchers has continued to collaborate regarding next steps, such as building a better database to provide improved access to sequencing information and listening to the needs of the scientists working on these issues. In conjunction with the NIH, BWF recently provided additional dollars to help complete the genome sequencing of the other parasite that causes malaria—*Plasmodium vivax*.

In North Carolina, the new North Carolina Science, Mathematics, and Technology Education Center, incubated by BWF, is bringing together business, government, and education sectors to coordinate and champion efforts to improve preK-12 science education in the state. We are working closely with the National Science Foundation and its N.C. funded programs to involve scientists in training and supporting teachers. Additionally, we are technically supporting the creation of new science-based schools arising from the Melinda & Bill Gates Foundation grant to help North Carolina reinvent its high schools.

Convening Awardees

Three years of volatile stock markets led the BWF board to decide not to offer three of our competitive programs this past year—Investigators in Pathogenesis of Infectious Diseases, Career Awards at the Scientific Interface, and Clinical Scientist Awards in Translational Research. Two programs—Career Awards in the Biomedical Sciences and the Student Science Enrichment Program—continued, albeit at a slightly reduced number of awards. Redirecting our efforts has paid off both in securing our future ability to field a full portfolio of awards and in allowing BWF to emphasize nurturing the careers of our awardees through providing convening activities and through our efforts to build alliances with other funders.

Staff redirected their efforts from managing the competitive programs to holding a series of awardee meetings in each of our program areas; these efforts will be discussed in more detail in the following sections on each program. In general, the purpose of these meetings is to identify new scientific insights, facilitate networking and forge new collaborations among our awardees, take a look at awardees' career development issues, and provide ongoing training. The meetings also provide an opportunity for our board, and the advisory committee members who oversee each of our programs, to assess the results of program awards and provide continuing mentorship and advice. We consider our awardees, board, committee members, and staff as part of the BWF family.

Beginning in 2004-2005, we will be back to a full program of support in the United States and Canada with 20 Career Awards in the Biomedical Sciences, 10 Career Awards at the Scientific Interface, 10 awards in Pathogenesis of Infectious Disease, 7 Clinical Scientist in Translational Research awards, and 10 awards to support student science enrichment experiences in North Carolina. These programs are described in more detail in the sections that follow.

The Career Awards in the Biomedical Sciences (CABS) program marked its tenth anniversary in 2004, having funded 195 young scientists with a total financial commitment approaching $100 million.

Of those awardees, 40 percent are physician-scientists; one-third work in the field of neuroscience; one-third are women; and 98 percent (excluding the most recent class) have tenure-track or equivalent faculty appointments.

The newest member of the CABS advisory committee, John York, Ph.D., is one of BWF's own. Dr. York, a Howard Hughes Medical Institute (HHMI) assistant investigator and an associate professor at Duke University Medical Center, received a Career Award in 1995. He will now be among those who review applications for the CABS program and recommend awardees to BWF's Board of Directors.

During the past decade, the CABS program has been in the forefront of biomedical program outcome evaluation. Since 1997, BWF has conducted an annual survey of all CABS awardees. Results from these surveys were published in *Academic Medicine* (Georgine Pion and Martin Ionescu-Pioggia, "Bridging postdoctoral training and a faculty position: Initial outcomes of the Burroughs Wellcome Fund Career Awards in the Biomedical Sciences," *Academic Medicine* 78(2): 177-185, February 2003). This study examined the effect of early career funding on career outcomes, and though not a controlled study, concludes that the CABS program is meeting its goal of fostering the research independence of young investigators. In a continuing commitment to evaluation, BWF will make available in 2005 results of a study comparing funded applicants to those who did not receive a BWF award.

Using survey data and feedback from face-to-face interviews with awardees, BWF has been able to tweak its CABS program to better serve awardees. Among the program's defining characteristics are:

- Flexibility
- Portable funding
- Freedom to pursue risky research ideas
- Liberal financial carryover policy
- Encouragement of research independence
- Career development training that supports high quality, innovative science

The unique characteristics of this program were described at the National Academies convocation, *Bridges to Independence: Identifying Opportunities for and Challenges to Fostering the Independence of New Investigators in the Life Sciences.*

In January 2004, Dr. Martin Ionescu-Pioggia of BWF, along with Dr. Maryrose Franko of HHMI, gave a presentation to the National Institutes of Health's Training Advisory Committee on the need for developing nationally based lab management courses. The following month, BWF and HHMI released a 250-page publication, *Making the Right Moves: A Practical Guide to Scientific Management for Postdocs and New Faculty*, at the American Association for the Advancement of Science annual meeting in Seattle. The two funders developed the publication from materials prepared for the 2002 laboratory management course held at HHMI and have made it available for free download at www.hhmi.org/labmamangement. Once it was published online, demand for the manual was high, with several thousand downloads during the first week and more than 43,000 downloads to date.

Following the publication of the lab manual, Dr. Thomas Cech, head of HHMI, and Dr. Enriqueta Bond, president of BWF, published an editorial in *Science* (Cech, Thomas R. and Enriqueta Bond, "Managing your own lab," *Science* 304 (5678), 1717, June 18, 2004) emphasizing the need for universities and other organizations to develop courses of their own in this area. The lab manual provides organizations with a starting point for such courses. A partnering program to help them develop independent courses is currently under way. BWF and HHMI will offer a revised version of the course in June 2005 and plan to update the manual.

profile

Dr. Vamsi Mootha: Computing the Pathways to Genetic Discoveries

Dr. Vamsi Mootha's innovative research on mitochondria has earned him not only a BWF award but also a 2004 MacArthur Foundation "genius grant."

In the early 1990s when Dr. Vamsi Mootha was in college, he wrote a computer program—dozens of pages of code that ran as a statistical algorithm for analyzing DNA—as his senior research project. His adviser, a mathematical biologist, had urged Dr. Mootha to develop mathematical and computational techniques for DNA sequence analysis. Back then it took weeks for Dr. Mootha to request and receive DNA sequences by mail, and he was able to run his code against only a dozen sequences before he graduated and moved on to medical school.

Times have changed, Dr. Mootha says now, marveling at how the Internet makes available millions of DNA sequences. In the decade since he wrote his code, Dr. Mootha—recipient of a 2004 Career Award in the Biomedical Sciences—has programmed himself into the forefront of genomic science with his work on mitochondria. His groundbreaking work also has been recognized with a 2004 MacArthur Foundation "genius grant" of $500,000 to use as he wishes.

In September 2004, Dr. Mootha joined the faculty of Harvard Medical School as assistant professor, the first faculty hire in the newly created Department of Systems Biology. Systems biology is an emerging field that "attempts to understand how all the individual pieces work together," Dr. Mootha says, and one where he can merge his training in medicine, mathematics, and computation. He also sees patients with mitochondrial diseases, which cause neuromuscular problems, seizures, and loss of vision. In addition, recent research has shown that mitochondria contribute to a variety of other diseases, including cancer, diabetes, and obesity.

"I strongly believe that many common diseases will be due to inherited or acquired mitochondrial dysfunction," Dr. Mootha asserts. Mitochondria are tiny cellular organelles (small structures that are located within cells and perform dedicated functions) that at one time were anaerobic bacteria but have since evolved into a crucial part of our bodies. Much of the body's energy production, as well as the apoptotic machinery, which programs cell death, is resident in the mitochondria, he says, explaining that mitochondria tell a cell whether or not to start dying. Too little apoptosis leads to unregulated cell growth and tumors. Mitochondria contain their own compact genome, mtDNA, which encodes just 13 polypeptides of the 1,200 proteins that make up the organelle. They are ripe for the computational picking.

The traditional approach in biology, says Dr. Mootha, is to study a single gene or protein in all its activities. But new tools in genomic science enable investigators to monitor all the genes at once and record all the protein expressions. "Computation is the key tool that is used in making sense of the vast experimental data," he says.

Dr. Mootha's approaches include using the neighborhood analysis algorithm, which compares public databases of DNA, protein expression, and RNA to scan for disease-causing genes. He then gives each human gene a score depending on its similarity to mitochondrial genes and the likelihood that the ways it gets expressed will lead to disease. With this technique, he and his colleagues were able to identify a genetic cause of Leigh syndrome, a fatal neurodegenerative disorder.

Using computational tools to delve into genomics at first seemed "like a pipe dream," says Dr. Mootha, but recent work by him and others in type 2 diabetes offered more proof of concept. Although there was no single gene or protein that seemed out of whack in this disease, computational analysis revealed an entire signaling pathway in which several minute changes added up to an important, health-altering change in diabetic patients' skeletal muscle.

Researchers using a computational technique developed by Dr. Vamsi Mootha were able to identify the genetic cause of a fatal pediatric disease that destroys the brain.

"Vamsi has an inherent ability to think quantitatively and thereby see new approaches combining computational and molecular methods to attack biological problems," says Dr. James Gusella, director of the Massachusetts General Hospital Center for Human Genetic Research, an interdisciplinary center in which Dr. Mootha's Harvard lab is located. "Combine that talent with his medical training and you have a physician-scientist with the promise to truly bridge the gap between the lab and the clinic in the post-genomics era."

"One of my major goals is to develop tools and techniques to help propel genomic biology," says Dr. Mootha. Researchers recently used his neighborhood analysis algorithm to identify a previously unknown genetic cause of a fatal pediatric disease, called ethylmalonic encephalopathy, that destroys the brain.

"I found that to be tremendously satisfying," he says.

His new boss finds that inspiring as well. "Needless to say," Dr. Gusella notes, "hearing about Vamsi's approaches gives me all kinds of ideas that could be applied in my own research."

Dr. Mootha's love of mathematics surfaced in high school, he says. "I was a math geek who played on the varsity tennis team." He was majoring in math and computer science at Stanford University when, in his junior year, he took biochemistry to fulfill his biology requirement. "I loved it," he says, and he made up his mind to go to medical school.

After his undergraduate work, Dr. Mootha earned his M.D. from the Harvard-MIT Division of Health Sciences and Technology. As a medical student, with the support of the Howard Hughes Medical Institute (HHMI), he went to the National Institutes of Health and studied mitochondrial physiology. His thesis work, on regulatory control in mitochondrial energetics, "got me hooked on mitochondria," he explains.

During his residency in internal medicine at Brigham and Women's Hospital, Dr. Mootha moonlighted in the lab of Dr. Stanley Korsmeyer, where he worked on apoptosis. Then it was over to Denmark to a biotech company for six months of research on the proteomics of mitochondria. With additional funding from HHMI, he subsequently completed a postdoctoral fellowship in Eric Lander's laboratory at the Whitehead Institute in Cambridge, Massachusetts, where he was able to re-kindle his interests in mathematics and biology. During his education and training, Dr. Mootha determined he wanted to apply his skills to finding clinical solutions for human health problems.

Dr. Mootha says he will go slowly in building his lab, but he hopes to achieve that special mix of mathematicians, biochemists, and clinicians, as well as undergraduate students. He says he enjoys sharing his enthusiasm for how an investigator can make the most of today's biological research opportunities and new high-tech approaches. "It's a tremendous time to work in biology," he adds.

The Investigators in Pathogenesis of Infectious Disease award program continues the Fund's 50-year tradition of supporting work aimed at understanding and conquering some of humanity's worst killers.

The program focuses BWF resources on work that moves toward understanding what happens at the point where the human host and its microbial residents interact, allowing researchers opportunities to ask important questions about how pathogenesis begins, how infections are established, how the host helps or harms itself in responding, and how to shift the balance between host and microbe away from damage and toward health. This award program, on hold in the 2004 grant cycle, has funded two groups of investigators. The awards are at the center of a suite of activities that BWF sponsors in the infectious diseases. Over time, the Fund has invested more than $43 million in infectious disease research.

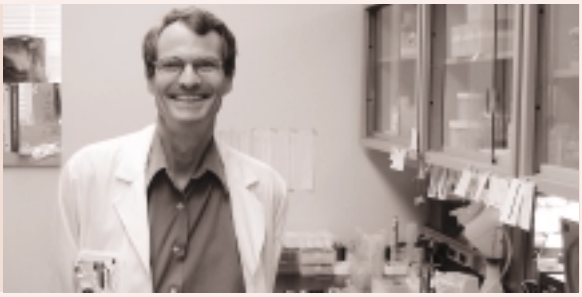
In his will, Henry Wellcome, who with Silas Burroughs founded the drug company that ultimately gave rise to the Fund, laid out a vision for how his wealth would keep working for the betterment of human health. "With the enormous possibility of development in chemistry, bacteriology, pharmacy and allied sciences," he wrote, "if my desires and plans are carried out in the way of research, in cooperation with the several industrial organisations, there are likely to be vast fields opened for productive enterprise for centuries to come."

The Fund's infectious disease program area is a proving ground for several of our strategies for investing in research. Using significant ad hoc grants over the past decade, we have stimulated team-driven projects and built new tools for basic research in malaria, the trypanosomatid parasites (which cause diseases such as Chagas disease, human leishmaniasis, and African sleeping sickness), and the pathogenic fungi. The connections and capacities developed through these efforts place researchers in these fields in excellent position to realize Sir Henry's vision.

As basic science becomes more interdisciplinary and more coordinated with applied work in the clinic, the field, and industry, investments such as those made by the Fund become more critical. BWF's strategy in promoting infectious disease research only rarely has been to deploy large grants to large projects. Rather, the Fund has looked for needs and opportunities, especially in the fatal parasitic diseases and emerging fungal diseases, where our flexibility and capacity for deploying dollars quickly can bring together the right group of researchers and funders to get a great idea off the ground. This summer, with the competitive awards dormant, we held a meeting, *Coexistence and Collisions at the Host/Microbe Interface*, to bring together researchers from across the BWF family of awardees and advisors to think about changes in what is experimentally possible and how to ask the questions that get to the heart of the interaction between human bodies and the organisms that live on, in, and among us. The Fund plans to explore some of the themes that arose in the meeting and look for new opportunities to build strong scientific networks that will advance the understanding of individual diseases and disease processes.

profile

DR. SCOTT FILLER WANTS TO CONQUER CANDIDA ONE GENE AT A TIME



Dr. Scott Filler wants to understand why Candida albicans*, a common fungus that causes thrush in newborns, can morph into a deadly systemic infection that can strike humans of any age who have been hospitalized.*

In healthy individuals, *Candida albicans*, a common fungus, can multiply to become a painful annoyance, showing up as what is called thrush or oropharyngeal candidiasis (OPC). Newborns sometimes contract OPC as they pass through the birth canal, because their immune systems are not fully developed. However, the fungus also can cause another, sometimes deadly, form of disease, called hematogenously disseminated candidiasis (HDC). HDC is *Candida albicans* run amok throughout the body, killing 20 percent to 50 percent of those stricken. This systemic form of candidiasis usually requires intravenous therapy, whereas OPC is treated with topical medication.

Dr. Scott Filler, a 1999 New Investigator in Molecular Pathogenic Mycology, is keenly interested in what distinguishes OPC from HDC, and he has a hunch that different virulence factors and regulatory pathways are activated in the two types of infections. "HDC is a recent disease associated with modern medicine," Dr. Filler says. Patients who contract HDC are typically in the hospital and have had major surgery of the gastrointestinal tract, have cancer, or have too few neutrophils (the white cells that surround and destroy bacteria). HDC also strikes premature infants in intensive care units and individuals on broad-spectrum antibiotics. "OPC doesn't usually progress into HDC even in immune-suppressed patients as long as their neutrophils are okay," Dr. Filler explains.

Another compelling reason for understanding the mechanisms that drive *Candida* is that the pathogen, in both OPC and HDC, increasingly is becoming resistant to antifungal drugs. Because HDC can kill, the developing resistance to current treatments is alarming. Dr. Filler's research could lead to identifying new drug targets in *Candida* infections or to developing vaccines to prevent the infection.

Candida is a dimorphic fungus—it can transform itself from a football-shaped yeast cell to long, many-celled filaments called hyphae. Sensors in the yeast are able to detect changes in its environment and activate a signal pathway that transforms the pathogen from yeast to hyphus—or football to filament. It is this process of transformation that most interests Dr. Filler. "If you infect mice with strains that are locked in yeast or hyphal phase, we find that they don't get sick," Dr. Filler notes, adding, "almost anything that blocks yeast to hyphus transition leads to reduced virulence." So he is looking at the signals that tell cells to morph from one form to the other. Kinases—proteins that add phosphates to other molecules—often trigger this kind of change, and protein kinase A regulates the transition in *Candida*.

"In *Candida albicans*, there are two different protein kinase A catalytic subunits (parts of an enzyme complex that transfer the phosphate to molecules)," Dr. Filler explains, "one encoded by a gene called *tpk1* and one by *tpk2*. Both act on a transcription factor (a protein that binds to DNA and alters the expression of other genes) called *efg1*." Do these two different subunits help tell the organism when conditions are right for a change to another form?

Dr. Filler and his colleagues set out to compare how cells lacking *tpk1*, *tpk2*, and *efg1* differ in their ability to interact with oral epithelial cells, the targets in OPC, and vascular endothelial cells, the targets in HDC. In a mouse model, they were able to confirm their hypothesis that *tpk1* and *tpk2*, as

well as *efg1*, have different contributions to candidal virulence in thrush versus a systemic infection. In the HDC mouse model, only *efg1* was required for normal virulence. But in the OPC mouse model, both *efg1* and *tpk2* were necessary to cause a significant infection.

"Right now," says Dr. Filler, "we're in the process of using microarrays to investigate the genes that are regulated by *efg1* and *tpk2*. We're making mutants that lack genes that are upregulated [turned on] in a virulent strain of *Candida* when it comes in contact with different host cells, and then we'll test the virulence of these mutants." Dr. Filler notes that it will be a challenge to decide which genes to examine. "Of the genes of unknown function, we're looking for those encoding proteins that are likely to be exposed on the cell surface, because they're more likely to be proteins that enable the organism to adhere to or invade the host cell surface." Such proteins, he says, could be targets of vaccines.

"Another compelling reason for understanding the mechanisms that drive Candida *is that the pathogen, in both OPC and HDC, increasingly is becoming resistant to antifungal drugs."*

Dr. Filler's route to infectious disease research was circuitous. A biology major at Dartmouth College, he says he went to medical school to become an orthopedic surgeon but then decided he was "better cut out to be an internist." During his residency at Harbor UCLA Medical Center, he conducted infectious disease research with Dr. Jack Edwards, and then applied for and won an infectious diseases fellowship.

Now a professor in the Department of Medicine at Harbor-UCLA Research and Education Institute, Dr. Filler says, "I really love the mixture of research and patient care." He is married to rheumatologist Dr. Bett Eng and is father to two daughters, two and six years old.

Dr. Filler and his wife experienced the patient side of the medical system when their now six-year-old was diagnosed with leukemia at age two. After two years of chemotherapy, his daughter is doing well, says Dr. Filler. But the going was rough in the beginning as he and his wife took turns with their daughter's care. "I handled most of the doctor visits," Dr. Filler says. "Because I worked mostly in the lab, my time was more flexible. What we went through with our daughter makes you see how important family is."

Balancing work and family can be a challenge, Dr. Filler says, but he has found the equilibrium he likes between the lab and the clinic. "I probably spend 75 percent of my time doing research," he says. "But I like doing both. Taking care of patients brings a more immediate reward and helps me focus on the important issues. Fortunately," he adds, "I've had a lot of support in my institution and am not pressured to spend more time in the clinic."

Dr. Filler credits his BWF award with jump-starting his faculty career. "As a result of my getting the BWF award, I was promoted to associate professor," he says, adding that he also used some of his BWF award to apply for an RO1 research project grant from the National Institutes of Health and got that as well. A promotion to full professor soon followed.

Outside work and his family, Dr. Filler's main hobby is long distance running. "I used to be an avid marathoner," he relates, "but I've cut back to half marathons and now do two a year here in California." Dr. Filler remembers his best marathon as one he ran while in college, finishing the course in 2 hours and 46 minutes. Perhaps most impressive, though, is that he finished in second place in an ultra-marathon, a punishing 41 mile test of endurance that he conquered in 5 hours and 15 minutes.

Attend almost any scientific conference in the biomedical sciences, and you will find that once-narrow biological disciplines are readily welcoming insights from physicists, mathematicians, and engineers.

Likewise, universities are creating multidisciplinary graduate programs that increasingly include students with backgrounds in theory or computation, and are building new, shared spaces where scientists from different disciplines can more easily interact and collaborate. Despite these promising trends, significant institutional and cultural barriers remain. Funds for trainees, for the most part, are still linked to departments or to a mentor's research grants. And the scientific culture in the biological disciplines is radically different from that within the computational and theoretical disciplines.

Recognizing the issues involved in collaboration across disciplines, in 1996 BWF launched a series of "social experiments" to educate students with backgrounds in the physical, computational, and mathematical sciences to tackle biological problems. BWF made 10 institutional training awards over three award cycles. Eight years into this experiment, it is still too early to assess career outcomes, since many of the program participants are still in training. A few principles have emerged from this experience, however, and these were summarized in a Policy Forum article in *Science* in fall 2003 (Sung, NS, Gordon, JI, Rose, GD, Getzoff, ED, Kron, SJ, Mumford, D, Onuchic, JN, Scherer, NF, Sumners, DL, and Kopell, NJ. 2003. Educating Future Scientists. *Science* 301:1485.) These principles include:

- Dual mentors are an effective way to ensure the trainee's immersion in the culture of two different scientific disciplines.
- Sharing trainees whose funding is independent of either mentor is an effective way of cementing a link between two research groups.
- Courses adapted to integrate theory with application in biology shorten the learning curve.
- It is important to immerse the physical, mathematical, and computational scientists in biology; otherwise, they risk being viewed as mere technical help for biologists rather than as participants in raising new research questions.
- The interdisciplinary culture should be as influential in the lives of the trainees as is the culture of their primary departments—this means that funding for community-building and social events is as necessary as funding for shared spaces. This community-building can take place at a distance through the use of Internet resources and periodic convening events.

During fiscal year 2004, BWF made no new awards in the area of Interfaces in Science. But in the spirit of community-building, the Fund convened trainees from three of our institutional programs in December 2003 in San Diego. More than 50 fellows from the University of Chicago, the University of California-San Francisco, and Princeton University gathered to present their work and discuss career issues unique to interdisciplinary scientists. David Botstein, Ph.D., director of the Lewis-Sigler Institute for Integrative Genomics at Princeton University, and Steve Chu, Ph.D., Nobel Laureate and professor of physics at Stanford University, gave keynote addresses. Not surprisingly, participants reported that their greatest benefit was the opportunity to network with peers.

In July 2004, BWF convened the latest recipients of our Career Awards at the Scientific Interface. Of the first two groups totaling 15 awardees and representing a $7.6 million investment, 11 have already made the transition into faculty positions at research universities. They share much in common with recipients of BWF's Career Awards in the Biomedical Sciences, with the added concern of building an academic career that straddles departmental boundaries. Through panel and roundtable discussions, BWF had the opportunity to listen to awardees' concerns with an eye to removing any obstacles that stand in their way. Through these convening events BWF hopes to contribute to the creation of a community in which the research careers of these bright young scientists can grow and flourish.

profile

Dr. Muhammad N. Yousaf Develops a Novel Process for Identifying Proteins

A chemist by training, Dr. Muhammad Yousaf is applying his background in surface chemistry to the task of identifying proteins, which could lead to developing potential drugs for a variety of ailments.

"Biology is where all the open questions are," says Toronto native Dr. Muhammad Yousaf, a 2003 recipient of a Career Award at the Scientific Interface. "I wanted to apply my surface chemistry tools to biology." With his BWF award, Dr. Yousaf is applying his extensive background in surface chemistry specifically to the challenge of identifying new proteins.

Armed with a Ph.D. in chemistry from the University of Chicago and a Harvard postdoc in cell biology, Dr. Yousaf set himself the daunting task of immobilizing small molecules and proteins on a two-dimensional surface while retaining their three-dimensional structures as they would appear in their normal biological environment. "It's no problem to get a protein to stick to a surface," Dr. Yousaf says, "but it becomes a mess." So, how do you capture a protein on a surface while at the same time preserving its structure? The answer, according to Dr. Yousaf, is by controlling the surface chemistry. And after solving the problem of immobilizing a protein in its pristine state, how do you then add a complex protein mixture to the immobilized protein and observe the reaction between proteins without the interaction of the surface and protein mixture getting in the way? The answer again is surface chemistry.

"The key to our surface technology is that the surfaces are based on self-assembled monolayers of alkanethiolates on gold," says Dr. Yousaf. "Essentially it is a molecular-level carpet. There are three main advantages with these particular surfaces: You can easily make mixed monolayers where there are many components presented on the surface; the alkanethiolates are synthetically flexible—routine organic synthesis allows you to decorate the surface with all sorts of chemical properties and molecules; and the surfaces are conductive, a feature that allows for many analytical surface spectroscopies to characterize the interactions on these surfaces," he adds. "These surfaces give us access to MALDI (matrix-assisted laser desorption ionization). In order to use MALDI mass spectrometry, the surfaces have to be conductive." And the surfaces must be extremely clean, he adds, because the MALDI-TOF/TOF (time of flight) instrument is so sensitive. That is why he uses gold for his surfaces instead of other metals, such as silver or copper, which oxidize over time.

A basic mass spectrometer enables peptide mass fingerprinting, which is the identification of a protein based on the specific group of peptide masses it produces. The MALDI spectrometer takes the process a step further by also providing peptide sequence information. Having the peptide sequence information enables the researcher "to unambiguously identify the protein using the protein database," Dr. Yousaf explains. Numerous proteins may have the same peptide mass, he notes, which makes it difficult to identify a protein unless the researcher also has the peptide sequence information.

To enable the MALDI spectrometer to identify a peptide sequence, the researcher must add to the surface an enzyme called trypsin, which chews the immobilized protein into fragments. "The key," Dr. Yousaf says, "is that trypsin chews up proteins in specific fragments because it recognizes a specific sequence. Then when the proteins are ionized, you see their peptides." However, only a percentage of the protein's peptides will ionize in the mass spectrometer.

The beauty of Dr. Yousaf's approach is that he and his team have combined controlled surface chemistry with MALDI

mass spectrometry to detect and identify proteins. He has termed his new process SpaM: self-assembled monolayers, in-situ proteolytic digestion and MALDI mass spectrometry.

Inside the MALDI mass spectrometer, lasers ionize proteins (turn them into a gaseous state) and then the protein ions speed down the flight tube as the spectrometer measures their mass based on their time of flight. In the MALDI-TOF/TOF, the first TOF measures the peptide's mass and the second breaks down the peptide into amino acids—the individual sequence of that peptide.

"The surface chemistry has to be well defined." Dr. Yousaf says. "There has to be no or very little nonspecific protein absorption on the surface" so that the researcher can identify the protein using MALDI.

"How do you capture a protein on a surface while at the same time preserving its structure? The answer, according to Dr. Yousaf, is by controlling the surface chemistry."

Dr. Yousaf says there are numerous applications for the new technology, including identifying unknown proteins, teasing out the difference between normal cells and cancer cells by identifying which proteins are over expressed in cancer cells, and discovering potential drugs by immobilizing small molecules to see which ones bind to which proteins. "Small molecules bind to partner proteins," Dr. Yousaf says. "We can identify the protein using mass spectrometry, and the small molecule is potentially a drug for that protein."

The chemist-turned-biomedical researcher has been strategic about his early career choices. "I was fortunate to work with a very dynamic and exciting assistant professor, Dr. Milan Mrksich," says Dr. Yousaf. "Dr. Mrksich was a surface chemist who wanted to make microarrays and model substrates. I was in his first class of students, and I chose to work with him because he was on the frontier of research.

"Dr. Mrksich introduced me to big science," he adds. "When you work with an assistant professor, you can get a thesis project and push it all the way to the end, tackle it from all angles. In a big lab, you're competing with other students."

Likewise, Dr. Yousaf turned down offers from other top institutions to take a position at the University of North Carolina-Chapel Hill as an assistant professor in both the chemistry department and the Carolina Center for Genome Science. He says he picked UNC because he was offered "a great interdisciplinary position." Dr. Yousaf says he is also a sports enthusiast and loves basketball. With a position at UNC, he will definitely be watching more basketball.

"All students need the level and quality of science, mathematics, and technology (SMT) education that successfully prepares them to solve a wide variety of problems, pursue graduate study in SMT, assume civic responsibilities by understanding SMT issues affecting a global society, and participate in a dynamic and internationally competitive economy."

(N.C. Mathematics and Science Coalition Governing Board 1994-95)

This vision—created by a statewide group of education, public policy, civic, community, and business leaders—is still relevant in 2005. We need to teach our children about SMT and its importance in our lives, because we are growing the next generation of young scientists.

Engaging children in SMT continues to be a focus of the Burroughs Wellcome Fund's science education program. We are convinced that all children, regardless of background or gender, need basic SMT literacy to participate fully in civic life. We believe that the best method for achieving the goal of science literacy is to get students involved in the scientific process and let them do what comes naturally: ask questions and participate in hands-on activities and experiments that convey basic scientific principles.

BWF's Student Science Enrichment Program (SSEP) has been supporting innovative science education projects since 1996 and provides over $1 million annually to nonprofit organizations—public and private schools, universities, colleges, museums, and community groups—that offer creative science education activities for N.C. middle- and high school students. These enrichment activities take place outside the classroom and are aligned with the North Carolina Standard Course of Study. We received 46 applications for the 2004 SSEP and made six awards totaling $876,155. During the program's eight-year history, BWF has invested $9.1 million, reaching more than 23,000 students through 67 SSEP awards. Through program evaluations, we learned that more than 46 percent of student participants in last year's program viewed science as a career option.

BWF is partnering with key organizations to develop an infrastructure for improving SMT education across the state. With the Public School Forum of North Carolina, BWF created an Institute for Educational Policymakers to forge relationships among legislators, members of the State Board of Education, and members of the media around issues related to school improvement. BWF and the North Carolina School of Science and Mathematics have collaborated to use multimedia technologies to interconnect schools across the state for teacher training and institutional reform in SMT education. The Grassroots Museum Collaborative supports hands-on science learning across North Carolina through programs and activities offered by more than 21 member science museums.

Our most recent major investment in SMT education has been launching and supporting the North Carolina Science, Mathematics, and Technology Education Center. The SMT Center represents a partnership of organizations that are stakeholders in advancing SMT education in North Carolina and serves as a catalyst to integrate plans to systematically improve the performance of N.C. secondary school students in SMT. The SMT Center also engages scientists in this process through its Teacher Link Program, which trains scientists to mentor teachers as they implement new research-based, hands-on science curricula. By establishing and supporting the SMT Center, our aim is to make science, mathematics, and technology education a high priority on the state's education agenda and keep it there.

profile

North Carolina State University's Science House Teaches Minority Youth that Physics is Shining the Way to Their Future

Photonics Xplorers, a program offered by North Carolina State University's Science House, intrigues students because it relates lessons to the gadgets in their lives—such as cell phones and MP3 players.

U.S. Senate candidate Barack Obama made headlines when he told the 2004 Democratic National Convention in the keynote address that inner city children "can't achieve unless we raise their expectations and turn off the television sets and eradicate the slander that says a black youth with a book is acting white."

"I agree 10,000 percent," says Dr. Joyce Hilliard-Clark, coordinator of the Imhotep Academy at The Science House, a learning outreach center at North Carolina State University.

Earlier in 2004, when Dr. Hilliard-Clark had been looking for a way to engage more minority youth in science education, she asked the director of The Science House, Dr. David Haase, to identify the hottest topic in science. The physics professor came back with "photonics."

That answer sent Dr. Hilliard-Clark, who has a Ph.D. in forestry and was a high school biology teacher, to faculty in N.C. State's science and engineering departments. From them, she learned about the science and technology of using light to carry information, and the more she learned, the more she wanted to share that knowledge with minority students.

"But what excites adults doesn't excite kids," she says. To get them interested in the applications of science and mathematics, she explains, teachers must relate the lessons to the gadgets in kids' lives, such as cell phones, MP3 players, and grocery bar code scanners.

With support from the Burroughs Wellcome Fund, Dr. Hilliard-Clark organized Photonics Xplorers—a two-year program in which 22 high school freshmen gather one week during the summer and one Saturday each month to explore the power of light in their lives. Along with receiving classroom instruction in physics and mathematics, the students get to tour the labs of N.C. State University and area technology companies.

The program kicked off in the summer of 2004. On one of their tours, the students visit Cisco Systems, a leading Internet networking company. Back in the laboratory the next day, Brandon Conover, the Photonics Xplorers teaching coordinator, quizzes the students on how incandescent light bulbs work and then explains that new traffic signals use clusters of light-emitting diodes (LEDs) instead. "When we went to Cisco," one student remembers, "all the indicator lights were LEDs." Brandon Conover then takes the class through an experiment with fiber-optic cables and angles of refraction.

Grasping how science and technology interact is important not just because a rising political star like Barack Obama says so. "The chance for these students to do well in physics is greater than in sports," says Dr. Hilliard-Clark. Harvard professor Dr. Henry Louis Gates Jr., writing in *The New York Times* this past summer, set the record straight on such dreams: "According to the 2000 census," he wrote, "there were more than 31,000 black physicians and surgeons, 33,000 black lawyers and 5,000 black dentists." But that year there were just 1,400 black athletes playing professional basketball, football, and baseball.

Dr. Hilliard-Clark laments that one of her greatest challenges is finding African American males who want to teach young people. She is excited, however, to have 10 African American young men enrolled in the program. Ninety percent of the students enrolled identified themselves as African American

and 10 percent as Caucasian or other. Students come from Harnett, Johnston, Lenoir, Pitt, and Wake Counties.

"I want to congratulate you on being here," Dr. Hilliard-Clark says to the students early on a Saturday in July. One young man has already been up since 4 a.m. and has gone to football practice; he will return to practice after the day's classes about lasers, mathematics equations, and time management.

Dr. Hilliard-Clark reminds them that the academy they are attending is named for Imhotep, the Egyptian physician-priest and architect of the famous stepped Pyramid of Djoser. "We want you to have those same skills and aptitudes," she says. She has divided the students into three groups, named for Edward Alexander, the first African American to earn a doctorate from an American university; Walter Massey, a physicist and the president of Morehouse College; and Kristina Johnson, dean of the Pratt School of Engineering at Duke University.

"With support from the Burroughs Wellcome Fund, Dr. Hilliard-Clark organized Photonics Xplorers—a two-year program in which 22 high school freshmen gather one week during the summer and one Saturday each month to explore the power of light in their lives."

Photonics Xplorers, says Dr. Hilliard-Clark, is meant to be a bridge program to help students prepare for the faster pace of high school science and mathematics classes, and later, for the rigors of college coursework. She recruited the cohort by asking area middle schools to recommend their brightest students. All but five of the students had already participated in the Imhotep Academy and other middle school pre-college programs.

In return for their two-year commitment to the Xplorers program, Dr. Hilliard-Clark promises each student $1,000 in scholarship money for college. Of course, she says, "we want them to come to N.C. State University with its cutting-edge technology."

In addition to being assigned homework by their instructors, the students are asked to write short responses about their favorite teachers or whether a field trip was worth repeating. Dr. Hilliard-Clark compiles their answers in a daily newsletter.

"I would definitely recommend Photonics to someone," writes one student. "But I would have to tell them that it's no walk in the park. They should come to learn and not to mess around." Another student writes that she wanted to attend the program because "I want the opportunity to do what others have not done."

Parents support the program as well. Lendell Wayne of Kinston, N.C., says she is thrilled that her son, Brian, is getting an introduction to physics. "I feel comfortable that when he hits high school he'll have an edge," she says. To help Brian keep that edge, Dr. Hilliard-Clark and her teachers have created an Internet chat room/discussion group in which the students can share their high school experiences.

Dr. Hilliard-Clark says she has just about convinced the students that education will pay off for them. She relates the lesson to her recent trip to Japan, where she encountered a fully automated food kiosk. "It doesn't take you long to figure out how many jobs will be eliminated by that technology," she says. She tells the students someone will have to create and repair those machines. "It might as well be you."

BWF's Translational Research focus area grew out of our longstanding commitment to the therapeutic sciences, which in the past supported award programs in the areas of clinical pharmacology, pharmaco-epidemiology, drug design, experimental therapeutics, toxicology, and pharmacology.

Since 1998, BWF has made a $39 million investment in more than 50 Clinical Scientist Awards in Translational Research —to foster the productivity and creativity of physician-scientists whose work translates basic science discovery into clinical knowledge and, ultimately, to patient care. The program selects for investigators with a strong track record not only as scientists but also as mentors.

BWF made no new awards in 2004, but we did continue our tradition of convening awardees for in-person progress updates roughly midway through the five-year award period. This year's meeting had a new twist: "bring your own trainee."

Because the Translational Research program emphasizes mentoring the next generation of physician-scientists, we asked each awardee to bring a medical student or fellow to the meeting, which was held in Chicago in April 2004. All awardees and trainees presented their work to the program advisory committee and participated in several discussions on issues they face as translational investigators.

There was no lack of confidence among the group of investigators regarding their ability to master the scientific challenges of their work. It was clear, however, that many felt daunted by the increasingly complex regulatory environment they encounter in launching clinical studies, and some of them expressed difficulty in gaining access to proprietary compounds with potential therapeutic effect. The group also discussed the benefits as well as the drawbacks of team science—the need to have diverse teams to carry out clinical studies while each member is seeking to survive professionally in an academic environment that rewards individual achievement above teamwork.

Each of these "environmental" issues reflects the complexity of the clinical research enterprise and illustrates the need for system-wide solutions. To that end, BWF has continued to participate actively in the Clinical Research Roundtable (CRR), based at the Institute of Medicine of the National Academy of Sciences. Chaired by BWF president Dr. Enriqueta Bond, the CRR has brought together the diverse stakeholders in the enterprise: academic health center leaders, clinical investigators, pharmaceutical companies, patient advocates, government funding and regulatory agencies, health insurers, and large employers who purchase health care. Among other issues, the group has focused on the need to streamline regulations, improve the success rate of clinical trials, ensure the safety of clinical trial participants, stimulate professional societies to collaborate, and remove the disincentives to clinical investigators within academic health centers.

BWF also provided modest support to the Consortium to Examine Clinical Research Ethics, which is studying the landscape of institutional review boards and their associated costs, as well as determining how effectively current processes are protecting human subjects. In addition, BWF has provided leadership to the growing Health Research Alliance, a consortium of foundations and voluntary health agencies whose history and work is summarized elsewhere in this report.

After a full year of involvement in activities that influence the environment in which our awardees work, BWF is looking forward to selecting and supporting another round of Clinical Scientist Awards in Translational Research in the coming year.

profile

Dr. David Scadden Exploits the Vast Potential of Stem Cells

Dr. David Scadden, who, among his other titles, is codirector of the new Harvard Stem Cell Institute, is launching a clinical trial using parathyroid hormone to aid in bone marrow transplant for lymphoma.

His curiosity about how the human immunodeficiency virus (HIV) is able to wreak havoc on a broad spectrum of immune cells led hematologist/oncologist Dr. David Scadden to investigate the chameleon of cells: stem cells—unspecialized cells that renew themselves through cell division and can morph into cells with specific functions, such as insulin-producing pancreatic cells.

"I was interested in the role of stem cells in HIV disease," says Harvard's Dr. Scadden, recipient of a 2002 Clinical Scientist Award in Translational Research, "particularly blood-forming stem cells that are important in the formation of all the blood and immune elements. Since all immune elements are depressed in advanced HIV disease, I wondered if those stem cells were a target of the virus," he adds. "From that, I became interested in understanding more basic mechanisms of the way stem cells are regulated, with an eye toward using those mechanisms to manipulate the stem cell for therapeutic purposes."

Dr. Scadden's research first focused on identifying the barriers that prevent stem cells from being used more broadly in treating a number of different diseases—not just in treating diseases of the blood or immune system, such as HIV, leukemia, and lymphoma. Three specific barriers surfaced as needing further investigation: stem cell number, cell localization, and targeted differentiation.

"Stem cells are very rare cells," Dr. Scadden explains. "Identifying and isolating them has been a complex undertaking, and being able to get enough of them to use clinically has been a real problem." Even in the context of bone marrow transplants, the number of cells needed for a human is extraordinarily high compared to the number needed in a mouse, Dr. Scadden says. "In humans, we need 5 million per kilogram for a bone marrow transplant in an adult," he says.

The limited number of stem cells poses problems for patients needing autologous stem cell transplantation: 10 percent to 20 percent of these patients do not have enough of their own stem cells to undergo the potentially life-saving procedure. And a third of patients waiting for a bone marrow donor will not find one. Umbilical cord blood, which could solve the donor problem, is not useful because the number of stem cells present in such blood is too small to effectively transplant into an adult.

One of the huge hurdles to overcoming the barrier of too few stem cells is that "stem cells are hard wired to be quiescent," Dr. Scadden explains. "I think the evolutionary reason is that stem cells can be quite dangerous. They could form a tumor, for example. So stem cell constraint gets imposed early on in the development of an organism and is maintained in the adult."

In general, stem cell populations in the body are resistant to growth. "They're geared to a maintenance function rather than regeneration," Dr. Scadden says. "We thought if we could understand what restricts their growth, we might be able to develop strategies to increase their numbers. So we've tried to identify the brakes on cell cycling and have defined a number of cyclin dependent kinase inhibitors (CDKI)—a class of molecules abundant in primitive cells that serve as brakes."

Dr. Scadden and his team found that eliminating CDKIs in a mouse model increases the stem cell pool and the ability of certain tissues to repair themselves after injury. When they tested their theory on human stem cells, they found that

reducing the expression of one of the CDKI molecules—p21—could actually increase the number of stem cells. "We don't know if this discovery will ultimately be useful, but we hope that it will," Dr. Scadden says.

Dr. Scadden's approach is to examine how stem cells function in the context of the niches they inhabit in complex tissue, specifically the hematopoietic stem cells niche. "We know that blood stem cells move in the course of development to different locations," he explains. "And with each of those transitions in location they have a different function," he adds. "It looks like location does have a big impact. We want to understand one of the components of where stem cells live that might be relevant to these changes of function."

"In general, stem cell populations in the body are resistant to growth... We thought if we could understand what restricts their growth, we might be able to develop strategies to increase their numbers."

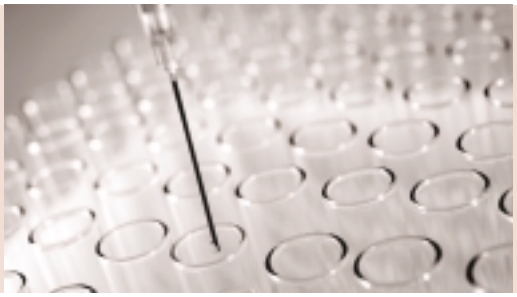
So Dr. Scadden decided to look at bone marrow stem cells and collaborated with endocrinologists to learn about the unique aspects of bone that distinguish it from other tissues. In the process, they identified three components of bone that would be amenable to genetic modification: osteoblasts (bone-forming cells), matrix (crystalline mineral salts, calcium, and collagen), and ionic calcium (calcium found in the blood). He and his colleagues found that each of the components has an impact on stem cells. In particular, they noticed that if they activated the osteoblasts, they could increase the number of stem cells. Using this discovery in a mouse model, they gave osteoblast-stimulating hormones to normal mice and then put them through a bone marrow transplant, giving them too few cells for a viable transplant. The results: the mice that received only stem cells had a 70 percent mortality rate; those that received the hormone in addition to stem cells had a zero mortality rate.

The hormone, parathyroid hormone, or PTH, was approved only a year ago for treating osteoporosis. "We are initiating a human trial using PTH in the setting of bone marrow transplant for lymphoma (both Hodgkin's disease and non-Hodgkins lymphoma)," Dr. Scadden says. "We couldn't do this without the BWF award; we're buying the drug and supporting the investigators in the clinic with BWF funding." The clinical trial is currently in the approval process.

Though he still sees patients, Dr. Scadden divides most of his time between the lab and his duties as director of the Center for Regenerative Medicine and Technology at Massachusetts General Hospital and codirector, with developmental biologist Dr. Doug Melton, of the newly inaugurated Harvard Stem Cell Institute.

For a physician-scientist so deeply involved in research and mentoring young scientists, Dr. Scadden came to his vocation circuitously: he earned a B.A. in English literature from Bucknell University and wrote a thesis on William Butler Yeats. But the stage was set early for scientific pursuits; he fondly remembers the lab his father built in the basement so young David could experiment with his chemistry set and anything else that aroused his curiosity. Years later, when he realized that his English degree was not proving useful in launching his career, Dr. Scadden decided to try medical school, based on his admiration for his family doctor. Decision became reality and Dr. Scadden acquired solid experience with clinical trials along the way. "I enjoy taking care of patients," he notes, "but I also like having a sense of both worlds, and this has allowed me to facilitate movement between the clinic and the lab."

The Health Research Alliance: A New Consortium of Funders



The Health Research Alliance has brought together major funders of health and biomedical research in a desire to enhance their effectiveness through collective action.

Health scientists routinely share their results at scientific meetings and in journals, but funders of health research have had no established forum in which to consider the changing scientific and medical landscape, to share information on which of their projects have worked and which have not, and to identify common ground for collaborations. With this reality in mind, a group of private funders of health research convened in 1998 at a meeting titled *Strengthening Health Research in America: Philanthropy's Role*. Jointly organized by the American Cancer Society, the Burroughs Wellcome Fund, the Howard Hughes Medical Institute (HHMI), and the Pew Charitable Trusts, this unique gathering attracted attendees from more than 50 grant-making organizations. Together, they considered the future of biomedical research in light of major changes in the funding streams for research within academic health centers.

The group met again in 2000 and 2002 to consider the role of private funders in training the next generation of biomedical scientists and to share best practices on basic operational processes, such as electronic grant making.

The ethos of these meetings was simple: they were organized by funders for funders and they focused on fact-finding rather than on pushing a particular agenda. The goals were to build a health research funders' network and to identify a few ideas around which smaller groups could take action. Following the meeting in 2000, one such group—calling itself the Clinical Research Alliance (CRA)—began to meet periodically. The group included a mix of private foundations and voluntary health organizations that focus on cancer, diabetes, arthritis, and heart disease. Although these organizations can rightly be considered competitors—for donor dollars and for talented clinical investigators in their disease areas—they recognized that they had to address the systemic disincentives that were driving the next generation of clinical investigators out of research. Accordingly, the CRA prompted the launch of several new award programs (by the Juvenile Diabetes Research Foundation and the American Heart Association, among others) that would provide not only generous, portable research funding for at least five years, but also educational loan repayment for the awardees.

Recognizing that the scope of private philanthropic funding for biomedical research was largely unknown, the CRA assembled data showing that between 1997 and 2001, collective support for career development of clinical investigators more than doubled, with the total annual commitment rising from $37 million to $78.5 million (*NEJM* 349:1860, 2003). Armed with this evidence of its substantial investment, the group felt it could creditably comment on remaining needs, in the hope of leveraging more funding for career development of clinical investigators. Members of the group then authored several prominently placed editorials (*Science* 293:573,2001; *NEJM* 346:2013, 2002) and met with leaders of the National Institutes of Health (NIH) to express a shared concern for clinical investigators' career development and to press for implementation of the NIH extramural loan-repayment program.

Beyond encountering hurdles in career development, clinical investigators who aim to translate basic science discoveries into clinical knowledge, and ultimately into better health, face myriad systemic barriers. Recognizing that these

issues are far too complex to be solved by any one organization, members of the CRA became active in the Institute of Medicine's Clinical Research Roundtable. This effort brought together system-wide stakeholders, representing not only the interests of academic investigators, but also those of pharmaceutical companies, government agencies, patient advocates, health insurance companies, and large employers who pay the bulk of health care costs. Emerging from this extended dialog was the concept of two translational blocks: translating basic biomedical discoveries into pre-clinical and clinical studies, and translating clinical knowledge into clinical practice and better health (*JAMA* 289:1278,2003).

"...the Clincal Research Alliance assembled data showing that between 1997 and 2001, collective support for career development of clinical investigators more than doubled, with the total annual commitment rising from $37 million to $78.5 million."

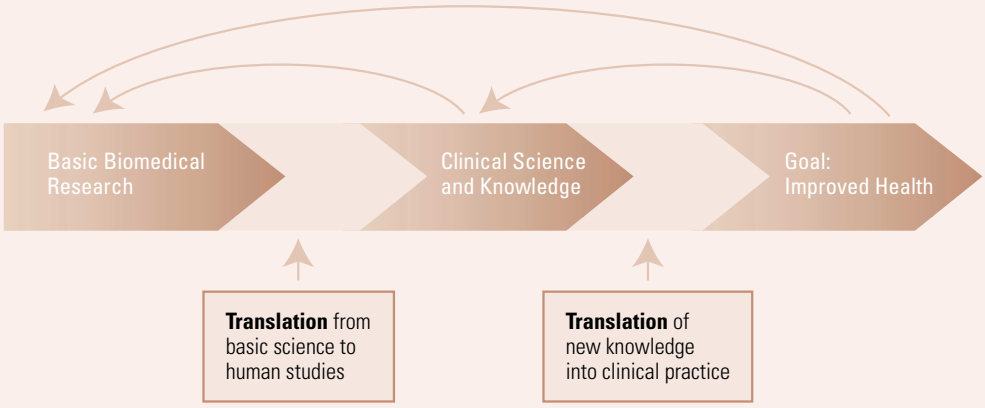
In the wake of the NIH "Roadmap" for medical research in the coming century, early in 2004 the CRA convened a large meeting—jointly planned by leaders from eight foundations and voluntary health organizations and led by BWF to explore the unique role of private funders of biomedical and health research in addressing the two translational blocks (see graphic below).

The agenda for this meeting—*Partnering to Advance Health Research: Philanthropy's Role*—centered on building partnerships among like-minded nongovernmental funders as well as governmental funders and for-profit entities. The first part of the meeting focused on accelerating the development of new therapeutics and vaccines, and the second part focused on partnership models that influence health outcomes.

Representatives from more than 70 biomedical research foundations and voluntary health agencies attended the meeting. Participating funders included some narrowly focused on one disease as well as some whose mandate was as broad as "health." The distribution of asset levels among the participating organizations formed a bell curve, including roughly equal numbers of those with annual budgets less than $1 million and more than $100 million, with the majority scattered in between.

The response to this event was overwhelmingly positive and underscored the need for nongovernmental funders of health research to forge collaborations around common interests and

THE TWO TRANSLATIONAL BLOCKS



Two translational blocks impede efforts to apply science to improve human health in a timely fashion. The first translational block involves the transfer of new understandings of disease mechanisms gained in the laboratory into the development of new methods for diagnosis, therapy, and prevention and their first testing in humans. The second translational block affects the translation of results from clinical studies into everday clinical practice and health decision making.

to share best practices. Participants also agreed that in an era of constrained resources and increased accountability, there is a need for greater coordination not only in making grants but also in evaluating their outcomes.

At the conclusion of the meeting, 17 of the participating organizations formed several working groups that reported on their plans at a follow-up meeting in May 2004, at HHMI. What emerged from this meeting was a strong consensus that the heretofore informal Clinical Research Alliance should be formalized and renamed the Health Research Alliance, to reflect our concern for research that leads to better health, not just the advance of biomedicine. The organization's mission is to improve communication, foster collaboration, and enhance the overall effectiveness of grant makers in the field of biomedical and health research.

In practical terms, a more formal organization will enable the working groups to make greater progress, will enable the inclusion of a larger number of interested funders, and, perhaps most importantly, will establish a unified voice for the community of nongovernmental funders of health research.

Member organizations approach their work with a wide variety of concerns, priorities, and strategies, but they share a common goal: fostering basic science discoveries and removing barriers that prevent discoveries from being translated into clinical studies, and, ultimately, into better health.

BWF is proud to have been a key leader in the development of the Health Research Alliance and will continue our commitment by hosting an office in our facility and hiring a part-time staff member to lead the HRA's activities. For more background on the group's activities, see ***http://www.bwfund.org/news/health_research_alliance_index.html.***

Partnering to Advance Health Research: Philanthropy's Role was planned by BWF, the American Heart Association, the Howard Hughes Medical Institute, the Doris Duke Charitable Foundation, the Arthritis Foundation, the Juvenile Diabetes Research Foundation International, the Robert Wood Johnson Foundation, and the American Cancer Society.

The Burroughs Wellcome Fund's investments totaled $627.9 million at August 31, 2004, 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 is placed in strategies that derive the bulk of their returns from exposure to U.S. and international capital markets. Consequently, fluctuations in BWF's investment results will be due largely to variability in capital market returns.

BWF develops our investment policies 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.

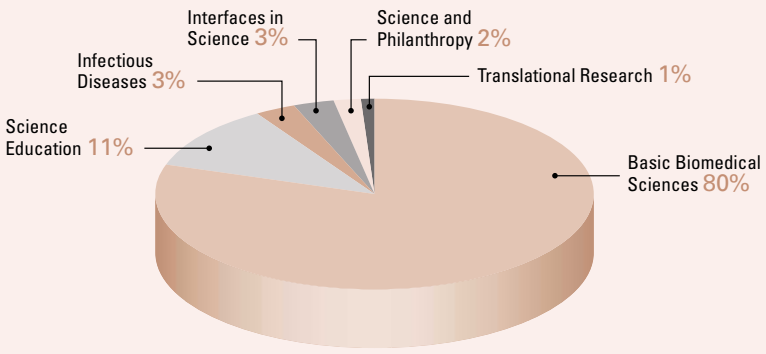
As part of BWF's investment strategy, we have established "allocation targets"—percentages of our total assets to be invested in particular asset classes. Investment managers hired by BWF pursue more focused mandates within each sector. As of the end of the fiscal year, BWF's asset mix and market values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

- U.S. large capitalization equity assets had a market value of $151.9 million. The sector's target allocation was 26 percent, and actual holdings stood at 24.2 percent.
- U.S. small capitalization equity assets had a market value of $103.3 million. The sector's target allocation was 19 percent, and actual holdings stood at 16.5 percent.
- International equity assets had a market value of $155.6 million. The sector's target allocation was 27 percent, and actual holdings stood at 24.8 percent.
- Fixed income assets had a market value of $122.6 million. The sector's target allocation was 25 percent, and actual holdings stood at 19.5 percent.
- Cash equivalent assets had a market value of $38.5 million. The sector's target allocation was 3 percent, and actual holdings stood at 6.1 percent.
- Alternative assets had a market value of $56 million. The sector did not have a target allocation, and actual holdings stood at 8.9 percent. The maximum permitted allocation to alternative assets stood at 14 percent.

The total market value of BWF's investments increased by $40.9 million, or 7 percent, from the end of the previous fiscal year. This increase in assets was due primarily to good returns in world equity markets in the fourth quarter of 2003 and the first two months of 2004. BWF's total investment return for the fiscal year was 12.2 percent. Returns in all three equity sectors and the fixed income sector were positive for the fiscal year. The U.S. large capitalization equity sector returned 10.9 percent; the U.S. small capitalization equity sector had a 19.5 percent return; the international equity sector posted a return of 17.6 percent; and fixed income produced a 6.5 percent return.

As of August 31, 2004, BWF employed 10 investment managers. In the U.S. large capitalization equity sector, the managers were Independence Investment Associates; LSV Asset Management; and Cohen, Klingenstein and Marks. Credit Suisse Asset Management, Kennedy Capital Management, and U.S. Bancorp Asset Management managed U.S. small capitalization equities. Pacific Investment Management Company and Smith Breeden Associates were the fixed income managers. Capital Guardian Trust Company and Hansberger Global Investors managed international equities. BWF also held investments in eight venture capital funds: Intersouth Partners IV, V, and VI; Spray Venture Funds I and II; Mission Ventures II; the North Carolina Bioscience Investment Fund; and A. M. Pappas Life Science Ventures II. Finally, Quellos Capital Management managed a fund of absolute return strategies.

Grants Awarded



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, 2004 and 2003, 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 2004 audit was conducted for the purpose of forming an opinion on the basic financial statements taken as a whole. The information presented 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
November 23, 2004

Statements of Financial Position

August 31, 2004 and 2003

(All dollar amounts presented in thousands)

	2004	2003
Assets		
Cash and cash equivalents	$95,769	$27,587
Marketable securities	508,623	549,712
Accrued interest and dividends receivable	1,564	2,139
Transactions receivable, net	22,158	7,964
Other assets	20	40
Total current assets	628,134	587,442
Property and equipment, net	12,652	13,230
Total assets	$640,786	$600,672
Liabilities and Net Assets		
Accounts payable and other liabilities	900	600
Federal excise tax payable	521	-
Deferred excise tax payable	308	498
Unpaid awards	52,988	64,566
Total liabilities	54,717	65,664
Unrestricted net assets	586,069	535,008
Total liabilities and net assets	$640,786	$600,672

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

Statements of Activities

Years Ended August 31, 2004 and 2003

(All dollar amounts presented in thousands)

	2004	2003
Revenues:		
Interest and dividends, less investment expenses of $3,805 and $2,767 in 2004 and 2003, respectively	$ 9,588	$ 11,167
Net realized (loss) gain on sales of marketable securities	52,330	(9,766)
Total revenues	61,918	1,401
Expenses:		
Program services	11,346	18,810
Management and general	5,590	4,269
Total expenses before net unrealized appreciation and deferred federal excise tax	16,936	23,079
Net unrealized appreciation of marketable securities, net of (benefit from) provision for deferred federal excise taxes of ($190) and $498 in 2004 and 2003, respectively	6,079	64,339
Change in net assets	51,061	42,661
Net assets at beginning of year	535,008	492,347
Net assets at end of year	$586,069	$535,008

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

Statements of Cash Flows

Years Ended August 31, 2004 and 2003

(All dollar amounts presented in thousands)

	2004	2003
Cash flows from operating activities:		
Change in net assets	$ 51,061	$ 42,661
Adjustments to reconcile change in net assets to net cash (used in) provided by operating activities:		
Depreciation	641	661
Net realized (gain) loss on sales of marketable securities	(57,330)	9,766
Net unrealized appreciation (depreciation) of marketable securities	(5,772)	(64,837)
Provision for deferred federal excise taxes	331	498
Awards granted, net of cancellations and change in unamortized discount	11,545	19,085
Award payments made	(23,123)	(25,458)
Changes in operating assets and liabilities:		
Accrued interest and dividends receivable	575	(5)
Other assets	20	(12)
Transactions receivable, net	(14,194)	(7,964)
Transactions payable, net	-	(15,459)
Accounts payable and other liabilities	300	(123)
Net cash used in operating activities	(30,946)	(41,187)
Cash flows from investing activities:		
Purchases of marketable securities	(964,058)	(1,237,408)
Proceeds from sales of marketable securities	1,063,249	1,281,158
Purchase of property and equipment	(63)	(21)
Net cash provided by investing activities	99,128	43,729
Net (decrease) increase in cash and cash equivalents	68,182	2,542
Cash and cash equivalents at beginning of year	27,587	25,045
Cash and cash equivalents at end of year	$95,769	$27,587
Supplemental disclosure of cash flow information:		
Cash paid during the year for federal excise taxes	$ 140	$ -

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

Years Ended August 31, 2004 and 2003

(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; 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 gains or losses 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 these forward currency contracts totaled $7,984 and $8,021 at August 31, 2004 and 2003, respectively. Realized gains on forward currency contracts totaled ($236) and $85 in 2004 and 2003, respectively. The market value of open forward currency contracts at August 31, 2004 and 2003 was $57 and $4, respectively. The market value is recorded as an asset in the Fund's financial statements. The average market value of open foreign currency contracts totaled ($119) and $218 for the years ending August 31, 2004 and 2003, 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, 2004 and 2003 were $1,179 and $958, 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, 2004 and 2003 is the net settlement relating to these contracts of $1,502 and ($102), 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 ($120) and ($8) at August 31, 2004 and 2003, respectively, which is recorded as an asset in the Fund's financial statements. The average fair value of open contracts totaled ($36) and ($27) for the years ending August 31, 2004 and 2003. Realized losses on options totaled $143 and $261 for the years ending August 31, 2004 and 2003, 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 or depreciation in the accompanying statements of activities. The Fund has investment advisors, which manage its 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 expensed at their fair value in the year in which the award is granted. Grants payable over several years are 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 statement of activities.

Estimated Fair Value of Financial Instruments

Financial instruments include cash and cash equivalents, marketable securities, accrued interest and dividends receivable, accounts payable, and unpaid awards. All financial instruments are reported at their estimated fair value. The carrying values of accrued interest and dividends receivable, accounts payable, and unpaid awards 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 generally accepted accounting principles 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 consisted of the following:

	2004	2003
Building	$13,451	$13,451
Furniture and fixtures	1,735	1,735
Computer equipment	757	694
	15,943	15,880
Less: accumulated depreciation	(3,291)	(2,650)
	$12,652	$13,230

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 tax liability on unrealized appreciation of marketable securities. At August 31, 2004, the Fund is in a net unrealized appreciation position, therefore, a deferred federal excise tax liability of $308 was recorded. At August 31, 2003, the Fund was in a net unrealized appreciation position, therefore, deferred federal excise tax liability of $498 was recorded.

4. Qualified Distributions

The Fund is required to distribute 5 percent 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 percent of the undistributed income of the Fund.

5. Unpaid Awards

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

	2004	2003
Payable in less than one year	$20,769	$24,660
Payable in one to five years	32,555	41,329
	53,324	65,989
Unamortized discount	(336)	(1,423)
Total	$52,988	$64,566

The expected future liability to the Fund has been calculated based on discount rates ranging from 1.24 percent to 3.80 percent.

6. Marketable Securities

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

	2004		2003	
	Cost	Estimated Market Value	Cost	Estimated Market Value
U.S. and foreign governmental obligations	$16,922	$18,920	$64,792	$66,954
Corporate bonds	21,315	22,111	29,980	30,802
Common and preferred stocks	254,562	272,888	258,779	276,802
Foreign stocks and foreign equity funds	123,765	138,869	117,258	121,083
Option and forward foreign currency investments	(87)	(120)	(9)	(8)
Venture capital investments	19,010	12,475	16,798	11,930
Mutual fund	42,454	43,480	37,232	42,149
	$477,941	$508,623	$524,830	$549,712

7. Employee Benefit and Retirement Plans

The Fund provides medical insurance to all employees working at least thirty hours per week. Coverage extends to each employee's spouse and dependent children, if applicable. The expense for this employee benefit was $204 and $148 during fiscal 2004 and 2003, respectively. The Fund has a defined-contribution retirement plan covering all employees working at least twenty hours per week. Under the terms of the plan, the Fund matches 50 percent of all employees' contributions up to 6 percent of the employee's annual compensation. Employees are 100 percent 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 percent of the employee's annual compensation. This plan covers all employees and vesting in contributions is immediate. The expense for these retirement plans was $46 and $177 in fiscal 2004, and $43 and $167 in fiscal 2003, respectively.

8. Classification of Expenses

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

	2004		2003	
	Program Services	Management and General	Program Services	Management and General
Awards granted, net of cancellations and refunds of $4,191 and $7,833 in 2003 and 2002, respectively	$11,286	$ -	$18,616	$ -
Federal excise tax	-	661	-	122
Salaries and other employee expenses	140	2,340	93	2,188
Depreciation expense	-	641	-	661
Travel and entertainment	14	628	13	256
Maintenance and supplies	1	559	2	438
Honoraria	-	267	-	310
Professional fees	43	190	82	223
Printing and design costs	-	86	4	46
Miscellaneous	1	79	-	25
Total expenses	$11,485	$5,451	$18,810	$4,269

9. Related Parties

North Carolina Science, Mathematics, and Technology Education Center, Inc. ("SMT") 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 granted $25,000 and $2,000 to SMT during the years ended August 31, 2004 and 2003, respectively. In addition, the Fund paid $60,213 and $194,204 of expenses on behalf of SMT during 2004 and 2003, respectively. Expenses included salaries, travel, entertainment, maintenance, supplies, professional fees, printing cost, and miscellaneous web enhancements.

The financial statements of the Fund and SMT are not presented on a consolidated basis, as the Fund is not the legal owner of SMT, does not have controlling interest of SMT's financial transactions, and does not have considerable representation on the board of SMT.

Schedule I: Statement of Award Transactions

Year Ended August 31, 2004

(All dollar amounts presented in thousands)

Unpaid awards, beginning of year	$64,566
Add – Awards granted (Schedule II)	13,298
Less – Award payments made	(23,123)
Award cancellations (excluding refunds)	(2,840)
Net increase in unamortized discount	1,087
Unpaid awards, end of year	$52,988

Schedule II: Statement of Awards Granted

Year Ended August 31, 2004

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.

Program Summary

	Approved	Paid	Transferred/ Cancelled*
Basic Biomedical Sciences			
Career Awards in the Biomedical Sciences	$8,621,201	$8,769,101	$1,221,649
Career Development of Postdoctoral Scientists	236,000	192,750	-
History of Medicine	-	-	15,000
Hitchings-Elion Fellowships	257,969	563,875	243,344
Reproductive Science	666,601	223,867	-
Total	$9,781,771	$9,749,593	$1,479,993
Infectious Diseases			
Investigators in Pathogenesis of Infectious Disease	$ -	$1,040,000	$ -
New Initiatives in Malaria Research Awards	100,000	269,003	100,000
New Investigator Awards in Molecular Parasitology	-	105,000	-
New Investigator Awards in Molecular Pathogenic Mycology	-	140,000	-
Scholar Awards in Molecular Parasitology	-	527,500	-
Scholar Awards in Molecular Pathogenic Mycology	127,500	400,000	127,500
Other Grants	328,897	692,326	-
Total	$ 556,397	$3,173,829	$ 227,500
Interfaces in Science			
Career Awards at the Scientific Interface	$ 556,723	$1,378,569	$ 382,800
Functional Genomics Innovation Awards	-	428,649	-
Institutional Awards at the Scientific Interface	-	1,720,714	-
Other Grants	120,000	120,000	-
Total	$ 676,723	$3,647,932	$ 382,800
Science Education			
Student Science Enrichment Program	$876,155	$596,202	$ -
Other Grants	312,451	300,700	-
Total	$1,188,606	$896,902	$ -

	Approved	Paid	Transferred/ Cancelled*
Science and Philanthropy			
Communications/Science Writing	36,000	36,000	$ -
General Philanthropy	$81,100	$81,100	-
Science Policy	75,000	125,000	-
Special Award	16,965	16,965	-
Total	$209,065	$259,065	$ -
Translational Research			
Clinical Scientist Awards in Translational Research	$750,000	$4,875,000	$ 750,000
New Investigator Awards in the Basic Pharmacological Sciences	-	245,000	-
New Investigator Awards in the Toxicological Sciences	-	140,000	-
Other Grants	135,500	135,500	
Total	$885,500	$5,395,500	$ 750,000
Totals	**$13,298,062**	**$23,122,821**	**$2,840,293**

GRAND TOTALS† APPROVED: $13,298,062
PAID: $23,122,821

* 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. 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 listed in the following sections, 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. 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.

TOTALS	APPROVED:	$9,781,771
	PAID:	$9,749,593
	TRANSFERRED/CANCELLED:	$1,479,993

Career Awards in the Biomedical Sciences

Career awards are postdoctoral-faculty bridging awards. During the fiscal year, some award recipients change institutions, modify the terms of their award at their current institution, or both change institutions and modify their award. In these cases, BWF's policy has been to cancel the remaining portion of the original award and, as necessary, approve a new award. When the award recipient has changed institutions, the new award is made to the new institution; when the award recipient has not moved but has modified the terms, the new award is made to the current institution. In the following descriptions, the name of the award recipient is listed first, the title of the project is listed second, the award recipient's current institution is listed third, and the amount approved or paid to the institution is listed fourth. For award recipients who either changed institutions or modified their award, the portion of the award paid to the original institution, as well as any portion that was transferred or cancelled, is listed last, in parentheses. For new award recipients still in the postdoctoral period, the portion of the award intended to cover a future faculty appointment is listed last, in parentheses.

Suzanne J. Admiraal, Ph.D.
Biosynthesis of hybrid natural products
University of Michigan Medical School
Paid $64,000
($29,000 of the original award to Harvard Medical School was paid)

Geoffrey K. Aguirre, M.D., Ph.D.
fMRI studies of the process architecture of face perception
University of Pennsylvania School of Medicine
Approved $58,000 Paid $29,000
($442,000 approved for future faculty appointment)

Matthew L. Albert, M.D., Ph.D.
Tumor immunity versus tumor-mediated immunosuppression: characterizing the cellular and molecular mechanism of cross-priming and cross-tolerance
Rockefeller University
($386,000 of the original award for future faculty appointment was transferred/cancelled)

Matthew L. Albert, M.D., Ph.D.
Support to attend the meeting of the European Life Science Organization
Rockefeller University
Approved $10,000 Paid $10,000

Matthew P. Anderson, M.D., Ph.D.
Role of T-type calcium channels in thalamic and hippocampal rhythmic activity
Harvard Medical School
Approved $583 Paid $127,500

Kaveh Ashrafi, Ph.D.
Comprehensive analysis of regulatory mechanisms of fat biology
University of California-San Francisco School of Medicine
Paid $100,000

Vahe Bandarian, Ph.D.
Biosynthesis of deazapurine secondary metabolites
University of Arizona
Approved $40,388 Paid $108,000

Jody L. Baron, M.D., Ph.D.
Role of the innate immune system in acute and chronic hepatitis B: studies in a novel transgenic mouse model of primary HBV infection
University of California-San Francisco School of Medicine
Paid $127,500

Greg J. Bashaw, Ph.D.
Molecular mechanisms of attractive and repulsive axon guidance at the midline of *Drosophila*
University of Pennsylvania Medical Center
Paid $65,500

Aaron P. Batista, Ph.D.
Neural gating within the cerebral cortex during sensory-motor behavior
Stanford University School of Medicine
Paid $58,000

Bradley E. Bernstein, M.D., Ph.D.
Proteomic studies of post-translational histone modifications
($500,000 approved for future faculty appointment)

David Bilder, Ph.D.
Genetic analysis of epithelial cell architecture
University of California-Berkeley
Paid $65,500

Cornelius F. Boerkoel, M.D., Ph.D.
Drosophila model for dissection SMARCAL1 function
Baylor College of Medicine
Paid $128,000

Carrie B. Brachmann, Ph.D.
Using *Drosophila* as a tool for the study of apoptotic regulation
University of California-Irvine
Paid $124,000

Edward S. Brodkin, M.D.
Genetic analysis of anxiety-related behaviors in mice
University of Pennsylvania School of Medicine
Paid $118,250

Chester W. Brown, M.D., Ph.D.
Understanding the reproductive roles of the activins using an activin beta B knock-in model
Baylor College of Medicine
Paid $65,500

Richard K. Bruick, Ph.D.
Investigation of hypoxia sensing and signaling pathways
University of Texas Southwestern Medical Center-Dallas
Paid $110,500

Michael D. Bulger, Ph.D.
Relationship between organization and function at the mammalian beta-globin locus
University of Rochester Medical Center
Paid $193,000

Kathleen M. Caron, Ph.D.
Reproductive and cardiovascular effects of the adrenomedullin system
University of North Carolina-Chapel Hill School of Medicine
Paid $127,500

Thomas R. Clandinin, Ph.D.
Dissecting neuronal target selection in the *Drosophila* visual system
Stanford University School of Medicine
Paid $127,500

Michael K. Cooper, M.D.
Modulation of sonic hedgehog signal transduction by cholesterol homeostasis
Vanderbilt University Medical Center
Paid $62,000

Nika N. Danial, Ph.D.
Integration of glycolysis and apoptosis by the pro-apoptotic protein BAD
Harvard Medical School
Approved $58,000 Paid $29,000
($442,000 approved for future faculty appointment)

Jeremy S. Dasen, Ph.D.
Role of Hox proteins in sensory-motor neuronal connectivity and identity
Columbia University
Approved $58,000
($442,000 approved for future faculty appointment)

Paul De Koninck, Ph.D.
Decoding rhythms in the nervous system
Laval University
Paid $65,500
($682 of the original award to Stanford University Medical Center was paid)

Abby F. Dernburg, Ph.D.
Chromosome architecture and the fidelity of meiotic segregation
University of California-Berkeley
Paid $76,959

Ricardo E. Dolmetsch, Ph.D.
Voltage-gated calcium channel signaling to the nucleus
Stanford University School of Medicine
Paid $127,500

Kelly S. Doran, Ph.D.
Penetration of the blood-brain barrier in GBS meningitis
University of California-San Diego
Paid $127,500

Charles G. Eberhart, M.D., Ph.D.
Analysis of medulloblastoma pathobiology and response to novel therapies using murine transgenic models
Johns Hopkins University School of Medicine
Approved $21,000 Paid $145,000

Peter J. Espenshade, Ph.D.
Molecular mechanism of cholesterol homeostasis in mammalian cells
Johns Hopkins University School of Medicine
Paid $124,000

Miguel Estevez, M.D., Ph.D.
Investigation of a calcium channel related to migraine and epilepsy in both an invertebrate and a mouse model
University of Pittsburgh Medical Center
Paid $193,000

Kathryn M. Ferguson, Ph.D.
Structural basis for erbB receptor activation by epidermal growth factor gonists and neuregulin
University of Pennsylvania School of Medicine
Paid $127,500

Seth J. Field, M.D., Ph.D.
Comprehensive analysis of phosphoinositide function
Harvard Medical School
Approved $58,000 Paid $29,000
($442,000 approved for future faculty appointment)

Nicholas R. Gaiano, Ph.D.
Neural stem cells in the mammalian forebrain: the roles of Notch and FGF signaling
Johns Hopkins University School of Medicine
Paid $150,807

Timothy P. Galitski, Ph.D.
Genetic networks
Institute for Systems Biology
Paid $131,000

Erin C. Gaynor, Ph.D.
Molecular basis of colonization and invasion in the foodborne enteric pathogen *Campylobacter jejuni*
University of British Columbia
Paid $165,750

Joseph A. Gogos, M.D., Ph.D.
Genetic analysis of connectivity in the mammalian olfactory system
Columbia University College of Physicians and Surgeons
Paid $60,500

Joshua I. Gold, Ph.D.
Neural basis of perceptual-decision formation
University of Pennsylvania School of Medicine
Paid $124,000

Ruben L. Gonzalez Jr., Ph.D.
Single-molecule fluorescence studies of eukaryotic translation initiation and regulation
($500,000 approved for future faculty appointment)

Or P. Gozani, M.D., Ph.D.
Regulation of chromatin remodeling events by nuclear phosphoinositides
Harvard Medical School
Paid $29,000

Michael Graziano, Ph.D.
From eye to hand: sensory-motor integration in the primate brain
Princeton University
Paid $65,500

Matthias Gromeier, M.D.
Principles of polio neuropathies: exploiting poliovirus of brain cancer
Duke University Medical Center
Paid $65,500

Jay T. Groves, Ph.D.
Studies of cell recognition and signaling with micropatterned lipid membranes
University of California-Berkeley
Paid $65,500

Karen J. Guillemin, Ph.D.
Genetic and cellular basis of pylori-associated malignancies
University of Oregon
Paid $65,500

Victoria G. Herman, Ph.D.
Defining the molecular code for synaptic target selection
University of Oregon
Paid $65,500

Joel N. Hirschhorn, M.D., Ph.D.
Genetic analysis of complex endocrine disorders
Harvard Medical School
Paid $131,000

Michael D. Hogarty, M.D.
BIN1: a *MYCN* interacting neuroblastoma suppressor
University of Pennsylvania School of Medicine
Paid $65,500

Lora V. Hooper, Ph.D.
Molecular analysis of commensal host-microbial interactions in the intestine
University of Texas Southwestern Medical Center-Dallas
Paid $127,500

Jennifer S. Hovis, Ph.D.
Understanding lipid and protein interactions at the molecular level in model cell membranes
Purdue University
Paid $127,500

Chyi-Song Hsieh, M.D., Ph.D.
Determining the antigen specificity of CD25+ CD4+ regulatory T cells
($500,000 approved for future faculty appointment)

Christina M. Hull, Ph.D.
Cell identity, sexual development, and virulence in the human fungal pathogen *Cryptococcus neoformans*
University of Wisconsin Medical School
Paid $100,000

Raymond H. Jacobson, Ph.D.
TBP-related factor and selectivity factor I: probing TBP function in alternative contexts
University of Texas M. D. Anderson Cancer Center
Paid $15,700
($1,800 was approved and paid to the University of California-Berkeley.)

Ursula H. Jakob, Ph.D.
Structural and functional characterization of new heat shock proteins
University of Michigan-Ann Arbor
Paid $131,000

James D. Jontes, Ph.D.
Role of protocadherins in neural development studied in living zebrafish embryos
Stanford University
Approved $65,500 Paid $32,750
($65,500 of the original award for a future faculty appointment was transferred/cancelled)

Susan M. Kaech, Ph.D.
Investigation of the mechanisms that regulate memory CD8 T cell development
Yale University School of Medicine
Approved $24,166
($29,000 of the original award to the Emory University School of Medicine was paid)

Dennis H. Kim, M.D., Ph.D.
Genetic analysis of innate immunity in *Caenorhabditis elegans*
Harvard Medical School
Paid $29,000

Laura J. Knoll, Ph.D.
Molecular genetic approaches to investigate developmental regulation in *Toxoplasma gondii*
University of Wisconsin-Madison
Paid $131,000

William R. Kobertz, Ph.D.
Molecular interactions of the lipid-exposed surfaces of integral membrane proteins
University of Massachusetts Medical School
Paid $127,500

Scott C. Kogan, M.D.
Use of a transgenic mouse model of acute promyelocytic leukemia to elucidate disease pathogenesis and to improve therapy
University of California-San Francisco School of Medicine
Paid $60,500

Eric C. Lai, Ph.D.
Genomewide analysis of microRNA function in *Drosophila*
($500,000 approved for future faculty appointment)

Brian C. Lewis, Ph.D.
Modeling tumor initiation, progression, and metastasis using tissue-specific somatic gene transfer
University of Massachusetts Medical School
Paid $165,750

George Y. Liu, M.D., Ph.D.
Role of Group B *Streptococcal* hemolysin/cytolysin and pigment in the pathogenesis of invasive neonatal infections
University of California-San Diego School of Medicine
Approved $116,000 Paid $29,000
($384,000 approved for future faculty appointment)

Minmin Luo, Ph.D.
Integration of pheromonal signals and hormonal cues in mammalian reproduction
Duke University Medical Center
Approved $58,000 Paid $58,000
($58,000 of the original award for future faculty appointment was transferred/cancelled)

Anna K. Majewska, Ph.D.
Imaging rapid plasticity in the visual cortex
Massachusetts Institute of Technology
Paid $29,000

Margaret E. McLaughlin, M.D.
Effects of heterotypic cell interactions and bloodborne signals on tumors of the nervous system
Massachusetts Institute of Technology
Paid $29,000

Marc D. Meneghini, Ph.D.
Regulating chromatin domains in yeast and during animal development
University of California-San Francisco
Approved $58,000 Paid $29,000
($442,000 approved for future faculty appointment)

Karen L. Mohlke, Ph.D.
Genetic analysis of type 2 diabetes susceptibility
University of North Carolina-Chapel Hill School of Medicine
Paid $131,000

Vamsi K. Mootha, M.D.
Genomic approaches to mitochondrial biogenesis
Massachusetts Institute of Technology
Approved $58,000
($442,000 awarded to Harvard Medical School for future faculty appointment)

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
Approved $116,000 Paid $29,000
($384,000 approved for future faculty appointment)

Catherine L. Peichel, Ph.D.
Genetic and molecular basis of reproductive isolation of threespine sticklebacks
Fred Hutchinson Cancer Research Center
Paid $128,000

Thomas T. Perkins, Ph.D.
Measurements of single DNA-based molecular motors
University of Colorado-Boulder
Paid $131,000

Bijan Pesaran, Ph.D.
Cortical mechanisms for hand-eye coordination
California Institute of Technology
Approved $58,000 Paid $29,000
($442,000 approved for future faculty appointment)

Matthew H. Porteus, M.D., Ph.D.
Regulation of gene targeting in vertebrate somatic cells
University of Texas Southwestern Medical Center-Dallas
Paid $110,500

Salman T. Qureshi, M.D.
Genetic analysis of innate resistance to bacterial pathogens
McGill University Faculty of Medicine
Paid $118,250

Matthew Redinbo, Ph.D.
Structural and functional characterization of human topoisomerase I and the Werner syndrome helicase
University of North Carolina-Chapel Hill
Paid $65,500

David E. Reich, Ph.D.
Applying population genetics to find genes for common diseases
Harvard Medical School
Paid $100,000

Douglas N. Robinson, Ph.D.
Studies of the mechanisms of cytokinesis using *Dictyostelium*
Johns Hopkins University School of Medicine
Paid $65,500

Noah A. Rosenberg, Ph.D.
Efficient genome-based inference of ancestry for use in genetic association studies
University of Southern California
Approved $58,000 Paid $29,000
($442,000 approved for future faculty appointment)

Bernardo L. Sabatini, M.D., Ph.D.
Role of localized biochemical signaling in the regulation of synaptic function and spine morphogenesis
Harvard Medical School
Paid $131,000

Alvaro Sagasti, Ph.D.
Development of morphological diversity in trigeminal sensory neurons
New York University School of Medicine
Approved $58,000 Paid $29,000
($442,000 approved for future faculty appointment)

Stephen W. Santoro, Ph.D.
Directed evolution of natural and unnatural proteins and oligomers for gene manipulation, drug discovery, and biochemical investigation
Harvard University
Paid $58,000

Erica O. Saphire, Ph.D.
Structural studies of Ebola pathogenesis
Scripps Research Institute
Paid $121,000

Bradley L. Schlaggar, M.D., Ph.D.
Development of cognition: fMRI studies
Washington University School of Medicine
Paid $110,500

Maria A. Schumacher, Ph.D.
Structural biology of cell growth, development, and regulation
Oregon Health & Science University
Paid $127,500

Kristin E. Scott, Ph.D.
Taste representation in *Drosophila* brain
University of California-Berkeley
Paid $165,750

Nirao M. Shah, Ph.D.
Genetic analysis of neural circuits mediating sexually dimorphic behaviors in mammals
University of California-San Francisco School of Medicine
Paid $131,000

Shu-ou Shan, Ph.D.
Mechanism of signal recognition particle-mediated protein targeting
University of California-San Francisco School of Medicine
Paid $58,000

Krishna V. Shenoy, Ph.D.
Early reach plans in posterior parietal cortex
Stanford University
Paid $65,500

Donald C. Sheppard, M.D.
Isolation and characterization of genes involved in morphogenesis and virulence of *Aspergillus fumigatus*
University of California-Los Angeles School of Medicine
Paid $29,000

Upinder Singh, M.D.
Transcriptional control in *Entamoeba histolytica*
Stanford University School of Medicine
Paid $118,250

Douglas E. Smith, Ph.D.
Single molecular studies of viral DNA packaging
University of California-San Diego
Paid $65,500

Michele M. Solis, Ph.D.
Telencephalic pattern generator for song
University of Washington School of Medicine
Approved $58,000 Paid $29,000
($442,000 approved for future faculty appointment)

Theodore S. Steiner, M.D.
Isolation and characterization of an interleukin 8 releasing protein from enteroaggregative *Escherichia coli*
University of British Columbia Faculty of Medicine
Paid $12,669

Collin M. Stultz, M.D., Ph.D.
Conformational free energy landscape of collagen and its relationship to atherosclerotic plaque rupture
Massachusetts Institute of Technology
Paid $55,250
($58,000 of the original award to Harvard Medical School was paid)

Xin Sun, Ph.D.
Understanding the endoderm in organogenesis and regeneration
University of Wisconsin Medical School
Paid $62,000

Surachai Supattapone, M.D., D.Phil.
Structure and biology of a soluble prion
Dartmouth Medical School
Paid $80,808

Roger B. Sutton, Ph.D.
Biophysical and structural investigation of Ca^2 in neurotransmitter release
University of Texas Medical Branch-Galveston
Paid $131,000

Susanne J. Szabo, Ph.D.
T-bet, a novel t-box transcription factor that directs T-helper cell type 1 lineage commitment
($323,000 of the original award for a future faculty appointment was transferred/cancelled)

Heidi A. Tissenbaum, Ph.D.
Genetic and molecular analysis of genes controlling longevity in *Caenorhabditis elegans*
University of Massachusetts Medical School
Paid $65,500

Stephen H. Tsang, M.D., Ph.D.
Unraveling genetic pathways leading to cell death in mice lacking the gamma subunit of the cGMP phosphodiesterase
Columbia University College of Physicians and Surgeons
Paid $193,000

Kevin B. Urdahl, M.D., Ph.D.
Role of MHC class I molecules against tuberculosis
University of Washington School of Medicine
Paid $58,000

Amy J. Wagers, Ph.D.
Dynamic circulation of hematopoietic stem cells: implications for stem cell function
Stanford University School of Medicine
Paid $29,000

John B. Wallingford, Ph.D.
Molecular control of cell motility during vertebrate gastrulation
University of Texas-Austin
Approved $9,932 Paid $165,750

Michael M. Wang, M.D., Ph.D.
Estrogen receptors and neuroprotection against excitotoxic injury
University of Michigan Health System
Approved $294,649 Paid $147,325
($25,851 of the original award to the Johns Hopkins University School of Medicine was paid; $294,649 of the original award to the Johns Hopkins University School of Medicine was transferred/cancelled)

Anthony P. West, Ph.D.
Identification of the natural ligand of Methuselah, a *Drosophila* GPCR associated with extended life span
California Institute of Technology
Approved $65,500 Paid $32,750
($65,500 of the original award for future faculty appointment was transferred/cancelled)

Michael B. Yaffe, M.D., Ph.D.
Scaffolding and chaperone proteins in signal transduction: 14-3-3 regulation of mitosis and programmed cell death
Massachusetts Institute of Technology
Paid $65,500

Jennifer A. Zallen, Ph.D.
Molecular analysis of dynamic cell rearrangements in *Drosophila*
Princeton University
Paid $58,000

Karen M. Zito, Ph.D.
Regulation of synapse formation in the mammalian cortex
Cold Spring Harbor Laboratory
Approved $29,000 Paid $29,000
($29,000 of the original award for future faculty appointment was transferred/cancelled)

SUBTOTALS	APPROVED:	$8,621,201
	PAID:	$8,769,101
	TRANSFERRED/CANCELLED:	$1,221,649

Hitchings-Elion Fellowships

Michael W. Black, Ph.D.
Secretion-dependent regulation of ribosome synthesis in *Saccharomyces cerevisiae*
California Polytechnic State University
Paid $45,250

John W. R. Copeland, Ph.D.
Activation of the transcription factor SRF by actin remodeling proteins
University of Ottawa Faculty of Medicine
Approved $171,000 Paid $80,500
($168,000 of the original award to the Imperial Cancer Research Fund was transferred/cancelled)

Aaron R. Dinner, Ph.D.
Molecular mechanism of free radical oxidative DNA damage
University of Chicago
Paid $84,000

Daniel Durocher, Ph.D.
Role of FHA domains during DNA damage signaling
University of Toronto
Paid $45,250

Reuben S. Harris, Ph.D.
Delineation of the mechanisms of immunoglobulin gene hypermutation
University of Minnesota-Twin Cities
Paid $122,750

Jonathan K. Pritchard, Ph.D.
Population structure and linkage disequilibrium in association mapping
University of Chicago
Paid $64,156
($37,969 of the original award to the University of Oxford was paid; $26,344 of the original award to the University of Chicago was transferred/cancelled)

David J. Rossi, Ph.D.
Mechanisms of ischemia-induced excitotoxicity
Oregon Health & Science University
Paid $84,000

Michael J. Schell, Ph.D.
Brain calcium homeostasis: functional roles of GAP1-IP4BP ($49,000 approved for future faculty appointment; $49,000 of the original award to the University of Cambridge was transferred/cancelled)

SUBTOTALS	APPROVED: $257,969 PAID: $563,875 TRANSFERRED/CANCELLED: $243,344

Reproductive Science

Marine Biological Laboratory
Support for the Frontiers in Reproduction course
Approved $424,101 Paid $141,367

Meharry Medical College
Support for the Dr. Henry W. Foster Obstetrics and Gynecology Educational Initiative
Approved $1,000 Paid $1,000

University of California-San Francisco School of Medicine
Support for a study on the effect of cigarette smoking on HPV and cervical neoplasia
Approved $240,000 Paid $80,000

University of Kansas Medical Center
Support for travel to the FASEB Summer Research Conference
Approved $1,500 Paid $1,500

SUBTOTALS	APPROVED: $666,601 PAID: $223,867 TRANSFERRED/CANCELLED: N/A

Other Grants

In addition to making competitive awards, BWF makes noncompetitive grants 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.

American Association for the Advancement of Science
Support for postdoctoral outreach sessions
Approved $6,125 Paid $6,125

American Association for the Advancement of Science
Support for *Science*'s Next Wave Career Development Center website
Approved $69,000 Paid $23,000

American Association for the Advancement of Science
Support for *Science*'s Next Wave career development program on interviewing skills
Paid $2,750

American Society for Cell Biology
Support for a management training seminar
Approved $5,000 Paid $5,000

American Society for Cell Biology
Support for producing a publication on career advice for women in the life sciences
Approved $7,500 Paid $7,500

American Society for Microbiology
Support for the society's Graduate and Postdoctoral Summer Institute in Preparation for Careers in Microbiology
Approved $30,000 Paid $30,000

Association of American Medical Colleges
Support for a project on research centers and institutes and their effects on medical school research
Approved $25,000 Paid $25,000

Commission on Professionals in Science and Technology
Support for general activities
Approved $3,000 Paid $3,000

International Congress of Immunology-Federation of Clinical Immunology Societies
Support for the International Congress of Immunology
Approved $5,000 Paid $5,000

International Society for Pharmaceutical Engineering
Support for a student to attend and present a poster at the society's annual meeting
Approved $250 Paid $250

National Academies
Support for revising the guidebook *A mentoring culture: on being a mentor to students in science and engineering*
Approved $50,000 Paid $50,000

National Postdoctoral Association
Support for general activities
Approved $8,125 Paid $8,125

National Postdoctoral Association
Support for travel awards for underrepresented postdoctoral fellows to attend the association's annual meeting
Approved $5,000 Paid $5,000

Sigma Xi, The Scientific Research Society
Support for the NIEHS/NTA Career Fair
Approved $1,500 Paid $1,500

Society for Neuroscience
Support for postdoctoral travel awards to the society's annual meeting
Approved $15,000 Paid $15,000

Society for the Advancement of Chicanos and Native Americans in Science
Support for travel scholarships to the society's annual meeting and to the Minority Postdoc Summit
Approved $3,000 Paid $3,000

University of North Carolina-Chapel Hill
Support for annual postdoc career symposium
Approved $2,500 Paid $2,500

Wellcome Trust
Support for the touring exhibit The Phantom Museum
($15,000 of the original award was transferred/cancelled)

Subtotals	Approved: $236,000 Paid: $192,750 Transferred/Cancelled: $15,000

TOTALS	APPROVED: $556,397 PAID: $3,173,829 TRANSFERRED/CANCELLED: $227,500

Investigators in Pathogenesis of Infectious Disease

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
Paid $40,000

Barbara A. Burleigh, Ph.D.
Functional characterization of the role of the host cell fibrogenic response in *Trypanosoma cruzi* infection
Harvard School of Public Health
Paid $80,000

Zhijian J. Chen, Ph.D.
Role of TRAF5-regulated IKK activators in innate immunity
University of Texas Southwestern Medical Center-Dallas
Paid $80,000

Dana A. Davis, Ph.D.
Control of phenotypic switching and pathogenesis by the Mds3 protein
University of Minnesota-Twin Cities
Paid $40,000

Maurizio Del Poeta, M.D.
Role of inositol phosphoryl ceramide synthase 1 in fungal-host interaction
Medical University of South Carolina College of Medicine
Paid $80,000

David A. Fidock, Ph.D.
Plasmodium falciparum transmembrane proteins and their role in parasite susceptibility to heme-binding antimalarials
Albert Einstein College of Medicine of Yeshiva University
Paid $40,000

Michael J. Gale Jr., Ph.D.
Control of hepatitis C virus replication
University of Texas Southwestern Medical Center-Dallas
Paid $40,000

Heidi Goodrich-Blair, Ph.D.
Pathogenesis of *Xenorhabdus nematophilus* in insects: a model for the innate immune response to bacterial pathogens
University of Wisconsin-Madison
Paid $80,000

David B. Haslam, M.D.
Mechanisms of *Shiga* toxin translocation and intoxication within host cells
Washington University School of Medicine
Paid $80,000

Margarethe J. Kuehn, Ph.D.
Toxin trafficking via vesicles
Duke University Medical Center
Paid $80,000

Andrew S. Neish, M.D.
Transgenic analysis of prokaryotic effector proteins in the eukaryote *Drosophila melanogaster*
Emory University School of Medicine
Paid $40,000

Eric J. Rubin, M.D., Ph.D.
Cell signaling by bacterial cytokines in *Mycobacterium tuberculosis*
Harvard School of Public Health
Paid $40,000

C. Erec Stebbins, Ph.D.
Structural studies of bacterial virulence factors
Rockefeller University
Paid $80,000

Ren Sun, Ph.D.
Identification of cellular factors that determine the fate of herpes virus infection: latency versus lytic replication
University of California-Los Angeles School of Medicine
Paid $80,000

Chloe L. Thio, M.D.
Identification of human genes associated with hepatitis B virus outcomes
Johns Hopkins University School of Medicine
Paid $80,000

Wenqing Xu, Ph.D.
Innate immunity: how do toll-like receptors recognize microbial pathogens?
University of Washington School of Medicine
Paid $40,000

Thomas C. Zahrt, Ph.D.
Mycobacterium tuberculosis regulators modulating reactivation
Medical College of Wisconsin
Paid $40,000

SUBTOTALS	APPROVED:	N/A
	PAID:	$1,040,000
	TRANSFERRED/CANCELLED:	N/A

New Initiatives in Malaria Research

Scott D. Bohle, Ph.D.
McGill University
Peter W. Stephens, Ph.D.
State University of New York-Stony Brook
Interaction of the quinoline antimalarials and malaria pigment
Paid $119,003 (McGill University)

Fred E. Cohen, M.D., D.Phil.
University of California-San Francisco
Joseph L. DeRisi, Ph.D.
University of California-San Francisco School of Medicine
Functional genomics approach to identification of new antimalarial drug targets
Paid $100,000

Keith A. Joiner, M.D.
Mechanism of hemoglobin uptake in malaria
University of Arizona
Approved $100,000
($100,000 of the original award to the Yale University School of Medicine was transferred/cancelled; $50,000 of the original award to the Yale University School of Medicine was paid)

SUBTOTALS	APPROVED:	$100,000
	PAID:	$269,003
	TRANSFERRED/CANCELLED:	$100,000

New Investigator Awards in Molecular Parasitology

Vernon B. Carruthers, Ph.D.
Defining the proteome of toxoplasma secretory proteins
Johns Hopkins University Bloomberg School of Public Health
Paid $35,000

Barbara Papadopoulou, Ph.D.
Functional genomics of stage-specific gene expression in the kinetoplastid protozoan *Leishmania donovani*
Laval University Faculty of Medicine
Paid $35,000

Gary E. Ward, Ph.D.
Chemical genetic approach to the study of host cell invasion by *Toxoplasma gondii*
University of Vermont College of Medicine
Paid $35,000

SUBTOTALS	APPROVED: N/A PAID: $105,000 TRANSFERRED/CANCELLED: N/A

New Investigator Awards in Molecular Pathogenic Mycology

J. Andrew Alspaugh, M.D.
Signal transduction and pathogenicity of *Cryptococcus neoformans*
Duke University Medical Center
Paid $35,000

Ashraf S. Ibrahim, Ph.D.
Molecular genetics approach for studying the role of iron permease in the virulence of *Rhizopus oryzae*
University of California-Los Angeles School of Medicine
Paid $35,000

Jose L. Lopez-Ribot, Pharm.D., Ph.D.
Gene and protein expression profiling in *Candida albicans* biofilms
University of Texas-San Antonio Health Science Center
Paid $70,000

SUBTOTALS	APPROVED: N/A PAID: $140,000 TRANSFERRED/CANCELLED: N/A

Scholar Awards in Molecular Parasitology

Alan A. Aderem, Ph.D.
Macrophage responses to *Leishmania* infection
University of Washington Institute for Systems Biology
Paid $85,000

Paul J. Brindley, Ph.D.
Schistosome transgenesis
Tulane University School of Public Health and Tropical Medicine
Paid $85,000

Patricia J. Johnson, Ph.D.
Investigation of potential chemotherapeutic targets and the pathogenesis of the human-infective parasite *Trichomonas vaginalis*
University of California-Los Angeles School of Medicine
Paid $20,000

Marc Ouellette, Ph.D.
Functional genomics of drug resistance in *Leishmania*
Laval University Faculty of Medicine
Paid $85,000

Edward J. Pearce, Ph.D.
Role of the TGF-ß superfamily in host signaling to schistosomes
University of Pennsylvania School of Veterinary Medicine
Paid $42,500

Margaret A. Phillips, Ph.D.
Design of inhibitors for *Trypanosoma brucei* ornithine decarboxylase using a combination of structure-based approaches and combinatorial chemistry
University of Texas Southwestern Medical Center-Dallas
Paid $42,500

David S. Roos, Ph.D.
Exploring the function of the apicomplexan plastid
University of Pennsylvania
Paid $40,000

L. David Sibley, Ph.D.
Molecular pathogenesis in toxoplasmosis
Washington University School of Medicine
Paid $85,000

Samuel L. Stanley, M.D.
Pathways for amebic induction of inflammation and programmed cell death
Washington University School of Medicine
Paid $42,500

SUBTOTALS	APPROVED: N/A PAID: $527,500 TRANSFERRED/CANCELLED: N/A

Scholar Awards in Molecular Pathogenic Mycology

Martin Bard, Ph.D.
Characterization of new target sites for antifungal intervention in the *Candida albicans* ergosterol pathway
Indiana University-Purdue University at Indianapolis
Paid $42,500

Alexander D. Johnson, Ph.D.
Analysis of a mating-type-like locus in *Candida albicans*
University of California-San Francisco School of Medicine
Paid $20,000

James W. Kronstad, Ph.D.
Temperature-regulated and infection-regulated gene expression in *Cryptococcus neoformans*
University of British Columbia
Paid $42,500

Carol S. Newlon, Ph.D.
Analysis of chromosome structure and function in the pathogenic basidiomycete *Cryptococcus neoformans*
University of Medicine and Dentistry of New Jersey
Paid $85,000

Peter A. B. Orlean, Ph.D.
Glycolipid anchoring of protein and wall biogenesis in fungal pathogens
University of Illinois at Urbana-Champaign
Paid $40,000

Michael P. Snyder, Ph.D.
Analysis of morphogenic differentiation in *Candida albicans*
Yale University
Paid $85,000

Paula Sundstrom, Ph.D.
Global regulatory circuits and candidiasis
Dartmouth College
Approved $127,500 Paid $85,000
($127,500 of the original award to the Ohio State University College of Medicine and Public Health was transferred/cancelled)

Subtotals	Approved:	$127,500
	Paid:	$400,000
	Transferred/Cancelled:	$127,500

Other Grants

In addition to making competitive awards, BWF makes noncompetitive grants 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.

American Society of Tropical Medicine and Hygiene
Support for the Burroughs Wellcome Fund/American Society of Tropical Medicine and Hygiene Fellowship in Tropical Infectious Diseases
Paid $52,000

American Society of Tropical Medicine and Hygiene
Support for the society's annual meeting and for the Burroughs Wellcome Fund/Wellcome Trust session held at the meeting
Approved $30,000 Paid $30,000

Boston University
Support for young investigators to attend the 6th International Conference on *Cryptococcus* and cryptococcosis
Approved $15,000 Paid $15,000

Cold Spring Harbor Laboratory
Support for the 3rd International Conference on Microbial Pathogenesis and Host Response
Approved $5,000 Paid $5,000

Cold Spring Harbor Laboratory
Support for a meeting titled "Toward a More Unified Understanding of Infectious Disease"
Approved $30,846.67 Paid $30,846.67

Federation of American Societies for Experimental Biology
Support for a conference titled "Microbial Pathogenesis: Mechanisms of Infectious Diseases"
Approved $10,000 Paid $10,000

Gordon Research Conferences
Support for a conference titled "Bacterial Cell Surfaces"
Approved $5,000 Paid $5,000

Gordon Research Conferences
Support for a conference titled "Cellular and Molecular Fungal Biology"
Approved $1,000 Paid $1,000

Gordon Research Conferences
Support for a conference titled "Host-Pathogen Interaction"
Approved $10,000 Paid $10,000

Gordon Research Conferences
Support for a conference titled "Microbial Toxins and Pathogenesis"
Approved $5,000 Paid $5,000

Institute for Genomic Research
Support for a meeting titled "The Genome and Biology of the Trichomonads"
Approved $1,000 Paid $1,000

Institute for Genomic Research
Support for a *Plasmodium vivax* symposium at the annual meeting of the American Society of Tropical Medicine and Hygiene
Approved $3,550 Paid $3,550

Institute for Genomic Research
Support for a workshop for selected members of the *Giardia* and trichomonad communities
Approved $7,500 Paid $7,500

Institute for Genomic Research
Support for completing the *Plasmodium vivax* genome sequencing project
Approved $100,000

Institute of Medicine
Support for the Forum on Microbial Threats
Approved $25,000 Paid $25,000

Johns Hopkins University Bloomberg School of Public Health
Support for the Wellcome Trust/BWF Infectious Diseases Initiative 2000
Paid $172,459

Keystone Symposia
Support for a conference titled "The Pathogen-Host Standoff"
Approved $7,500 Paid $7,500

Marine Biological Laboratory
Support for the training course titled "Biology of Parasitism: Modern Approaches," for 2003-2006
Paid $100,000

Multilateral Initiative on Malaria Secretariat
Support for the Fourth Pan-African Malaria Conference
Approved $10,000 Paid $10,000

New York University School of Medicine
Support for work on a promising new approach to developing a malaria vaccine, involving the use of the yellow fever vaccine 17D
Approved $5,000 Paid $5,000

Pace University
Support for a meeting titled "Polyamine metabolism of parasitic protozoa as a drug target"
Approved $2,500 Paid $2,500

Smith College
Support for a symposium on genome evolution in eukaryotic microbes, held in conjunction with the annual meeting of the Society of Protozoologists
Approved $5,000 Paid $5,000

Society of Toxicology
Support for the BWF New Investigator Session titled "Reprogramming gene expression in response to insult," held at the society's annual meeting
Approved $10,000 Paid $10,000

University of Iowa Center for Conferences and Institutes
Support for the Tenth Annual Midwest Microbial Pathogenesis Conference
Approved $5,000 Paid $5,000

University of Massachusetts-Boston
Support for Phyllis Freeman to complete a monograph on scientific capacity building
Approved $5,000 Paid $5,000

University of Pennsylvania
Support for the 2nd International Meeting on Molecular Approaches to Malaria
Approved $5,000 Paid $5,000

University of Virginia Health System
Support for a meeting of scientists in the *Entamoeba histolytica* community
Approved $15,000 Paid $15,000

Wellcome Trust
Support for the Tri-Tryp meeting
Approved $10,000 Paid $10,000

Yale University
Support for the Wellcome Trust/BWF Infectious Diseases Initiative 2000
Paid $138,970

SUBTOTALS	APPROVED: $328,897 PAID: $692,326 TRANSFERRED/CANCELLED: N/A

TOTALS	APPROVED: $676,723 PAID: $3,647,932 TRANSFERRED/CANCELLED: $382,800

Career Awards at the Scientific Interface

Lindsay G. Cowell, Ph.D.
Duke University Medical Center
Novel statistical approach to deducing the function of regulatory DNA: examples from analyses of recombination signal sequences
Paid $60,000

Michael B. Elowitz, Ph.D.
California Institute of Technology
In vivo modeling: a synthetic approach to regulatory networks
Paid $130,000

Adrienne L. Fairhall, Ph.D.
University of Washington
Neural computation, adaptation, and information processing
Approved $103,071 Paid $130,000
($60,000 of the original award to Princeton University was transferred/cancelled)

Jeffrey R. Kuhn, Ph.D.
Yale University
Total internal reflection fluorescence microscopy of actin branching dynamics *in vivo*
Paid $60,000

Patrick W. Nelson, Ph.D.
University of Michigan-Ann Arbor
Theoretical study of HIV-1 pathogenesis: from primary infection, through latency, to effective drug therapy or progression to AIDS
Paid $130,000

Todd E. Peterson, Ph.D.
Vanderbilt University
Ultra high-resolution *in vivo* imaging
Approved $49,897 Paid $179,897

Jianghong Rao, Ph.D.
Stanford University School of Medicine
Imaging gene expression and protein phosphorylation in living organisms
Approved $398,883 Paid $53,800
($322,800 of the original award to the University of California-Los Angeles was transferred/cancelled)

Ronald S. Rock Jr., Ph.D.
University of Chicago
Exploring the protein folding energy landscape at the single molecule level
Paid $130,000

Jason K. Sello, Ph.D.
Harvard Medical School
Taking a chemical genetic scalpel to a *Streptomyces* colony
Paid $60,000

Brent R. Stockwell, Ph.D.
Columbia University
Chemical profiling of cellular disease states
Paid $130,000

Keith R. Weninger, Ph.D.
North Carolina State University
Single molecule study of the role of SNARE protein assisted membrane fusion in calcium-triggered neurotransmitter release
Approved $4,872 Paid $134,872

Ryohei Yasuda, Ph.D.
Cold Spring Harbor Laboratory
Visualization of biochemical signaling in single dendritic spines
Paid $60,000

Matthew A. Young, Ph.D.
University of California-Berkeley
Allosteric regulation in cell signaling proteins
Paid $60,000

Muhammad N. Yousaf, Ph.D.
Harvard Medical School
Surface chemistry and materials approach to develop model substrates to study PI(4,5)P2 lipid raft dependent actin polymerization
Paid $60,000

SUBTOTALS	APPROVED: $556,723 PAID: $1,378,569 TRANSFERRED/CANCELLED: $382,800

Functional Genomics Innovation Awards

Listed by names, institutions, and research subjects. In the case of collaborators at two different institutions, the institution listed first received the award payment. These special one-time awards were made in conjunction with the dedication of BWF's building in 2000. BWF also provides support for functional genomics through our other programs.

Christopher B. Burge, Ph.D.
Phillip A. Sharp, Ph.D.
Massachusetts Institute of Technology
Whole genome approaches to pre-mRNA splicing specificity and regulation
Paid $75,000

Wah Chiu, Ph.D.
Baylor College of Medicine
Gregor Eichele, Ph.D.
Max Planck Institute of Experimental Endocrinology
Spatial and temporal database of gene expression patterns of mouse brain
Paid $18,500

R. Mark Henkelman, Ph.D.
University of Toronto Hospital for Sick Children
Eugene Fiume, Ph.D.
University of Toronto
Automated image analysis of genetically modified mice
Paid $35,149

Sudhir Kumar, Ph.D.
Arizona State University
Computational genomic analysis to identify and dissect functionally important mutations in protein sequences
Paid $37,500

Elaine A. Ostrander, Ph.D.
University of Washington
Leonid Kruglyak, Ph.D.
Fred Hutchinson Cancer Research Center
Mapping cancer susceptibility genes in dogs by linkage disequilibrium
Paid $100,000

Eric D. Siggia, Ph.D.
Frederick R. Cross, Ph.D.
Rockefeller University
Computational and experimental analysis of promoters in the genome of budding yeast
Paid $50,000

Oliver Smithies, D.Phil.
Nobuyuki Takahashi, M.D., Ph.D.
University of North Carolina-Chapel Hill School of Medicine
Computer simulation and animal modeling of complex genetic systems
Paid $75,000

Alan R. Templeton, Ph.D.
Washington University
Cladistic analyses of epistasis among candidate genes influencing common disease
Paid $37,500

SUBTOTALS	APPROVED: N/A PAID: $428,649 TRANSFERRED/CANCELLED: N/A

Institutional Awards at the Scientific Interface

Listed by name of the training program, the institution or consortium conducting the program, and the researchers directing the program.

Cross-Disciplinary Training Program in Biophysical Dynamics
University of Chicago
Stephen J. Kron, M.D., Ph.D.
Norbert F. Scherer, Ph.D.
Paid $375,000

Graduate Program in Quantitative Biology
University of California-San Francisco School of Medicine
David A. Agard, Ph.D.
University of California-San Francisco School of Pharmacy
Ken A. Dill, Ph.D.
Paid $375,000

Interdisciplinary Training Program in Brain Science
Brown University
John P. Donoghue, Ph.D.
David Mumford, Ph.D.
Paid $345,714

LaJolla Interfaces in Science Training
Consortium of the University of California-San Diego, the Scripps Research Institute, the Salk Institute of Biological Studies, and the San Diego Supercomputing Center; grant administered by the University of California-San Diego
Elizabeth D. Getzoff, Ph.D.
Scripps Research Institute
José N. Onuchic, Ph.D.
University of California-San Diego
Paid $375,000

Program in Mathematics and Molecular Biology
Consortium of 17 laboratories and 12 institutions nationwide; administered by Florida State University
Wilma K. Olson, Ph.D.
Rutgers, the State University of New Jersey-New Brunswick
DeWitt L. Sumners, Ph.D.
Florida State University
Paid $250,000

SUBTOTALS	APPROVED: N/A PAID: $1,720,714 TRANSFERRED/CANCELLED: N/A

Other Grants

In addition to making competitive awards, BWF makes noncompetitive grants 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.

American Physical Society
Support for the Topical Conference on Opportunities in Biology for Physicists II
Approved $10,000 Paid $10,000

Aspen Center for Physics
Support for a workshop titled "Coherence and coordination in the brain: perspectives from olfaction and birdsong"
Approved $5,000 Paid $5,000

Biophysical Society
Support for a meeting titled "Bridging the Sciences Coalition Review Mechanism"
Approved $15,000 Paid $15,000

Biophysical Society
Support for postdoctoral and graduate student breakfasts and an early career development panel discussion at the society's annual meeting
Approved $5,000 Paid $5,000

Canadian Genetic Diseases Network
Support for the Canadian Bioinformatics Workshop series
Approved $15,000 Paid $15,000

Kavli Institute for Theoretical Physics
Support for an interdisciplinary workshop titled "Pattern Formation in Physics and Biology"
Approved $50,000 Paid $50,000

New York University
Support for an international conference titled "Algorithms for Macromolecular Modeling"
Approved $5,000 Paid $5,000

University of Michigan-Ann Arbor
Support for the Society for Mathematical Biology annual meeting
Approved $5,000 Paid $5,000

Washington University
Support for the 4th International Conference on Systems Biology
Approved $10,000 Paid $10,000

SUBTOTALS	APPROVED: $120,000 PAID: $120,000 TRANSFERRED/CANCELLED: N/A

TOTALS	APPROVED: $1,188,606 PAID: $896,902 TRANSFERRED/CANCELLED: N/A

Student Science Enrichment Program

Campbell University School of Pharmacy
High School Science Seminars
Approved $83,800 Paid $22,600

Duke University Comprehensive Cancer Center
Summer on the Edge
Approved $180,000 Paid $60,000

Duke University Nicholas School of the Environment and Earth Sciences
Connecting Coastal Communities
Approved $140,685 Paid $46,358

Friends of Great Smoky Mountains National Park
Smoky Mountain Heights: Science Education in Western North Carolina
Paid $54,200

Laboratories for Learning
BioSummer
Approved $176,571 Paid $56,571

North Carolina Museum of Life and Science
Mentors Opening Doors: Experiential Links to Science
Approved $178,637 Paid $58,779

North Carolina Science Olympiad
Science Olympiad Student Enrichment Program
Paid $60,000

North Carolina State University Science House
Photonics Xplorers
Approved $116,462 Paid $33,416

Onslow Community Ministries
Sturgeon City Student Science Series
Paid $59,058

Ranger Elementary/Middle School
Wild Rides!
Paid $25,380

Shodor Education Foundation
Mentor Center at Shodor
Paid $60,000

Wake Forest University School of Medicine
Mini-Fellowships in Science Fields: Linking Career Choices to Student Experiences
Paid $59,840

SUBTOTALS	APPROVED: $876,155 PAID: $596,202 TRANSFERRED/CANCELLED: N/A

Other Grants

In addition to making competitive awards, BWF makes noncompetitive grants 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.

American Chemical Society, North Carolina Local Section
Support for Project Seed
Approved $25,000 Paid $25,000

Delta Sigma Theta, Durham Alumnae Chapter
Support for the Delta Science and Everyday Experiences project, in lieu of an honorarium for SSEP advisory committee member Dr. Marian Johnson-Thompson
Approved $3,000 Paid $3,000

Durham Public Education Network
Support for the K-8 Science Initiative
Approved $20,000 Paid $20,000

Grantmakers for Education
Support for general activities
Approved $3,000 Paid $3,000

James B. Hunt Jr. Institute for Educational Leadership and Policy
Support for the annual North Carolina Legislators Conference focused on examining the state's exemplary educational policies and practices
Approved $25,000 Paid $25,000

National Association of Academies of Science
Support for the "Breakfast with Scientists" session at the association's annual meeting
Approved $2,500 Paid $2,500

North Carolina Center for International Understanding
Support for general activities
Approved $5,000 Paid $5,000

North Carolina School of Science and Mathematics Foundation
Support for Science Now
Approved $151,751

North Carolina School of Science and Mathematics Foundation
Support for the North Carolina Student Academy of Science
Approved $12,900 Paid $12,900

North Carolina Science, Mathematics, and Technology Education Center
Support for general activities
Approved $50,000 Paid $50,000

North Carolina State University
Support for a series of conferences on K-12 science outreach
Paid $50,000

Public School Forum of North Carolina
Support for general activities
Approved $3,000 Paid $3,000

Public School Forum of North Carolina
Support for North Carolina education leaders to participate in the China Studies Program
Approved $8,300 Paid $8,300

Public School Forum of North Carolina
Support for the N.C. Institute for Educational Policymakers
Paid $90,000

United Negro College Fund
Support for general activities, in lieu of an honorarium for SSEP advisory committee member Dr. Julia Clark
Approved $3,000 Paid $3,000

SUBTOTALS	APPROVED:	$312,451
	PAID:	$300,700
	TRANSFERRED/CANCELLED:	N/A

TOTALS	APPROVED: $885,500 PAID: $5,395,500 TRANSFERRED/CANCELLED: $750,000

CLINICAL SCIENTIST AWARDS IN TRANSLATIONAL RESEARCH

During the fiscal year, some award recipients change institutions or modify the terms of their award at their current institution, or both. In these cases, BWF's policy is to cancel the remaining portion of the original award and, as necessary, approve a new award. When the award recipient has changed institutions, the new award is made to the new institution; when the award recipient has not moved but has modified the terms, the new award is made to the current institution. In the following descriptions, the name of the award recipient is listed first, the title of the project is listed second, the award recipient's current institution is listed third, and the amount approved or paid to the institution is listed fourth. For award recipients who either changed institutions or modified their awards, the portion of the award paid to the original institution, as well as any portion that was transferred or cancelled, is listed last, in parentheses.

Sunil K. Ahuja, M.D.
HIV-1 AIDS pathogenesis: bridging the gap between host genotype and HIV transmission/disease phenotype
University of Texas-San Antonio Health Science Center
Paid $150,000

David M. Altshuler, M.D., Ph.D.
Genomic approaches to the genetics of type 2 diabetes and response to antidiabetic medication
Massachusetts General Hospital
Paid $150,000

Nina Bhardwaj, M.D., Ph.D.
Vaccination of HIV-1 positive individuals by antigen-pulsed dendritic cells
New York University School of Medicine
Paid $150,000

Cameron S. Carter, M.D.
Multimodal brain imaging and the pharmacotherapy of cognitive disability in schizophrenia
University of California-Davis
Approved $375,000 Paid $75,000
($375,000 of the original award to the University of Pittsburgh School of Medicine was transferred/cancelled)

Judy H. Cho, M.D.
Characterization of expression patterns in monocyte-derived cells in inflammatory bowel disease
University of Chicago Pritzker School of Medicine
Paid $150,000

George Q. Daley, M.D., Ph.D.
Chemotherapy and stem cell transplantation in leukemia
Harvard Medical School
Paid $75,000

Robert B. Darnell, M.D., Ph.D.
Detection and activation of tumor-specific killer cells in animal models and cancer patients
Rockefeller University
Paid $150,000

Claire M. Doerschuk, M.D.
Response of neutrophils during inflammatory lung disease
Case Western Reserve University School of Medicine
Paid $75,000

Jeffrey A. Drebin, M.D., Ph.D.
Targeted suppression of B-catenin in colorectal cancer
University of Pennsylvania School of Medicine
Approved $375,000
($375,000 of the original award to the Washington University School of Medicine was transferred/cancelled)

Brian J. Druker, M.D.
Mechanism-based therapy for chronic myelogenous leukemia
Oregon Health & Science University
Paid $150,000

Erol Fikrig, M.D.
Borrelia gene expression and lyme arthritis
Yale University School of Medicine
Paid $75,000

Barry A. Finette, M.D., Ph.D.
Mechanisms of malignant transformation in humans
University of Vermont College of Medicine
Paid $150,000

Glenn I. Fishman, M.D.
Gap junction channels as novel anti-arrhythmic targets
New York University School of Medicine
Paid $150,000

Thomas F. Gajewski, M.D., Ph.D.
Development of a second-generation melanoma vaccine
University of Chicago Pritzker School of Medicine
Paid $150,000

Lisa M. Guay-Woodford, M.D.
Genetic modifiers in recessive polycystic kidney disease: implications for pathogenesis and therapeutics
University of Alabama-Birmingham School of Medicine
Paid $150,000

Eva Guinan, M.D.
Extending the donor pool by inducing alloantigen specific T-cell anergy *ex vivo* for human hematopoietic stem cell transplantation
Dana-Farber Cancer Institute
Paid $75,000

Barbara L. Hempstead, M.D., Ph.D.
Growth factor regulation of coronary angiogenesis
Weill Medical College of Cornell University
Paid $75,000

Marshall S. Horwitz, M.D., Ph.D.
Therapeutic inhibition of aberrant protease activity in inherited neutropenias
University of Washington School of Medicine
Paid $75,000

Thomas J. Hudson, M.D.
Genomic approaches to identify genes predisposing to asthma
McGill University Faculty of Medicine
Paid $150,000

Daniel C. Javitt, M.D., Ph.D.
NMDA-based treatment development for schizophrenia
New York University School of Medicine
Paid $150,000

Jane E. Koehler, M.D.
Genomic and clinical correlates of human *Bartonella quintana* infection
University of California-San Francisco School of Medicine
Paid $75,000

Jonathan D. Licht, M.D.
Targeting aberrant repression as a therapeutic strategy in hematological malignancy
Mount Sinai School of Medicine
Paid $150,000

David M. Markovitz, M.D.
New approaches to inhibiting HIV replication
University of Michigan-Ann Arbor
Paid $75,000

Joseph M. McCune, M.D., Ph.D.
Regulation of human thymic function *in vivo*
University of California-San Francisco School of Medicine
Paid $150,000

M. Juliana McElrath, M.D., Ph.D.
Induction of cellular immunity in HIV-1 exposed seronegative individuals
Fred Hutchinson Cancer Research Center
Paid $150,000

Elizabeth M. McNally, M.D., Ph.D.
Microvascular spasm in the progression of cardiomyopathy
University of Chicago
Paid $150,000

Sofia D. Merajver, M.D., Ph.D.
Genetic determinants of aggressive breast cancer phenotypes: translation to the clinic
University of Michigan-Ann Arbor
Paid $75,000

Hector D. Molina, M.D.
Mechanisms of complement-induced abnormalities in fetomaternal tolerance
Washington University School of Medicine
Paid $150,000

Jason D. Morrow, M.D.
Isoprostanes as markers and mediators of oxidant stress in humans
Vanderbilt University Medical Center
Paid $75,000

Anthony J. Muslin, M.D.
Signaling mechanisms in cardiovascular disease
Washington University School of Medicine
Paid $75,000

W. Cam Patterson, M.D.
Oxidative profiles in cardiovascular diseases
University of North Carolina-Chapel Hill School of Medicine
Paid $75,000

Mark R. Philips, M.D.
Endomembrane trafficking of Ras: novel molecular targets for anticancer agents
New York University School of Medicine
Paid $150,000

Steven A. Porcelli, M.D.
Defining the protective human CD8+ T cell response against *Mycobacterium tuberculosis*
Albert Einstein College of Medicine of Yeshiva University
Paid $150,000

Daniel J. Rader, M.D.
Novel therapeutic approach to atherosclerosis through modulation of HDL metabolism
University of Pennsylvania School of Medicine
Paid $150,000

W. Edward Robinson Jr., M.D., Ph.D.
Structure-function analyses of clinically relevant HIV integrases
University of California-Irvine College of Medicine
Paid $75,000

Don C. Rockey, M.D.
Cellular and molecular basis of portal hypertension: an endothelialopathy in cirrhosis
Duke University Medical Center
Paid $150,000

Antony Rosen, M.B., Ch.B.
Altered structure and clearance of autoantigens during apoptosis: implications for autoimmunity
Johns Hopkins University School of Medicine
Paid $75,000

Marc E. Rothenberg, M.D., Ph.D.
Experimental analysis of eosinophil-associated gastrointestinal inflammation
University of Cincinnati College of Medicine
Paid $150,000

David T. Scadden, M.D.
Developing control mechanism-based stem cell therapies
Massachusetts General Hospital
Paid $150,000

Ann Marie Schmidt, M.D.
Novel therapeutic strategy for the prevention and treatment of diabetic complications: antagonism of receptor for advanced glycation end products
Columbia University College of Physicians and Surgeons
Paid $75,000

Donald Small, M.D., Ph.D.
Translating FLT3 inhibition into improved therapy for pediatric AML and infant ALL
Johns Hopkins University School of Medicine
Paid $75,000

Matthew L. Warman, M.D.
Delineating the proteins and pathways that maintain human joints and their potential for treating heritable and acquired forms of arthritis
Case Western Reserve University School of Medicine
Paid $150,000

Subtotals	Approved:	$750,000
	Paid:	$4,875,000
	Transferred/Cancelled:	$750,000

New Investigator Awards in the Basic Pharmacological Sciences

Peter J. Belshaw, Ph.D.
Combinatorial synthesis of non-ribosomal peptide-based electrophilic libraries
University of Wisconsin-Madison
Paid $35,000

Anton M. Bennett, Ph.D.
p21Ras signaling by protein tyrosine dephosphorylation
Yale University School of Medicine
Paid $35,000

Calvin J. Kuo, M.D., Ph.D.
Physiologic and pathologic roles of vascular endothelial growth factor
Stanford University School of Medicine
Paid $35,000

David P. Siderovski, Ph.D.
GoLoco motif-derived peptides as selective G-protein "perturbagens"
University of North Carolina-Chapel Hill School of Medicine
Paid $35,000

Scott K. Silverman, Ph.D.
Phototriggered folding approaches to RNA structural motifs and RNA-protein interactions
University of Illinois at Urbana-Champaign
Paid $35,000

Lu-Yang Wang, Ph.D.
Regulation of synaptic strength by subtype-specific coupling between Ca<^2+ ^>channels and metatropic receptors
University of Toronto
Paid $70,000

Subtotals	Approved:	N/A
	Paid:	$245,000
	Transferred/Cancelled:	N/A

New Investigator Awards in the Basic Toxicological Sciences

Mohanish P. Deshmukh, Ph.D.
Caspase activation during apoptosis: a novel mechanism of regulation in neurons
University of North Carolina-Chapel Hill School of Medicine
Paid $35,000

Su Guo, Ph.D.
Mechanism of action of neurotoxins that induce parkinsonism: a molecular genetic study in zebrafish
University of California-San Francisco School of Pharmacy
Paid $35,000

Anna K. Mapp, Ph.D.
Small molecules for reprogramming gene expression
University of Michigan College of Pharmacy
Paid $35,000

Terry L. Sheppard, Ph.D.
Chemical toxicology of oxidative DNA damage lesions
Northwestern University
Paid $35,000

SUBTOTALS	APPROVED: N/A PAID: $140,000 TRANSFERRED/CANCELLED: N/A

Other Grants

In addition to making competitive awards, BWF makes noncompetitive grants 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.

American Society for Clinical Investigation/Association of American Physicians
Support for a joint meeting of the society and the association
Approved $2,500 Paid $2,500

Clinical Research Alliance
Support for the Clinical Research Alliance meeting
Approved $40,000 Paid $40,000

Institute of Medicine
Support for the Clinical Research Roundtable
Approved $40,000 Paid $40,000

Johns Hopkins University
Support for the Consortium to Examine Clinical Research Ethics
Approved $50,000 Paid $50,000

North Carolina Center for Women's Health Research
Support for the 5th Annual Women's Health Research Day at the University of North Carolina-Chapel Hill
Approved $3,000 Paid $3,000

SUBTOTALS	APPROVED: $135,500 PAID: $135,500 TRANSFERRED/CANCELLED: N/A

Science and Philanthropy Ad Hoc Grants

TOTALS	APPROVED: $209,065 PAID: $259,065 TRANSFERRED/CANCELLED: N/A

Communications/Science Writing

American Association for the Advancement of Science
Support for the Mass Media Science and Engineering Fellowship Program
Approved $16,000 Paid $16,000

Council for the Advancement of Science Writing
Support for the New Horizons in Science Briefing and the New Horizons in Science Traveling Fellowship Program
Approved $20,000 Paid $20,000

SUBTOTALS	APPROVED: $36,000 PAID: $36,000 TRANSFERRED/CANCELLED: N/A

General Philanthropy

Boston University
Support for a conference to bring university and technology transfer people together to improve practices in patenting and licensing intellectual property generated with public funds
Approved $10,000 Paid $10,000

Council on Foundations
Support for general activities
Approved $39,600 Paid $39,600

Friends of the National Library of Medicine
Support for general activities
Approved $5,000 Paid $5,000

Grantmakers in Health
Support for general activities
Approved $5,000 Paid $5,000

North Carolina Association for Biomedical Research
Support for collaborations between the association and the North Carolina Science, Mathematics, and Technology Education Center
Approved $10,000 Paid $10,000

North Carolina Community Foundation
Support for the North Carolina Network of Grantmakers
Approved $1,500 Paid $1,500

Philanthropic Research
Support for general activities
Approved $5,000 Paid $5,000

Southeastern Council of Foundations
Support for general activities
Approved $5,000 Paid $5,000

SUBTOTALS	APPROVED: $81,100 PAID: $81,100 TRANSFERRED/CANCELLED: N/A

Science Policy

American Association for the Advancement of Science
Support for the AAAS Center for Science, Technology, and Congress
Paid $50,000

Emory University
Support for publishing and distributing the Blue Ridge Academic Health Group report *Converging on Consensus: Planning the Future of Health and Health Care*
Approved $10,000 Paid $10,000

Institute of Medicine
Support for the Kellogg Health of the Public Fund
Approved $10,000 Paid $10,000

National Academy of Sciences
Support for planning a study to assess research doctorate programs
Approved $25,000 Paid $25,000

New York Academy of Medicine
Support for a symposium titled "The International Pandemic of Obesity: Scientific, Clinical, Public Health, and Health Policy Challenges"
Approved $5,000 Paid $5,000

Research!America
Support for an internship program
Approved $25,000 Paid $25,000

SUBTOTALS	APPROVED: $75,000 PAID: $125,000 TRANSFERRED/CANCELLED: N/A

Special Award

National Journal of Young Investigators
Support for developing a website feature for undergraduates, focusing on career trends in the scientific community
Approved $16,965 Paid $16,965

SUBTOTALS	APPROVED: $16,965 PAID: $16,965 TRANSFERRED/CANCELLED: N/A

The Burroughs Wellcome Fund makes approximately 90 percent of our grants through competitive award programs, which support investigators in targeted areas of basic scientific 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. Program application deadlines for the 2006 award series are listed in the "Program Application Deadlines" section on page 69.

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 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.

BWF does not support activities that are primarily clinical in nature (such as disease diagnosis and treatment) or 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.

To obtain the most up-to-date information about our award programs, visit our website at www.bwfund.org

Competitive Award Programs

Basic Biomedical Sciences

Career Awards in the Biomedical Sciences

These awards are made in honor of Gertrude B. Elion, D.Sc., and George H. Hitchings, Ph.D., who shared the 1988 Nobel Prize in Physiology or Medicine and were long associated with the Burroughs Wellcome Fund. The awards are intended to foster the development and productivity of biomedical researchers who are early in their careers and to help them make the critical transition to becoming independent investigators. The grants provide $500,000 over five years to bridge advanced postdoctoral training and the first three years of faculty service. Recipients may spend part of the grant period at institutions in the United Kingdom. BWF expects to award up to 20 of these grants annually. Approximately half of the awards will go to researchers with a Ph.D. degree and half to those with an M.D. or M.D.-Ph.D. degree. Candidates must have completed at least 12 months but not more than 48 months of postdoctoral research training by the application deadline. For candidates with M.D. degrees, postdoctoral training excludes clinically oriented residencies that do not contain a major research component. 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.

Infectious Diseases

Investigators in Pathogenesis of Infectious Disease
These 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 $80,000 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. Up to eight of these grants will be awarded annually.

Interfaces in Science

Career Awards at the Scientific Interface
These awards are intended to 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. BWF expects to award up to eight of these grants annually. 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 temporary residents whose H1B visa was granted on or after January 1, 2003. Degree-granting institutions may nominate up to two candidates.

Translational Research

Clinical Scientist Awards in Translational Research
These awards are intended to 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). BWF expects to award up to eight of these grants annually. 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. In exceptional circumstances, non-M.D. candidates will be considered if their work is likely to contribute significantly to the clinical enterprise; these candidates should hold an appointment or joint appointment in a clinical department. Candidates must be tenure-track investigators at the late assistant professor level or the 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.

Science Education

Student Science Enrichment Program
These awards are limited to nonprofit organizations in BWF's home state of North Carolina. BWF provides around $1 million annually for this program, and grants provide up to $60,000 per year for three years. The program's goals include improving students' competence in science, nurturing their enthusiasm for science, 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 students in the sixth through twelfth grades 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.

Science and Philanthropy

BWF makes noncompetitive grants for activities that fall outside of our competitive award programs but are closely related to our targeted areas, such as career development of scientists or the pathogenesis of infectious disease. 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.

Program Application Deadlines

2006 Award Series

Basic Biomedical Sciences

Career Awards in the Biomedical Sciences	October 3, 2005

Infectious Diseases

Investigators in Pathogenesis of Infectious Disease	November 1, 2005

Interfaces in Science

Career Awards at the Scientific Interface	May 2, 2005

Science Education

Student Science Enrichment Program	April 11, 2005

Translational Research

Clinical Scientist Awards in Translational Research	September 1, 2005

Science and Philanthropy

Received all year

Advisory Committees

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 Fund's investment policies. This committee is appointed by and reports to the Board of Directors.

Career Awards in the Biomedical Sciences

Jack Antel, M.D.
McGill University Faculty of Medicine

Aravinda Chakravarti, Ph.D.
Johns Hopkins University School of Medicine

Patricia K. Donahoe, M.D. (Cochair)
Massachusetts General Hospital
Harvard Medical School

Shelton H. Earp, M.D.
University of North Carolina-Chapel Hill School of Medicine

Elaine Fuchs, Ph.D.
Howard Hughes Medical Institute
Rockefeller University

Margaret K. Hostetter, M.D.
Yale University School of Medicine

Thomas M. Jessell, Ph.D.
Columbia University

Lawrence C. Katz, Ph.D.
Howard Hughes Medical Institute
Duke University Medical Center

George M. Langford, Ph.D.
Dartmouth College

Martin M. Matzuk, M.D., Ph.D.
Baylor College of Medicine

Roderick R. McInnes, M.D., Ph.D.
University of Toronto
Hospital for Sick Children

J. Anthony Movshon, Ph.D.
New York University

Cecil B. Pickett, Ph.D.
Schering-Plough Research Institute

John F. Sheridan, Ph.D.
Ohio State University

David Tank, Ph.D.
Princeton University

Jeffrey A. Whitsett, M.D.
University of Cincinnati Children's Hospital Medical Center

Ian A. Wilson, D.Phil., D.Sc., F.R.S. (Cochair)
Scripps Research Institute

John York, Ph.D.
Howard Hughes Medical Institute
Duke University Medical Center

Investigators in Pathogenesis of Infectious Disease

Arturo Casadevall, M.D., Ph.D.
Albert Einstein College of Medicine

Mary K. Estes, Ph.D.
Baylor College of Medicine

Diane E. Griffin, M.D., Ph.D.
Johns Hopkins University Bloomberg School of Public Health

Philippe Gros, Ph.D.
McGill University Faculty of Medicine

Stephen L. Hajduk, Ph.D.
University of Alabama Marine Biological Laboratory

Jerry R. McGhee, Ph.D
University of Alabama-Birmingham

David G. Russell, Ph.D.
Cornell University College of Veterinary Medicine

Magdalene So, Ph.D.
Oregon Health & Science University

P. Frederick Sparling, M.D. (Chair)
University of North Carolina-Chapel Hill School of Medicine

Interfaces in Science

Laurence F. Abbott, Ph.D.
Brandeis University

Robert H. Austin, Ph.D.
Princeton University

James B. Bassingthwaighte, M.D., Ph.D.
University of Washington

Susan N. Coppersmith, Ph.D.
University of Wisconsin-Madison

Julio M. Fernandez, Ph.D.
Columbia University

Douglas A. Lauffenburger, Ph.D. (Cochair)
Massachusetts Institute of Technology

Michael C. Reed, Ph.D.
Duke University

Eric Siggia, Ph.D.
Rockefeller University

Susan S. Taylor, Ph.D. (Cochair)
Howard Hughes Medical Institute
University of California-San Diego School of Medicine

Clinical Scientist Awards in Translational Research

Martin J. Blaser, M.D.
New York University Medical Center

John W. Griffin, M.D. (Cochair)
Johns Hopkins University School of Medicine

Alan Krensky, M.D.
Stanford University Medical Center

Beverly S. Mitchell, M.D.
University of North Carolina-Chapel Hill School of Medicine

John E. Niederhuber, M.D.
University of Wisconsin Medical School

Jennifer M. Puck, M.D. (Cochair)
National Human Genome Research Institute
National Institutes of Health

Marlene Rabinovitch, M.D.
University of Toronto Faculty of Medicine
University of Toronto Hospital for Sick Children

Christine E. Seidman, M.D.
Howard Hughes Medical Institute
Harvard Medical School

Michael J. Welsh, M.D.
Howard Hughes Medical Institute
University of Iowa College of Medicine

Wayne M. Yokoyama, M.D.
Howard Hughes Medical Institute
Washington University School of Medicine

New Investigator Awards in the Pharmacological or Toxicological Sciences

This program was discontinued after the 2001 award series; however, the advisory committees will continue to monitor awardees' progress.

Pharmacological Sciences Subcommittee

Lorraine J. Gudas, Ph.D.
Weill Medical College of Cornell University

T. Kendall Harden, Ph.D.
University of North Carolina-Chapel Hill School of Medicine

Lee E. Limbird, Ph.D. (Chair)
Vanderbilt University Medical Center

Victor Ling, Ph.D.
British Columbia Cancer Research Centre

Palmer Taylor, Ph.D.
University of California-San Diego School of Medicine

Jeffrey M. Trent, Ph.D.
Translational Genomics Research Institute

Toxicological Sciences Subcommittee

Barbara F. Hales, Ph.D.
McGill University Faculty of Medicine

Philip Hanawalt, Ph.D.
Stanford University

Victor A. Levin, M.D.
University of Texas M. D. Anderson Cancer Center

Baldomero M. Olivera, Ph.D.
University of Utah

Stephen H. Safe, D.Phil.
Texas A&M University College of Veterinary Medicine

Thomas J. Slaga, Ph.D. (Chair)
AMC Cancer Research Center

Student Science Enrichment Program

Julia Clark, Ph.D.
National Science Foundation

Luciano Corazza, Ph.D.
University of California-Berkeley

G. Thomas Houlihan, Ph.D.
Council of Chief State School Officers

Marian Johnson-Thompson, Ph.D.
National Institute of Environmental Health Sciences

Carolyn Mahoney, Ph.D.
Elizabeth City State University

Willie Pearson Jr., Ph.D.
Georgia Institute of Technology

Sylvia Sanders, Ph.D.
Palo Alto, California

Sally G. Shuler (Chair)
Smithsonian Institution

Liz Woolard
W. G. Enloe High School

Douglas Y. Yongue
North Carolina General Assembly

Investment Committee

The committee is composed of four members from outside BWF and three members from BWF's Board of Directors. The board's chair, BWF's president, and BWF's vice president for finance also serve on the committee as nonvoting members.

Stephen D. Corman (Chair)
BWF Board of Directors

Michael Even
Citigroup

Geoff Gerber
Twin Capital Management

W. Curtis Livingston
Western Asset Management

I. George Miller, M.D.
BWF Board of Directors

Walter Niemasik
Snyder Capital Management

Philip R. Tracy
BWF Board of Directors

Board of Directors

Enriqueta C. Bond, Ph.D.
President
Burroughs Wellcome Fund

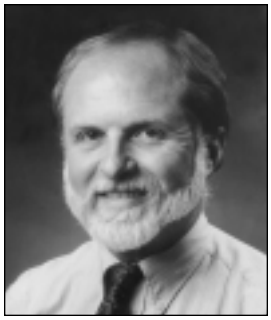
Carlos J. Bustamante, Ph.D.
Professor of Physics and Molecular and Cell Biology
University of California-Berkeley

Gail H. Cassell, Ph.D.
Vice President, Infectious Diseases Drug Discovery Research and Clinical Investigation
Eli Lilly and Company
Lilly Research Laboratories

Stephen D. Corman
Founder and former Chair and Chief Executive Officer
PharmaLink Inc.

Marye Anne Fox, Ph.D.
Chancellor
University of California-San Diego

Phil Gold, M.D., Ph.D.
Douglas G. Cameron Professor of Medicine
McGill University
Professor of Physiology and Oncology
Montreal General Hospital



Albert James Hudspeth, M.D., Ph.D.
Investigator, Howard Hughes Medical Institute
F. M. Kirby Professor and Head, Laboratory of Sensory Neuroscience
Rockefeller University

I. George Miller, M.D.
John F. Enders Professor of Pediatric Infectious Diseases
Professor of Epidemiology and Molecular Biophysics and Biochemistry
Yale University School of Medicine

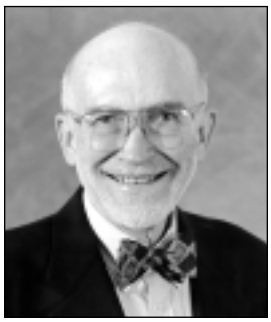
Board of Directors

Mary-Lou Pardue, Ph.D.
Boris Magasanik Professor
of Biology
Massachusetts Institute
of Technology

Jerome F. Strauss II, M.D., Ph.D.
Luigi Mastroianni Jr. Professor
of Medicine
Director, Center for Research on
Women's Health and Reproduction
University of Pennsylvania Medical Center

Judith Swain, M.D.
Arthur L. Bloomfield Professor
of Medicine
Chair, Department of Medicine
Stanford University Medical Center

Philip R. Tracy
Of Counsel
Smith, Anderson, Blount, Dorsett,
Mitchell & Jernigan, L.L.P.



Jean D. Wilson, M.D.
Charles Cameron Sprague
Distinguished Professor
of Biomedical Science
University of Texas Southwestern
Medical Center-Dallas

EXECUTIVE

LEFT TO RIGHT:
Scott G. Schoedler, Vice President, Finance
Enriqueta C. Bond, Ph.D., President

ADMINISTRATION, FINANCE, MEETINGS, AND TECHNOLOGY

SITTING, LEFT TO RIGHT:
Sam Caraballo, Systems and Web Engineer
Martie Nolan, Senior Manager, Facility and Administrative Services
Betsy Stewart, Secretary
Glenda Oxendine, Document/Web Specialist

STANDING, LEFT TO RIGHT:
Wendell Jones, Technology Coordinator
Mara Johnson, Accountant
Brent Epps, Administrative Support
Ken Browndorf, Senior Asset and Accounting Manager
Catherine Voron, Meeting Professional
Barbara Evans, Administrative Assistant

Programs and Communications

SITTING, LEFT TO RIGHT:
Debra Vought, Senior Program Associate
Rolly Simpson Jr., Senior Program Associate
Jean Kramarik, Senior Program Associate
Carr Thompson, Senior Program and Communications Officer

STANDING, LEFT TO RIGHT:
Debra Holmes, Program Assistant
Melanie Scott, Senior Program Associate and Database Specialist
Mirinda Kossoff, Communications Officer
Nancy Sung, Ph.D., Senior Program Officer
Victoria McGovern, Ph.D., Senior Program Officer
Martin Ionescu-Pioggia, Ph.D., Senior Program Officer

Contact Information for Major Programs

Staff E-Mail Addresses and Focus Areas

Basic Biomedical Sciences
Martin Ionescu-Pioggia, Ph.D., mionescu@bwfund.org
Senior Program Officer

Rolly L. Simpson Jr., rsimpson@bwfund.org
Senior Program Associate

Infectious Diseases
Victoria P. McGovern, Ph.D., vmcgovern@bwfund.org
Senior Program Officer

Jean A. Kramarik, jkramarik@bwfund.org
Senior Program Associate

Interfaces in Science; Translational Research
Nancy S. Sung, Ph.D., nsung@bwfund.org
Senior Program Officer

Debra A. Vought, dvought@bwfund.org
Senior Program Associate

Science Education
D. Carr Thompson, cthompson@bwfund.org
Senior Program and Communications Officer

Melanie B. Scott, mscott@bwfund.org
Senior Program Associate and Database Specialist

To Obtain Information About Programs

Burroughs Wellcome Fund
The most up-to-date information about our programs, including complete application information, can be found on our website at www.bwfund.org

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