

BURROUGHS
WELLCOME
FUND




2006 ANNUAL REPORT


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ABOUT THE BURROUGHS WELLCOME FUND



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 \$750 million and awards \$30 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—biomedical sciences, infectious disease, 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.

BWF was founded in 1955 as the corporate foundation of Burroughs Wellcome Co., the U.S. branch of the Wellcome pharmaceutical enterprise, based in the United Kingdom. The Wellcome enterprise was started in 1880 by two young American pharmacists, Henry Wellcome and Silas Burroughs, who moved to London to manufacture and sell “compressed medicines”—that is, pills—which they believed could replace the potions and powders of the day.

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

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

In 1993, after nearly four decades as a corporate foundation, BWF received from the Trust a \$400 million gift to become a fully independent foundation.

The importance of curiosity-driven research, as endorsed by Henry Wellcome, continues to be our guide. More than a century after two 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.

PRESIDENT'S MESSAGE



INSCRIBED ON THE BASE OF THE DOME AT THE NATIONAL ACADEMY OF SCIENCES ARE THESE WORDS: "TO SCIENCE, PILOT OF INDUSTRY, CONQUEROR OF DISEASE, MULTIPLIER OF THE HARVEST, EXPLORER OF THE UNIVERSE, REVEALER OF NATURE'S LAWS, ETERNAL GUIDE TO THE TRUTH."



Enriqueta Bond, Ph.D.

The Burroughs Wellcome Fund's mission—to advance the biomedical sciences by supporting research and other scientific and educational activities—resonates with that view.

Within our broad mission, BWF places primary emphasis on supporting the basic biomedical sciences—research aimed at discovering fundamental knowledge that will help in improving human health. Our Board of Directors has chosen a strategy that emphasizes investing in the "human capital" of the research enterprise in the United States and Canada, by providing support for promising scientists early in their careers and for investigators working in areas of science that are underfunded or undervalued.

BWF channels our financial support primarily through competitive peer-reviewed award programs. These programs provide support for career development in the biomedical sciences, for physician-scientists conducting translational research, for physical or computational scientists working at the interface with biology, for scientists working at the host/pathogen interface, and for K-12 science and mathematics education in BWF's home state of North Carolina. To complement these competitive programs, we award ad hoc and catalytic grants to nonprofit organizations working to improve the environment for science or carrying out other projects that correlate with our program areas.

CLIMATE IN PHILANTHROPY

In recent years, the media and Congress have increased their scrutiny of the philanthropic sector, paying particular attention to various financial and legal abuses that have occurred at some organizations. The Council on Foundations is now undertaking a two-year program to identify the most appropriate legal practices for nonprofit organizations and to promote adherence to high ethical standards in

grant making. I served on the committee that developed a set of standards and stewardship principles for independent foundations. At BWF's annual meeting in October 2005, our Board of Directors carefully scrutinized our programs and policies, comparing them to the identified standards and principles, to ensure that we are operating as a model of best practices.

As the philanthropic sector grows—Warren Buffet's recent remarkable gift of \$44 billion to the Bill & Melinda Gates Foundation and to other foundations established by his wife and children speaks to the anticipated transfer of wealth—public scrutiny and requirements for good stewardship will follow.

TRENDS FOR R&D FUNDING

Despite the budget increases called for in President Bush's American Competitiveness Initiative—which would double funding over the next 10 years for the National Science Foundation, the Department of Energy's Office of Science, and the Department of Commerce's National Institute of Standards and Technology—the total federal investment in basic and applied research will decline in fiscal year 2007. Funding for the National Institutes of Health will remain flat or decline for the second year in a row, funding for homeland security research and development will decrease for the first time, and other federal research portfolios will experience steep cuts.

NIH Director Elias Zerhouni has called his agency's current funding environment the “perfect storm,” caused by factors such as federal deficits and increased spending on such things as homeland security, entitlement programs, and relief from natural disasters. The current constraints on the NIH budget have generated many myths and misconceptions among scientists worried about their chances of being funded. A recent NIH newsletter examined this issue, comparing myths against realities. Among its findings:

The Myth of Declining Investigator Grants: Some scientists believe that the current declining success rates for investigator-initiated research project grants (RPGs) are due to a shift of resources away from projects focused on advancing basic science and toward larger initiatives, such as clinical trials, or toward NIH-driven requests for applications (RFAs).

The Facts: How NIH has spent its budget has changed little between 1998 and 2005. The percentage of the budget spent on basic science grew from 53.9 percent to 55.8 percent during that period, while the percentage spent on applied science remained the same.

A temporary dip in relative basic science funding occurred in 2003 due to the large biodefense commitment for construction of BSL 3 and BSL 4 laboratories that year and in 2004. In 2007, basic science is expected to grow to a level of 56.1

percent and applied science (which includes clinical trials) to a level of 40.8 percent, from 40 percent in 1998.

In terms of dollars, there has not been a shift away from RPGs or R01s, which are grants initiated by individual investigators. Also, the proportion of R01s and RPGs issued through RFAs has not dramatically changed from 1998 to 2005.

Investigator-initiated proposals remain the mainstay of NIH's efforts. They represent 93 percent of all R01s and 84.4 percent of all RPGs, as compared with 91 percent for R01s in 1995.

Because the NIH's total budget doubled between 1998 and 2003, more RFAs and Program Announcements (PAs) were launched, but as a proportion of the budget they have decreased since 1999.

The Myth of Roadmap Effects: Some observers have maintained that the NIH Roadmap for Medical Research has helped to drain resources from investigator-initiated research.

The Facts: The Roadmap is not a single large project but is both a framework and a dynamic process that NIH designed through extensive consultations with the scientific community. The Roadmap enables the agency to be more proactive and synergistic in addressing areas of emerging scientific needs that no single institute can provide but that benefit all of NIH. In an era of rapid convergence in science, the Roadmap process has allowed NIH to support innovative, high-risk research; incubate new ideas; stimulate transformative strategies in interdisciplinary research with the basic science of complex biological systems; and advance translational science.

The Roadmap consists of a multiplicity of peer-reviewed projects. In 2005, projects were led by more than 300 individual investigators through 345 grants at 133 institutions in 33 states. The science conducted under the Roadmap is extremely competitive, with applicants receiving grants at a rate that is lower than for NIH as a whole.

The Roadmap currently represents approximately 1.2 percent of the NIH budget. It is scheduled to grow progressively, but to no more than 1.7 percent of the budget by 2009 and into the foreseeable future.

The Roadmap portfolio is balanced, with 40 percent of its funding going to basic research, 40 percent to clinical and translational research, and 20 percent to interdisciplinary and high-risk research that would be difficult to support otherwise.

The Roadmap responds to the need for NIH to develop better mechanisms of coordination and collaboration across institutes and their specific missions through a bottom-up, regular, consultative process of evaluation of shared needs supported through shared resources that engages the entire research community. It has been well received and supported by Congress as a clear demonstration of stewardship by all institutes and centers.

In order to help guide NIH's direction, Dr. Zerhouni has called for the agency to develop a set of adaptive strategies guided by the following principles:

- ✱ Protect core values and mission: discovery and new knowledge.
- ✱ Protect the future: new investigators via a new program of support called Pathways to Independence and by Institute and Center efforts to assist new investigators.
- ✱ Manage the key drivers of the current leveling and low funding levels: that is, the supply and demand of grants. In 1998, NIH received 24,151 new applications for new and competing research project grants; NIH expected to receive more than 46,000 in 2006 and more than 49,000 in 2007 largely due to the new scientists applying for grants. This creates the current scenario of low funding levels. While 10 percent of applications are funded, closer to 25 percent of applicants are funded.
- ✱ Develop proactive communications within the scientific community that convey a unified message about the value of NIH's investment and need for sustainability.
- ✱ Promote NIH's vision for the future.

BWF concurs with these principles. We provide modest support to the non-profit group Research America! to help it continue to advocate for increased budgets for NIH and other federal agencies that conduct research. It may surprise many people that the average cost of health care per person in the United States is \$7,100, but the government invests only \$95 per resident in NIH to support research. The constrained climate for federal funding makes BWF support for investigators more critical to enable our awardees to take risks and to innovate.

BWF PROGRAMS

Later in this annual report, our program officers describe some of the accomplishments and plans of their programs. Here, I offer a few highlights.

Career Awards in the Biomedical Sciences

In recent years, the National Institutes of Health recognized that academic biomedical scientists were increasingly receiving their first research grant at a later age, and the agency grew concerned about how this factor might affect the researchers' careers and their ability and willingness to undertake high-risk research. In response, NIH asked the National Academies to recommend mechanisms to foster the independence of new investigators in the biomedical sciences. The Academies established a committee, led by Nobel laureate Thomas Cech, president of the Howard Hughes Medical Institute, to explore this issue. The committee issued its

report, *Bridges to Independence: Fostering the Independence of New Investigators in Biomedical Research*, in 2005.

For the report, the committee drew, in part, on experience gained through BWF's Career Awards in the Biomedical Sciences (CABS) program. One report recommendation, which drew on CABS outcome data demonstrating the positive impact of awards that "bridge" the postdoctoral and early faculty years, called for NIH to make 200 awards annually modeled on our program. In response, NIH announced in January 2006 that it would offer 175–200 new five-year awards in its Pathway to Independence program. BWF's Board of Directors applauds this step—and cites it as an example of how a foundation can play an important catalytic role by demonstrating the value of a particular approach to supporting young scientists that can then be adopted by a larger funder.

The CABS program began in 1995, and BWF has invested more than \$100 million to support 241 young scientists.

With NIH's commitment to supporting young scientists, BWF's board at its February 2006 meeting decided to reformulate the CABS program into a new program to support another group of "undervalued" scientists. Called Career Awards for Medical Scientists, the program will support physician-scientists working in biomedical sciences or translational research, as well as researchers working in molecular, genetic, or pharmacological epidemiology. In the past, physician-scientists often have found it difficult to obtain NIH funding, so our board saw this as a logical place for BWF to position new awards. BWF staff members Rolly Simpson and Debra Holmes have led the way in quickly and effectively transforming the program.

Health Research Alliance

In 2004, BWF's board authorized funding to help establish a new alliance of not-for-profit, nongovernmental funders of health research and training. The goals of the Health Research Alliance are to improve communication and collaboration among all grantmakers that fund health research, as well as among grantmakers and the broader health research and policymaking communities; to provide information about member organizations' grant programs; and to enhance the overall effectiveness of grantmakers in supporting biomedical and health research and training through the sharing of information and best practices.

Much progress has been made this past year under the leadership of BWF senior program officer Nancy Sung, Ph.D., and Kate Ahlport, the alliance's executive director. The organization has received its not-for-profit status, and its Board of Directors and Steering Committee continue to work apace. Approximately 20 organizations are in the process of signing up for membership. The alliance spearheaded a conference, Building Strategic Partnerships to Advance Health Research, held in May 2006, and is nearing completion of a database listing awards made by

not-for-profit, nongovernmental funders. BWF has great hopes that this organization can provide a significant forum to promote development of more strategic public-private partnerships.

Infectious Disease and the Wellcome Trust Collaboration

For nearly 10 years, BWF and the Wellcome Trust, our sister philanthropy in the United Kingdom, have funded a program to support collaborative research on health issues that have a center of gravity in the developing world. The program is intended to bring together a U.S. or Canadian principal investigator, a U.K. principal investigator, and a principal investigator in a developing country. In November 2005, we hosted a meeting of all the investigators and selected trainees to evaluate the outcome of the grants and to consider future collaborations. The meeting affirmed that the collaborations produced major scientific advances and helped to expand and improve training capacity in the developing world.

The Wellcome Trust will continue to support these projects through a peer-reviewed process. BWF and the Wellcome Trust have agreed in principle to continue our collaboration and are in the process of “mapping the terrain” through a series of “Frontier” meetings hosted by the Wellcome Trust on issues such as emerging zoonotic infections (that is, infections passed from animals to humans) and disease surveillance in a postgenomics era.

K-12 Science and Mathematics Education in North Carolina

Rising Above the Gathering Storm: Energizing and Employing America for a Brighter Economic Future, a report produced by the National Academies in 2006, has had a remarkable impact on public policy. The report, which describes a world being “flattened” by globalization, declares: “The most effective way for the United States to meet the challenges of a flatter world would be to draw heavily and quickly on its investments in human capital. We need people who have been prepared for the kinds of knowledge-intensive occupations in which the nation must excel. Yet the United States has for a number of decades fallen short in making the kinds of investment that will be essential in a global economy.”

The committee that produced the report, chaired by Norman Augustine, the retired chairman and chief executive officer of Lockheed Martin Corporation, recommended a number of actions that policymakers could take to assure that the United States remains globally competitive and prosperous. Four of the recommendations focus on improving K-12 education. BWF sees these recommendations as confirming the programs we support to strengthen K-12 science and mathematics education in North Carolina. The recommendations also provide ideas for how we can build new strategies to augment our work of the past decade.

Since 1994, BWF has invested approximately \$20 million on K-12 science and mathematics education grants in North Carolina. We began by creating the Student Science Enrichment Program (SSEP) to provide hands-on inquiry-based informal experiences to middle- and high school students. As testimony to the value of this approach, many members of BWF's board recall being enticed into science by some informal science experience in a museum or laboratory, or on a field trip.

Several years into our efforts, the advisory committee that oversees SSEP decided that BWF needed to take a broader approach to supporting science education. The committee called on BWF to support the development of informed public policy and research in science education, help build educational capacity and partnerships, and champion systemic change for all students in North Carolina. In response, BWF made a series of grants to institutions and organizations that not only could support the informal science community but also inform state and local policymakers about policy needs, build model demonstrations, and advocate for change. More recently, BWF has created an entirely new institution, the North Carolina Science, Mathematics, and Technology Education Center, to provide a central and enduring organization for addressing the needs of students, communities, and the state. A case study of our efforts, prepared by BWF senior program officer Carr Thompson and myself and published in fall 2006, provides an example of one foundation's drive to improve K-12 science and mathematics education during the past decade. The full report can be found on the BWF website: www.bwffund.org.

Future Directions

With the stock market recovering, BWF expects to be able to increase modestly the number of awards in each of our programs. In addition, our ad hoc funding pool is strategic—providing a flexible funding reservoir to manage our assets as they fluctuate over time. We also make catalytic awards to significantly advance an emerging field, build infrastructure in an area, create venues to help increase the number of young scientists, or participate in innovations to advance biomedical sciences.

For example, we have set aside funds for a new collaboration with the Wellcome Trust currently under discussion, and we have awarded a catalytic grant to the American Society for Tropical Medicine and Hygiene to renew and enhance a joint fellowship program designed to attract top researchers in infectious disease and to “anchor” their interest in pursuing clinical research in the field. We have made a catalytic grant to the National Science Resources Center to work with the North Carolina Science, Mathematics, and Technology Education Center, as well

as grants to other key groups to develop and implement a comprehensive, research-based science education reform program for North Carolina. We have made a grant to Project Suc-Seed, an American Chemical Society program for attracting minorities into science and encouraging them to pursue a Ph.D. This program once focused on the Triangle area of North Carolina, but with our grant it will draw on students statewide. This program was supported by SSEP, and we have gathered outcome data showing that it has had a successful track record.

BWF will continue to support meetings and other activities that provide opportunities for our awardees to gain insight and information that will help them in their careers. In 2005, the Howard Hughes Medical Institute and BWF offered for the second time a course in laboratory management, and in October 2006 we published a report encapsulating the information from the course. A companion guide on how to develop a course within an institution will also be available to guide the growing efforts of universities and professional societies to offer similar courses. In order to expand the value of the lab management course, BWF and the Howard Hughes Medical Institute continue to work in partnership with the NIH's Fogarty International Center and the Wellcome Trust on developing a manual that will meet the needs of scientists working in the developing world.

In the past year, we have brought together recipients of our Career Awards in the Biomedical Sciences and Career Awards at the Scientific Interface as well as recipients of the Investigators in Pathogenesis of Infectious Disease award. The two meetings provided participants with opportunities for career development, for asking new scientific questions, for building collaborations, and for networking with each other and with senior scientists from BWF's board and advisory committees.

In considering our future, we feel that BWF is well positioned to advocate for strengthening the biomedical research enterprise, which can be achieved only through adequate support from both the private and public sectors. We will continue to "invest in people" and to foster innovation and risk-taking in research, and we will continue to seek opportunities where our investments will truly multiply outcomes.



BIOMEDICAL SCIENCES



THE PAST AWARD YEAR MARKED THE FINAL CYCLE FOR THE BURROUGHS WELLCOME FUND'S CAREER AWARDS IN THE BIOMEDICAL SCIENCES (CABS) PROGRAM, WHICH WAS AIMED AT HELPING POSTDOCTORAL FELLOWS OBTAIN FACULTY POSITIONS AND ACHIEVE RESEARCH INDEPENDENCE.

BWF modeled the program after the Markey Charitable Trust Scholars Program, one of the original "bridging award" programs, which funded 113 scholars from 1985 through 1991. The Markey Trust ceased operations in 1998.

During the CABS program's 12-year history, BWF received more than 2,200 applications and made 241 awards, for a financial commitment exceeding \$100 million. An advisory committee of distinguished scientists—four of whom were Nobel laureates—selected the awardees.

Nearly 40 percent of the awards went to physician-scientists. A third went to women scientists. A quarter went to neuroscientists. Many awardees are now tenured faculty and a few of them are Howard Hughes Medical Institute assistant investigators. Excluding the most recent classes, almost all awardees have tenure-track or equivalent faculty appointments. About 4 percent of awardees left the program to take positions as independent investigators at the National Institutes of Health or faculty appointments in Europe or Asia, or to work in the pharmaceutical industry.

BWF's ongoing formal evaluation of the program has documented its success. The first report detailing its results, "Bridging postdoctoral training and a faculty position: Initial outcomes of the Burroughs Wellcome Fund Career Awards in the Biomedical Sciences," was published in *Academic Medicine* in 2003. The study found that awardees were accomplishing the program's major goal of facilitating the career development of young scientists in becoming successful independent investigators. Career success was judged by evaluating awardees' performance against a variety of outcome markers, including receipt of a tenure-track faculty appointment, amount of start-up funding provided by the hiring institution, receipt of research funding from NIH, and publication in top-tier scientific journals. BWF has completed a second study, comparing outcomes of awardees and applicants who did not receive awards, which will be published in the near future.

In addition to its evaluation component, the CABS program had various other features that made it unique when compared with awards made by other funding agencies—and many of these features will continue so long as awardees are still in the pipeline. BWF conducts some type of convening activity every other year to help awardees establish networks with peers and senior scientists. In addition, we

intensively survey awardees about career development issues. As one result, BWF and the Howard Hughes Medical Institute jointly developed a course in scientific management, which was given in 2002 and 2005. BWF also has used the feedback to change the award's structure and utility. And as a service to our awardees, we provide independent mentoring for awardees as they negotiate faculty appointments.

The CABS program outcome studies not only have established the program's reputation within the academic community, but have had broader effects as well. Notably, the studies have influenced NIH funding policy. For years, the CABS program, along with its sister program, Career Awards at the Scientific Interface, were among the nation's few bridging awards. In early 2006, NIH announced a program intended to foster the independence of new investigators. The program, patterned largely on our CABS program, will issue 175 to 200 awards annually, with the first awards made in the fall of 2006. To be known as Pathway to Independence Awards, they provide \$500,000 over five years and consist of two parts: a postdoctoral phase and an independent investigator phase. Eligible institutions include universities, research institutes, and hospitals.

In light of NIH's new program, which will support far more awardees than BWF's modest resources would allow, we made the decision to refocus our CABS award into a program for physician-scientists. The Career Awards for Medical Scientists, put into operation in early 2006, is open to candidates with clinical degrees (M.D., D.V.M., D.D.S., etc.) who work in basic biomedical and translational research or in the areas of genetic epidemiology, molecular epidemiology, and pharmacoepidemiology.

Physician-scientists play critical roles in the biomedical research enterprise, but their participation has been decreasing. The percentage of physicians engaged in research has dropped from a high of 4.6 percent in 1985 to 1.8 percent in 2003. Even though the total number of physician-scientists has increased over the years, their relative decline in the research enterprise marks a troubling trend.

BWF hopes that our new award, which provides \$700,000 in support during the critical transition from a mentored position to an independent investigator, will have a significant impact on keeping the physician-scientist on a path to a career in research.

✱ PROFILE: JOHN YORK, PH.D.

FROM THE BEGINNING



John York, Ph.D.

John York, Ph.D., who holds a dual appointment as associate professor of pharmacology and cancer biology and biochemistry at Duke University, recalls vividly his interview more than a decade ago for a Burroughs Wellcome Fund Career Award in Biomedical Sciences (CABS). As a member of the first CABS cohort in 1995, Dr. York has seen the program from every perspective: as an awardee and, later, as a member of its advisory committee. But through everything, that interview stands out.

As he recalls, he was told that he would have just 20 minutes with the committee and that two of its members, Paul Berg and Mike Bishop, were Nobel laureates. Today, Dr. York still isn't sure whether his heart sunk or whether his adrenaline took over.

"It was probably one of the most amazing experiences of my life," he said. "We got into a scientific discussion that lasted 45 minutes. I thought the interview went well, but because it went long I worried that I may not have communicated effectively and that I wasn't going to get an award. But I also knew that I had just finished a conversation with two Nobel laureates—and that the experience would be with me for the rest of my life. Thinking back on it, that was really a defining moment."

BWF, which had recently received a \$400 million endowment from the Wellcome Trust, had just moved from its space at the Burroughs Wellcome Co. into a new—rented and modest—headquarters in Research Triangle Park. The office lacked a meeting room, so BWF conducted the CABS interviews at the North Carolina Biotechnology Center.

"I'll say one thing about that room," Dr. York remembers, with a laugh. "It was shaped like a triangle, and they stuck you at its very point—like an arrow going right through your midsection."

At the time, Dr. York was a postdoctoral fellow at Washington University. He already was running an independent laboratory, with support from the pharmaceutical company Merck. His lab studied lithium-inhibited enzymes—proteins that are rendered ineffective and, perhaps, toxic with therapeutic doses of lithium. His mentor, Philip Majerus, a professor of biochemistry and molecular biophysics, and

Stuart Kornfeld, codirector of the university's hematology division, suggested that he apply for the new career development award that BWF had announced.

Dr. York's academic path up to then had been different from most postdoctoral fellows. Rather than going straight from undergraduate work into graduate school, he entered the private sector as a technician at Merck—and he began a family.

"I tend to think of my training at Merck as my Ph.D.," he said. "I entered graduate school at Washington University when I was 27 years old, while most of my peers were 22 or 23 years old. I think I had a little edge because I already had a good deal of experience."

In addition to studying lithium-inhibited enzymes, he also had been conducting studies on intracellular signaling pathways, the networks and mechanisms that cells use to communicate with each other. Newly funded as a CABS award recipient, he began working in yeast biology, looking for a system that could be exploited both biochemically and genetically.



*Dr. John York's eventual career path found him early.
He fondly remembers early childhood chemistry
experiments conducted in his "garage lab."*

"Yeast was becoming a popular medium because it was the first published genome," he said. "We could do a lot with cell signaling." His initial work in yeast led to papers in *Science* in 1999 and 2000.

"There's no way I could have done what I did without BWF money," he said. "All the exploratory work led to winning my first grant from the National Institutes of Health as an independent investigator, to having a running start when I started my faculty position at Duke, and then to being named a Howard Hughes Medical Institute investigator."

Dr. York, who occasionally had advised BWF program staff on various ad hoc grants, joined the CABS advisory committee in 2005. "I felt strongly that if someone was willing to take a chance on me, then I was going to help that organization in spreading the word about this award," he said.

As a committee member, Dr. York now sits on the other side of the interview table. “When I started on the committee, I noticed that when applicants came into the room, their bodies were contorted as a result of the pressure and intensity,” he said. “I could relate to the applicants and what they were going through. It is one of those indescribable emotions—the excitement about the work and the pressure to try to walk out of there with money in your pocket.”

Dr. York offered some insight on the advisory committee’s thought processes while reviewing applications.

“When I read through proposals, I try to find questions to ask that will engage the most scientific discussion,” he said. “Who is the driving force behind this person’s career path? You can really test their knowledge on how deeply they have thought about their problem. We’re looking for people who are thinking outside the box. Progress depends on asking the unreasonable.”

When the National Institutes of Health announced in 2006 its major initiative to support early career development for basic biomedical science, BWF shifted its investment to increasing the pool of physician-scientists by providing early career development funds. While BWF’s CABS program is no longer making new awards, Dr. York has remained on board to review progress reports from the roughly 140 awardees still receiving funding.

As Dr. York sees it, “It seems clear that NIH looked at BWF’s career awards program as the proving ground and proof of principle that this approach is important—and that it can work.”



INFECTIOUS DISEASE



THE BURROUGHS WELLCOME FUND'S COMPETITIVE AWARD PROGRAM IN THE PATHOGENESIS OF INFECTIOUS DISEASE (PID) NOW SUPPORTS 42 INVESTIGATORS WHO ARE TAKING NEW APPROACHES TO UNDERSTANDING THE COMPLEX RELATIONSHIPS BETWEEN THE BIOLOGY OF THE HUMAN SYSTEM AND THAT OF MICROBES.

The program and ancillary grant-supported activities continue to enhance understanding not only of specific diseases but also of the broader question of how microbes interact with the human host.

As with most other BWF award programs, PID is aimed at career development. It supports U.S. and Canadian researchers at the assistant professor level. We made 14 awards in 2006, to investigators whose work aims at such diverse goals as developing animal model systems and exploring how bacteria communicate within the gut of a human host.

The program is intended to give awardees a chance to take a longer view of infection, getting at underlying questions of how humans and microbes change one another and how they live together within one another's context. Such a broader view of infection and human health may help both the scientific community and society move beyond the conventional "us versus them" approach. With an expanded perspective, it may be possible to understand the more invasive or harmful aspects of humans' relationship with the microbes around us, and perhaps eventually to develop strategies beyond antibiotic chemotherapy for mitigating microbe-associated damage.

In August 2006, BWF brought together our awardees, along with awardees in the Ellison Medical Foundation's now-discontinued New Scholars in Global Infectious Diseases program, to discuss the ways that human and microbial complexity, both at the level of organisms and the level of populations, impact health and disease. Participants offered a number of suggestions for how individual scientists might move beyond the important but ultimately reductionist questions to look at the broader themes underlying why microbial encounters can have such a broad range of outcomes. BWF is giving serious consideration to what we heard, much of which centered on the need to better integrate questions at the population level and the need to provide researchers with adequate time and resources so they can move more easily between fields.

Although researchers have long used microbes as tools for understanding general biology, BWF's particular focus in this program area has always been on studying infection and the methods that humans use for dealing with it. While our competitive award program is oriented toward basic science, BWF also uses ad hoc grants to support a variety of other activities, including the training of physicians who are immersing themselves in clinical research in the tropical developing world. Since 2000, we have supported a fellowship program, managed by the American Society for Tropical Medicine and Hygiene, to attract top researchers and "anchor" their interest in pursuing clinical research on tropical infectious diseases. In 2006, we expanded our commitment to the fellowship program, and plans call for supporting 15 new fellows over the next five years. The grants will support the fellows during their training overseas and continue during their early faculty years.

The BWF/Wellcome Trust Joint Program in Infectious Diseases of the Tropical Developing World, launched in 1998, came to a conclusion in late 2005 with a meeting at the University of Cape Town, in South Africa. Researchers in the program participated in partnerships drawn from three regions—the United States or Canada, the United Kingdom, and the developing world. The program is now being evaluated, and BWF looks forward to future international collaboration.

Within BWF's home state of North Carolina, we have been working with the scientific honorary society Sigma Xi to develop a grant-writing course tailored for researchers working within a particular field. In 2006, we piloted the course with a group of 24 postdoctoral fellows and new faculty in molecular parasitology. During the course, the researchers worked in small groups to develop fundable proposals, and each researcher also worked individually with senior scientists in the field. Evaluation of the pilot phase is still under way. If the results prove as hoped, Sigma Xi, as the primary "property owner," will have a strong course to offer to researchers in other fields, and BWF will have new insights to share with our awardees and their trainees on how to succeed at landing early funding.

In other activities, BWF in November 2006 released a new edition of the laboratory management manual *Making the Right Moves*, which was based on a series of workshops that we organized in collaboration with the Howard Hughes Medical Institute. Our organizations are now developing an international version of the laboratory management manual, which will be published in 2007.

✱ PROFILE: ZHIJIAN “JAMES” CHEN, PH.D.
CHASING SURPRISES IN THE CELL’S IMMUNE RESPONSE



Zhijian Chen, Ph.D.

From his first days in graduate school, Zhijian “James” Chen, Ph.D., was hooked by the beauty of the biochemical pathway of a small protein called ubiquitin, so named because it occurs in the cells of all types of organisms. At the time, during the mid-1980s, fewer than a dozen laboratories were working on how and why ubiquitin became tagged onto other proteins in the cell.

“No one expected ubiquitin would win the Nobel Prize,” Dr. Chen said, adding that three researchers studying ubiquitin did, indeed, capture the 2004 prize in chemistry. Today, every college biology major knows that chains of ubiquitin tag proteins are slated for destruction by the cell’s garbage disposal specialist, the proteasome. For the past decade, Dr. Chen has explored the intersection of the ubiquitin pathway with the cell’s immune response pathway—and he has found surprises at every turn.

“That is the fun of doing science—finding unexpected things,” said Chen, a 2002 BWF Investigator in Pathogenesis of Infectious Disease, an investigator of the Howard Hughes Medical Institute, and a professor of molecular biology at the University of Texas Southwestern Medical Center at Dallas. On weekends, he’s also a chauffeur to violin, piano, and ice-skating lessons for his daughters, ages 11 and 9.

Colleagues say Dr. Chen is scientifically fearless, with a serious-but-friendly demeanor that carries over when he challenges others to ping-pong or poker at conferences. That competitive streak paid off when Dr. Chen made a startling discovery about a new function for ubiquitin—that it could serve to actually activate some proteins instead of dooming them to the proteasome.

While working at a biotechnology company, ProScript, in Boston, Dr. Chen began investigating what role ubiquitin played in the NF- κ B signaling pathway in his “spare time.” Individual cells use the NF- κ B pathway to convert critical signals that occur within the cell or on its surface—signals such as when the immune system has detected the presence of a foreign invader—into a “high alert” system inside the cell’s nucleus that turns on the right combination of genes to respond appropriately.

NF- κ B is a key switch in the system. When activated, NF- κ B moves from the cytoplasm into the nucleus where it can turn on more than 200 genes to start specific cellular programs such as immune responses, inflammation, or cell death. In 1996, Dr. Chen, working with Tom Maniatis of Harvard University, showed that for proper NF- κ B signaling, a protein kinase must be activated by ubiquitin. A kinase is an enzyme, or biochemical catalyst, that modifies other proteins in a way that changes their functional properties.

“How does ubiquitin activate a kinase? That was a very important question and it was better pursued in an academic setting,” Dr. Chen said. He moved from his company job to UT-Southwestern, in 1997, where he started his own lab to follow that question. His group soon showed that this new form of ubiquitin tagging was distinct from the tagging used for protein degradation, and moreover that the tags could be recognized by potential protein partners.

“Ubiquitin tags are like what I call a big phosphate group,” said Dr. Chen, referring to the other method cells use to activate or inhibit proteins. “It serves as a mark for other proteins to interact with the polyubiquitinated protein, to recruit other proteins into a signaling cascade.”

With his BWF award, Dr. Chen moved his research into the area of infectious disease, to look at how NF- κ B plays a role in responding to RNA viruses, such as influenza, hepatitis C, West Nile, and SARS. (RNA viruses get their name because they are composed of only this particular genetic molecule.) Scientists already knew that NF- κ B and other specialized proteins called transcription factors respond to viral invaders by turning on proteins called interferons. Interferons can then suppress the replication of viruses and assembly of new virus particles. But the cascade—how the signal travels from detection of viral RNA to activating NF- κ B to interferons, eventually turning on genes to stop virus replication—was riddled with knowledge gaps.

“The funding from BWF was very important, because it allowed us to get into new territory for our lab,” Dr. Chen said. As a return on investment, his laboratory identified a key player in the virus-stimulated NF- κ B pathway, called mitochondrial antiviral signaling, or MAVS, that sits on the mitochondrion and is required to activate NF- κ B.

“What makes this exciting is that this is the first mitochondrial protein known to play a direct role in immunity,” Dr. Chen said. “Mitochondria are well known for their role in providing the energy that drives cellular reactions and for initiating

a programmed cell death pathway called apoptosis. Being on the lookout for viral invaders is an altogether new function of these organelles.”

MAVS led Dr. Chen’s group to discover that some viruses, such as hepatitis C, can escape detection by the cell by clipping MAVS off the mitochondrial membrane and rendering it useless for transmitting the signal on to NF- κ B. Dr. Chen said this may be why hepatitis C infections can be stubbornly persistent in about 80 percent of people infected.

Dr. Chen’s group also has shown that mice with little or no MAVS are super-susceptible to viruses, dying from infections that a normal mouse’s immune system would fight off. In collaboration with physicians, the group is trying to determine if genetic differences in the human MAVS protein might influence immunity to viruses in different people.

In the future, Dr. Chen wants to investigate whether MAVS is involved in certain autoimmune diseases, such as lupus, in which patients produce too much interferon that leads to painful, chronic inflammation. A method to inhibit MAVS might offer some relief to such patients, he said.

Dr. Chen and his colleagues also are pursuing exactly how MAVS, which is anchored to the mitochondrial membrane, stimulates the protein kinases that activate NF- κ B, which reside in the cytosol, or internal fluid, of cells. “How do you signal from the mitochondria to the cytosol?” Chen said. “The ubiquitin signaling mechanism we discovered is likely to play a role here as well, and it would be a nice convergence of our two research areas.”

—Article by Kendall Powell, a freelance science journalist based in Colorado.



INTERFACES IN SCIENCE



RECENT YEARS HAVE SEEN MATHEMATICIANS, PHYSICISTS, AND ENGINEERS INCREASINGLY ATTRACTED TO BIOLOGY AS A NEW SCIENTIFIC FRONTIER THAT POTENTIALLY IS RICH WITH APPLICATIONS TO HUMAN HEALTH. FOR THEIR PART, UNIVERSITIES ARE BRINGING THESE PREVIOUSLY ISOLATED DEPARTMENTS CLOSER TOGETHER, BOTH PHYSICALLY AND PHILOSOPHICALLY, IN ANTICIPATION OF THE FEDERAL RESEARCH FUNDING THAT LOGICALLY FOLLOWS NEW SCIENTIFIC OPPORTUNITIES.

As a reflection of such scientific sea changes, the applicant pool for the Burroughs Wellcome Fund's Career Awards at the Scientific Interface (CASI) program in 2006 was 37 percent larger than when it began in 2001. To date, the program has made 36 awards, representing an investment of more than \$18 million. More than a third of the awardees are physicists by training, while another quarter are mathematicians, computer scientists, or statisticians. The rest are chemists, or they have been trained in an interdisciplinary field such as biophysics. Like awardees in CASI's sister BWF award program, Career Awards in the Biomedical Sciences, CASI awardees have no trouble moving into faculty positions at top universities. Most of them receive multiple offers and very competitive startup packages.

BWF will be tracking the progress of CASI awardees closely. Nearly half of them moved into physical science or mathematics departments—in some cases, as the first experimentalist within the department to focus on biological questions. Will they be able to compete for research funding from the National Institutes of Health, the nation's major nonindustry funder of biomedical research, despite being relative newcomers to biology? Will they succeed in developing experimental research programs to complement their theoretical or computational backgrounds? Will they attract students? Will they win tenure? BWF believes the answer to each of these questions will be "yes." Yet we recognize that as interdisciplinary scientists, their learning curve as new faculty members will be steeper than average.

To help our awardees scale the curve, BWF convenes each year's cohort within a year of their awards to discuss such issues as negotiating a faculty position, setting up and managing a research group, and making strategic use of resources to be as productive as possible. The networking that occurs among awardees often leads to new scientific collaborations, as well as to peer relationships that may last throughout their careers. The awardees also benefit from talking with and receiving candid advice from senior scientists who serve on BWF's Board of Directors and program advisory committees.

The predecessor of the CASI awards was the Institutional Awards at the Scientific Interface program, through which BWF launched 10 “experiments” in interdisciplinary training. Awards went to institutions that proposed rigorous programs to educate students with backgrounds in physics, chemistry, mathematics, computer science, and engineering who were interested in tackling biological problems. Programs had two codirectors—one in the biological sciences; one in the physical or mathematical sciences—who were selected on the basis of how thoughtfully they addressed the cultural barriers among the disciplines.

During 2006, eight of the programs were still receiving BWF funding. Collectively, the programs provided stipend support to 100 students and fellows. Because the programs are by definition not tied to a particular department, and because dual mentorship is recommended, these trainees have freedom to build collaborations across departments. In the words of one trainee in the program at Boston University, “I have been provided with greater intellectual autonomy to pursue interdisciplinary work than it appears many other graduate students have.” Another trainee at Princeton University said, “One of the most important things I learned is to knock down the inhibition and fear of learning and using new tools from different fields.”

With BWF’s funding, the various programs also hold interdisciplinary seminar series and symposia that facilitate dialogue and understanding across fields for the young trainees and their mentors. The gatherings help the trainees envision not only how new techniques and ways of thinking might help them answer their research questions, but also how their careers might unfold. Presenting their own work in these venues also helps them build crossdisciplinary scientific communication skills.

BWF tracks the success of these institutional programs in several ways. One way is to track the early careers of program alumni. In this regard, we have found that more than half of the alumni have moved into academic faculty positions, with most of the rest going into positions in industry. Another important measure is whether the institutions have sustained the interdisciplinary training approach, since a primary goal of the program was to change institutional structures. BWF has been pleased to see that several of the institutions have competed successfully for multiyear funding for interdisciplinary training from the Howard Hughes Medical Institute. Several others have incorporated courses developed for the BWF-supported students into entirely new interdisciplinary graduate programs, which the institutions intend to sustain into the future.

✱ PROFILE: JOSHUA PLOTKIN, PH.D.

UNDERSTANDING EVOLUTION



Joshua Plotkin, Ph.D.

Joshua Plotkin, Ph.D., uses mathematics and computation to study evolution on its most basic level—the genome, the genetic blueprint of life. “I want to understand the whole molecular kit and caboodle behind Darwin’s big idea,” said Dr. Plotkin, a 2005 recipient of a Burroughs Wellcome Fund Career Award at the Scientific Interface.

In its most basic sense, evolution occurs when mutations in genes lead to changes in an organism. If a change is advantageous to the organism’s survival, the mutated gene is likely to be preserved in subsequent generations. Such mutations are described as being spontaneous, but even behind this spontaneity are factors that make one gene more susceptible to change than another.

Dr. Plotkin wants to understand what causes changes in an organism’s genome from one generation to the next. In his research at Harvard University, where he is a Junior Fellow in the Society of Fellows, he probes the workings of “positive” and “negative” selective pressures. Positive pressures comprise attributes of a gene that promote changes to take place, and negative pressures are those that cause a gene to remain stable or unchanged.

“It’s a major goal to sort out which proteins fall in which of these categories,” according to Dr. Plotkin. “By identifying the rapidly evolving proteins, we can start to figure out which genes are responsible for the specializations that distinguish one species from another, such as chimpanzees from humans.”

Many evolutionary biologists study such changes by comparing several different genomes in order to determine which genes stay the same and which change. Dr. Plotkin’s approach is to use mathematics and computation to create tools that can measure the positive or negative selective pressures across an entire genome.

One advantage to this approach, he said, is that he does not need multiple sequences of genes to compare and contrast, but rather he can elucidate hot spots for change or conservation within a single genomic sequence. This capability is particularly advantageous when only one set of data is available, as might be the case when studying a pathogen with only one known strain.

He tests his mathematical models by applying them to genomic data that other researchers previously have obtained by more traditional means. Models that hold up can then be used to predict change in species with limited available data.

Such evolutionary studies aren't merely interesting history lessons—they may, in fact, help save lives. The same genetic forces that produce adaptations in animals also influence the virulence of viruses and bacteria that cause diseases. Flora and fauna evolve over years and decades, but microbes can go through several life cycles a day, thus contributing to a rapid rate of evolution.

For this reason, Dr. Plotkin devotes much of his research to pathogens. Identifying rapidly evolving genes in pathogens may help researchers gain information about potential vaccine targets, he said. Conversely, identifying stable genes may help researchers develop new drug targets by pointing out what is essential to the pathogen's survival.

Dr. Plotkin is particularly interested in the influenza virus. Composed of only 11 genes, the virus is a master of disguises. The virus's surface is coated with a protein, called hemagglutinin, that undergoes rapid mutation, and each “new” coat fools the body's immune system into thinking it has never seen the virus before. Ordinarily, the immune system would develop antibodies to fight off familiar invaders, but each time a mutated form of the flu virus appear, the immune system has to start from scratch.

According to Dr. Plotkin, the flu virus manages to infect 20 percent of the human population each year. The more the virus interacts with a variety of human immune systems, the more it experiences pressure to change its disguise by producing novel variants of its hemagglutinin coat protein. Dr. Plotkin's evolutionary models may prove valuable in predicting how the coat protein will change and which strain of the flu will be predominant during the next flu season.



*Curiosity caught Dr. Plotkin early
as he examines his finding at the shore.*

Dr. Plotkin describes his journey into biology research as circuitous. As an undergraduate at Harvard, he first studied pure mathematics. His interest in biology was sparked during a year of study at Oxford University, in the United Kingdom, where he met William “Bill” Hamilton, one of the leaders of what has been called “the second Darwinian revolution.” Dr. Plotkin set about to learn more about the molecular underpinnings of the life sciences.

“When I learned more about the structure of DNA, it all seemed so implausible to me,” he now recalls. “For instance, how could it be that all of life was encoded in a simple digital alphabet of nucleic acids? I couldn’t help but think about these questions.”

Although he was slated to attend graduate school in pure mathematics, Dr. Plotkin decided instead to combine his mathematics background and his new-found excitement about the biological sciences. He entered an applied mathematics Ph.D. program at Princeton University, studying under Simon Levin and Martin Nowak, both renowned for applying mathematical tools to the study of biology. “They had an enormous impact in shaping my scientific interests,” Dr. Plotkin said.

Likewise, Dr. Plotkin made an impact on his advisers and colleagues. “Many things are impressive about Joshua,” said Dr. Levin, who continues to work on projects with his former student. “He’s able to bring perspectives, on one hand from molecular biology and on the other hand from ecology, to bear on everything he addresses. He addresses each problem in a very serious way.”

In June 2007, Dr. Plotkin will leave Harvard for the University of Pennsylvania, where he will be an assistant professor in the departments of biology and computer science. He said he intends to pursue his research on pathogen evolution, and also to continue with another of his interests, using mathematical modeling to support biodiversity research in the tropical forests of Southeast Asia.

As a young researcher trying to apply new approaches to questions in both evolutionary biology and biomedicine, Dr. Plotkin found his BWF career award especially helpful. “The funding has allowed me to explore new areas in molecular evolution using unorthodox approaches,” he said. “Even though evolutionary biology has traditionally been viewed as an academic subject, it is increasingly clear that evolutionary approaches will shed new light on fundamental problems in molecular biology.”

—Article by Nicole Garbarini, a freelance science journalist based in Tennessee.



TRANSLATIONAL RESEARCH



THE CORNERSTONE OF THE BURROUGHS WELLCOME FUND'S EFFORTS TO SPEED THE TRANSFER OF LABORATORY DISCOVERIES INTO BETTER THERAPIES IS THE CLINICAL SCIENTIST AWARDS IN TRANSLATIONAL RESEARCH PROGRAM. WE MADE 10 NEW AWARDS DURING THE PAST YEAR. SINCE THE PROGRAM BEGAN IN 1998, BWF HAS INVESTED MORE THAN \$50 MILLION, MAKING AWARDS TO 69 INVESTIGATORS AT 37 INSTITUTIONS IN THE UNITED STATES AND CANADA.

When we launched this program, “translational research” was a new concept, and the National Institutes of Health concurrently began offering grants for patient-oriented research, known as K23 and K24 awards. BWF's application rate remained strong even as NIH doubled the budget for its awards, and the number of applications we have received has increased sharply since 2003. We believe this increase reflects not only the current stagnation of NIH's budget but also the growing number of investigators who have completed K23 and K24 awards and are now in a position to compete for our awards, which are designed to serve their next career stage. At the same time, NIH is strongly emphasizing translational research, as signaled in the agency's 2003 Roadmap for Medical Research and in its implementation in 2006 of the Clinical and Translational Science Award program.

Other scientific trends also have influenced the direction of translational research. Perhaps most notably, the past several years have seen a nearly complete description of the human genome, the blueprint of human life, and the generation of vast quantities of gene-expression data. The availability of this data, combined with powerful new computational methods and high throughput technologies, has created vast new frontiers for disease research and translation to better therapies.

Among the new opportunities is accelerated generation of hypotheses regarding the molecular mechanisms of disease, more reliable prediction of patients' responses to therapies, and development of new targets for attacking genetically complex diseases. These opportunities bring an increasing need for researchers who are skilled not only in basic science and clinical medicine but also in the use of large clinical and genomic datasets for generating and testing hypotheses. BWF will be encouraging proposals from such investigators in the future.

BWF has been concerned about the dearth of women who are building careers not only in translational research but across academic medicine in general. This gap is evidenced both nationwide and in the pool of applicants for BWF's award program. In 2005, just 16 percent of applications came from women. We are convinced that this rate should be higher, given that women now comprise more than half of the medical student population and that about 37 percent of new faculty

positions at medical schools now go to women. By adjusting our communication efforts and adding nomination slots, we were able to increase the proportion of female applicants to 25 percent in 2006. Over the history of the program, when women are nominated, they compete just as well as their male colleagues. In addition to encouraging nomination of female candidates, BWF has contributed to the national dialog on this issue. BWF senior program officer Nancy Sung, Ph.D., served on the Institute of Medicine's Committee on Opportunities to Address Clinical Research Workforce Diversity Needs for 2010, which issued a report in 2006.

To complement our competitive award program, BWF supports a variety of activities through ad hoc grants to advance the broader field of translational research. For example, we recognize the importance of understanding the environment in which our awardees work, so that we can address obstacles that research funding alone cannot solve. This interest has led us to provide modest funding for the Clinical Research Task Force of the American Association of Medical Colleges. The task force has examined training and career paths for clinical investigators and made a number of recommendations for changes in the medical school curriculum and residency requirements. These changes, it is hoped, will facilitate earlier independence of new investigators and bring more attention to clinical research infrastructure, including clinical informatics and harmonization of federal regulations regarding research that uses human subjects.

Many of BWF's awardees tell us that they face barriers in translating their discoveries into clinical development. In some cases, the awardee lacks a connection to industry investors; in other cases, the awardee works in an "orphan" disease area with a patient base too small to attract funding from a pharmaceutical company. To help inform the national conversation around such issues, BWF has provided modest funding to the Institute of Medicine's Forum on Drug Discovery, Development, and Translation. One output of the forum, made possible by joint funding from BWF and the Doris Duke Charitable Foundation, was an online course in Drug Development, hosted at Stanford University but made available to more than 500 investigators nationwide. BWF will continue to participate in the forum, and we plan to devote particular interest to its work on intellectual property issues that academic investigators face and on conflict-of-interest issues that arise within public-private partnerships aimed at developing therapies for orphan or neglected diseases.

Beyond supporting the competitive award program, BWF's most significant effort in working to improve the environment for translational research has been our incubation of the Health Research Alliance, which has gathered representatives from a broad range of other private funders of biomedical and health research.

✱ PROFILE: JANE KOEHLER, M.D.

PASSION AND PERSISTENCE



Jane Koehler, M.D.

Perhaps success in research comes down to two things: passion and persistence.

Jane Koehler, M.D., recipient of a 2003 Burroughs Wellcome Fund Clinical Scientist Award in Translational Research and a professor of medicine at the University of California at San Francisco (UCSF), seemed to have both as a little girl.

“I was always doing experiments,” she recalls. In sixth grade, she bred mice to study the inheritance of coat color—until she had accumulated 49 of them and even her scientist mother told her to stop. Still, her path into research wasn’t without detours. She left graduate school, after three and a half years of studying species of soil-dwelling bacteria, because “I really wanted to do something relevant to patient care,” she said.

She worked in a laboratory at UCSF for a year and a half and volunteered at night in the hospital’s intensive care unit. “I absolutely loved it,” she said of the volunteer experience.

Inspired, she enrolled at the George Washington University School of Medicine and Health Sciences. The newly minted M.D. then returned to UCSF for her residency, then a clinical fellowship in infectious diseases, and eventually to lab work.

Initially, she wasn’t sure if lab work was quite right for her. But during the first week of her fellowship, she saw something that would jump-start her career: a strange kind of lesion in AIDS patients that looked like Kaposi sarcoma, a type of cancer. On further examination, however, the lesions were really a bacterial infection, now known as bacillary angiomatosis. This meant the potentially fatal infection could be treated with antibiotics.

Identifying the bacteria that caused the infection was no small job, as no one had been able to culture them. Her microbiology experience from grad school helped her to succeed—which happened on July 4, 1991, she said, perhaps the most crucial moment of her career. The trick: she added human blood vessel cells to the cultures, because the bacteria grew next to such cells in the lesions.

When she came to the lab that day and found her cultures to be cloudy, she initially thought they were contaminated. But under the microscope, the cloudy stuff looked like bacteria different from those usually found as contaminants. “This was an exciting clue,” she said. “So I stayed the rest of the day and night to prepare, preserve, and freeze the cultures.”

She identified two species of bacteria, *Bartonella henselae* and *Bartonella quintana*. “So here we had evidence that both *B. henselae* and *B. quintana* were causing the same disease,” she said. She published the work in 1992 in the *New England Journal of Medicine*.

In a later collaboration with an epidemiologist, she found that cats are the source of *B. henselae* bacteria that infect some AIDS patients. This finding also suggested that in people without AIDS, the same bacteria may be the cause of “cat scratch disease,” which affects some 24,000 Americans each year, causing such minor symptoms as lymph node swelling.

Initially, this suggestion was met with some skepticism, as other researchers thought they had isolated a different agent as a cause for cat scratch disease. But the skepticism disappeared when Dr. Koehler published a study in 1994 which concluded that 41 percent of the cats in the San Francisco Bay area had *B. henselae* in their blood. “This was a major moment in my career,” she said, adding that the study caused a media frenzy. “I was on CNN and had my own PR person here at the university.”

But she didn’t stop there. Where did the other 47 percent of AIDS patients who didn’t own cats get their bacillary angiomatosis infection? she asked. Again collaborating with an epidemiologist, she found that these patients were infected with *B. quintana*. The patients also were often homeless and exposed to body lice. This made sense, Dr. Koehler said, because *B. quintana* was known to cause trench fever, which is transmitted by body lice, in soldiers during World War I.



In the third grade Dr. Koehler conducted experiments by growing grass on a sponge.

With that finding, she had come full circle to understand the disease. She sat on a panel of the federal Centers for Disease Control and Prevention and the U.S. Public Health Service to draft national guidelines advising AIDS patients about potential health risks posed by their pets.

And in 1999, researchers who described a new *Bartonella* species isolated from cats named it after her: *Bartonella koehlerae*.

As her next challenge, Dr. Koehler set out to understand how the bacteria work at the molecular level to infect people. She focused on proteins the bacteria produce on their surfaces up to 70 days after they have infected a host, at which time the proteins disappear. This behavior suggests that the proteins, known as VOMPs, must somehow be important, she said, because in some other diseases, such as malaria, the parasite removes certain proteins from its surface to escape detection by the immune system.

But again, Dr. Koehler faced resistance. She said the National Institutes of Health expressed skepticism about whether these proteins represented virulence factors, and that they were reluctant to fund the more clinical aspects of her study. So she approached the Burroughs Wellcome Fund. “Reviewers there apparently like to think about the big picture,” she said, adding that BWF’s support has helped her do much of her recent translational work. This work, she said, has demonstrated that the bacteria do, in fact, need the VOMP proteins to adhere to and infect host cells.

Now, Dr. Koehler wants to figure out how the bacteria regulate the expression of VOMPs so they disappear.

And every few months, she takes off her lab coat to serve as the attending physician in UCSF’s infectious disease service. “It keeps me in touch with patients,” she said, adding that being able to combine research and clinical work makes hers “the perfect job.”

Outside of work, her passion expresses itself in orchids, which she grows in abundance in both her office and her home. Orchids, like bacteria, “take consistency and a lot of patience,” she said.

—Article by Andreas von Bubnoff, a freelance science journalist based in Washington, D.C.



CATALYTIC PROGRAM IN TRANSLATIONAL RESEARCH: HEALTH RESEARCH ALLIANCE



*Kate Ahlport, executive director
Health Research Alliance*

The Health Research Alliance's (HRA) national conference, Building Strategic Partnerships to Advance Health Research, held May 3-4, 2006, in Washington, D.C., capped a year of achievement. Representatives of 75 organizations heard updates on the funding and scientific environments for research, learned about innovative funding partnerships, and participated in workshops on operational issues common to many funders of health research and training. The conference also debuted the HRA to its targeted community of funders of health research.

The Health Research Alliance is intended to foster collaboration among not-for-profit, nongovernmental organizations that fund health research and training. HRA's goals are to improve communication among funders of health research and the broader health research and policymaking communities, provide information

about the research supported by nongovernmental funders of health research and training, and enhance the effectiveness of these funders through facilitating the sharing of information and best practices.

The Burroughs Wellcome Fund has provided significant leadership and infrastructure support to HRA during its initial period of development, such as providing office space, administrative assistance, and salary support for HRA Executive Director Kate Ahlport. BWF senior program officer Nancy Sung, Ph.D., serves as chair of the HRA Board of Directors. BWF President Enriqueta Bond, Ph.D., senior program officer Victoria McGovern, Ph.D., and Gail Cassell, Ph.D., a member of BWF's Board of Directors, gave presentations at the national conference.

HRA reached several organizational milestones during the past year. These markers include becoming incorporated as a not-for-profit organization in North Carolina, being designated as a tax-exempt organization under section 501(c)(3) of the Internal Revenue Code, electing a Board of Directors, and establishing

membership eligibility criteria and a dues structure. Twenty organizations, representing a mix of private foundations, voluntary health agencies, and disease-specific funders, have joined as founding members.

Among their benefits, members can participate in HRA Advisory Committee meetings, held two to three times a year. The Juvenile Diabetes Research Foundation International and the March of Dimes hosted this past year's meetings. Attendees discussed evaluations of BWF's career development programs for clinical investigators, the new National Institutes of Health Clinical and Translational Science Awards, the NIH public access policy, the drug discovery and development process, and mentoring of early-career clinical investigators, among other issues. At the meetings, members of HRA's working groups meet face-to-face to plan and assess projects.

One of HRA's major projects during the past year has been the continued development of the Grants in the Health Research Alliance Shared Portfolio (gHRAsp) database, which will be a central repository of health research awards made by not-for-profit, nongovernmental grantmakers. The database will be the only one of its kind in the nation. HRA member organizations are required to submit information on their awards to gHRAsp annually, and to designate a "gHRAsp administrator" to submit the awards data and to participate in a gHRAsp users group. Debi Vought, a senior program associate at BWF, has played a key role in coordinating this users group.

HRA's other working groups include Grants Administration, Program Evaluation, and a new group focused on examining models for commercial and nonprofit partnerships to accelerate the development of new therapeutics.

Additional information is available at www.healthra.org.

Founding Members of the Health Research Alliance

AACR Foundation for the Prevention and Cure of Cancer	Doris Duke Charitable Foundation*
Alzheimer's Association	The Flinn Foundation
American Cancer Society*	Fondation Leducq
American Diabetes Association	Food Allergy and Anaphylaxis Network
American Heart Association*	Foundation Fighting Blindness
Arthritis Foundation*	Howard Hughes Medical Institute*
Autism Speaks	Juvenile Diabetes Research Foundation International
Avon Foundation*	March of Dimes*
Burroughs Wellcome Fund*	The Medical Foundation*
Damon Runyon Cancer Research Foundation	Multiple Myeloma Research Foundation

**Organizations represented on the HRA Board of Directors*

SCIENCE EDUCATION



THE YEAR 2006 MARKED THE BURROUGHS WELLCOME FUND'S 10TH ANNIVERSARY OF FUNDING SCIENCE EDUCATION IN OUR HOME STATE OF NORTH CAROLINA.

From the beginning, BWF's Board of Directors and Science Education Advisory Committee have taken a strategic approach to helping strengthen the state's educational infrastructure by supporting four key categories—student enrichment, public policy and research, capacity building, and partnership development. The collective aim is to foster systemic change in science, mathematics, and technology education for all students in North Carolina.

Over the past decade, BWF has invested nearly \$20 million in education-oriented grants and other activities. We invested almost \$13 million in the Student Science Enrichment Program (SSEP), a competitive award program that supports innovative hands-on, inquiry-based education activities that take place outside the conventional school environment. We invested the remainder through an array of ad hoc grants intended to improve the general environment in which science, mathematics, and technology education takes place.

The SSEP program makes approximately 12 awards per year, which provide up to \$180,000 over three years. We have funded 54 different nonprofit organizations, including public and private schools, universities, colleges, museums, and community groups. The awards are intended to nurture middle- and high school students' enthusiasm for science, improve their competence in science, and encourage them to pursue careers in research or other science-related areas. In recent years, BWF has taken care to ensure that the activities we support align with the requirements spelled out in the newly developed North Carolina Standard Course of Study.

Nearly 24,000 students have participated in the various programs. The students learn to “do” science in engaging, creative ways, and their activities affect their schools, their families, and their communities. Through their activities, the students experience firsthand the scientific process—a way of thinking that is transferable to other subjects in school.

As a cornerstone of our activities beyond the SSEP program, BWF continually searches for ways to form collaborations and partnerships with other groups that are working to improve inquiry-based learning and to increase students' access to high-quality classes in science, mathematics, and technology.

Among various efforts, we have encouraged a growing cadre of scientists to work with teachers, helped the state's Department of Public Instruction create tools for assessing students' science knowledge as a step toward meeting require-

ments of the federal No Child Left Behind Act, and provided elected officials with opportunities to learn firsthand about innovative educational systems in other countries. We also have helped form networks of university scientists who want to lend their expertise and a helping hand to various K-12 educational outreach programs, and we have supported the development of “virtual” online coursework and training opportunities for teachers and students, in keeping with the emerging trend in which learning happens around both the clock and the calendar.

The North Carolina Grassroots Museum Collaborative perhaps epitomizes what partnerships can accomplish. With BWF support during its formative years, the collaborative brought together 25 science museums and aquariums across the state. It is the first such museum collaborative in the United States. The collaborative, headed by Fran Nolan, Ed.D., testifies to the “strength in numbers” adage. It empowers the member museums, many of them relatively small, by connecting them to each other’s exhibits, resources, and staff. Larger museums will often share exhibits with smaller ones. Staff members will work with other museums to help develop programs. The collaborative also works to increase students’ interest in science and related fields by sponsoring competitions, such as the recent North Carolina International Science Challenge in which three state high school students traveled to China to compete. In recognition of the collaborative’s success, the North Carolina state government now contributes to a portion of its operational expense.

BWF values such partnerships as essential. But our years of experience also revealed that North Carolina needed a “champion for science”—a single entity devoted solely and actively to fostering reform in science, mathematics, and technology education. Toward this end, we established in 2002 the North Carolina Science, Mathematics, and Technology Education Center. Headed by Sam Houston, Ed.D., the center plays a central role in building a statewide consensus about the importance of science, mathematics, and technology education and in developing, directing, and catalyzing efforts to ensure that all students have access to “best practice” educational opportunities in these areas.

In looking ahead, we take inspiration from a 2006 report issued by the National Academies. *Rising Above the Gathering Storm: Energizing and Employing America for a Brighter Economic Future* recommends 10 actions that policymakers can take to assure that the United States remains globally competitive and prosperous. Four of the recommendations focus on K-12 education. We intend to explore these areas for opportunities where BWF can apply our decade’s worth of experience—with the ultimate goal of enhancing science, mathematics, and technology education for the good of students, our home state, and the nation.

✱ PROFILE: STURGEON CITY

A COMMUNITY ENGAGES ITS STUDENTS IN SCIENCE



*Students in Jacksonville, NC
conducting experiments*

High school students in Jacksonville, N.C., are stepping out of the classroom and into the crime lab.

They conduct their investigations at the Sturgeon City Environmental Education Center, where they analyze DNA evidence and examine blood and hair samples in a mock crime laboratory as part of an exercise patterned after the popular TV drama “CSI: Crime Scene Investigation.” Students work with educators and area police officers to learn the real-world applications of science facts they pick up in the classroom.

The mock lab is one of several hands-on science-enrichment programs offered at the center, which is located on the banks of Wilson Bay, in Onslow County. The goal is to widen students’ exposure to science by providing meaningful, science-rich activities away from the school environment. The programs, supported in part by the

Burroughs Wellcome Fund, are intended to help students learn and become enthusiastic about science—and perhaps start thinking about a science-related career.

“A lot of the students see the experience as exciting because they are getting out of school and the confines of the classroom,” said Glenn Hargett, operations director at the center and community affairs director for Jacksonville. “But I think when they get here, even the folks who have their hands stuck in their pockets, they really get excited.”

Among other science-enrichment activities offered at the center, a Saturday program lets students participate in independent research, and the Summer Science Academy lets students engage in engineering, physics, biotechnology, and biology.

BWF supports the activities through the Student Science Enrichment Program (SSEP), which makes awards of up to \$60,000 per year for three years to nonprofit organizations serving North Carolina middle- and high school students.

Since SSEP began in 1996, BWF has awarded 92 grants, totaling \$12.7 million, to 54 organizations. Nearly 24,000 students have taken part. Awards support

practical programs that provide creative science activities for students who have shown exceptional skills and interest in science, as well as those perceived to have high potential but who have not had opportunity in their classrooms to demonstrate their abilities.

The idea behind the Sturgeon City center traces back several years, to when officials in Jacksonville decided the time had come to clean up Wilson Bay, a 108-acre body of water that empties into the New River. After 40 years of accepting run-off from the city's wastewater treatment facility, the bay's waters had been muddied and its population of sturgeon—a kind of bottom-feeding fish—had been greatly reduced.

*Sturgeon City introduces students
to how science can effect a community.*



City leaders abandoned the concept of river discharge in 1998 and built an environmentally friendly treatment facility in the northeast section of Onslow County. The new plant uses a lagoon filtration system, and treated water is sprayed over a pine plantation that is designed to absorb water through the ground and tree roots. Collectively, the process cleans the water and naturally recharges the groundwater in the area.

When the new facility was built, a local scientist suggested that the old treatment plant be used to raise sturgeon. The plant thus was transformed into the Sturgeon City science education complex, which its leaders say is a monument to the idea that environmental restoration is compatible with economic development. When scientists and developers began work on the new treatment facility, they found that kids were fascinated by the development and the technology behind it.

“We were never so amazed as we were with the number of young people who wanted to come out and be with the scientists,” city official Hargett said. “That’s really what inspired our environmental science education program.”

To respond to the interest, organizers launched a trio of programs in 2001: the Science Institute, the Wilson Bay Keepers, and the Science Explorers. The programs take place on weekends and during the summer, and they are designed for different age groups and activities. BWF provided the initial funding to get the programs off the ground.

“The Burroughs Wellcome Fund money provided the impetus to do something that was only an imagined dream, and because of this we have been able to sustain those programs,” Hargett said.

In addition to getting students excited about science, the programs serve to introduce Onslow County high schoolers to career opportunities right in their backyard. The practical application to local job options is part of an effort to retain talented individuals in the county. Working with local law enforcement officers and representatives from the University of North Carolina-Wilmington forensic science department, officials at the Sturgeon City center are trying to make local career options come alive in the eyes of students.

“We are seeing a decline in folks taking advanced sciences in high school,” Hargett said. “So we have targeted students who are taking the physical science courses, and we are bringing them to Sturgeon City and using the metaphor of ‘CSI’ to try and excite them about science.”

So far, Hargett said, the program is working. He said the students are having fun and learning about science, and the community is educating its students about valuable science and mathematics job opportunities in the area.

“I think the key is that the kids see other people who are excited about this,” Hargett said. “They can feel it. If someone is just lecturing out of a book, the students can figure that out. But with this approach, we have graduate students from UNC-Wilmington and other people out there who are working in the bay. These are real people.”

—Article by Jim Walsh, a senior journalism student at the University of North Carolina at Chapel Hill.



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



*Sam Houston, Ed.D.,
President and CEO
SMT Education Center*

In 2002, the Burroughs Wellcome Fund helped to establish the North Carolina Science, Mathematics, and Technology Education Center (SMT Education Center) to drive science education policy reform, help legislators improve public policy affecting science education, and serve as the centralized voice of reason in guaranteeing high-quality science education for all children in North Carolina. In the ensuing years, the SMT Education Center has gone from a concept created with input from education, business, and legislative leaders to an organization shaping how science, mathematics, and technology is taught and learned in North Carolina.

One of the SMT Education Center's most successful programs is the Teachers Link Program, which brings scientists into the classroom to work alongside teachers. Part of Duke University's Teachers and Scientists Collaborating Program, nine school districts work with more than 80 scientists to enhance inquiry-based science education. The scientists—known as Teacher Link Fellows—also serve as science advocates in their communities, assisting with science competitions and career days.

In concert with the SMT Education Center, the Teacher Link Fellows helped advise the N.C. Department of Public Instruction on science assessments for N.C. schools. The SMT Education Center supports the shift to a problem-based curriculum to empower students to think, question, and work through tasks, rather than simply memorizing formulas. Learning these skills will help students better understand concepts and apply their knowledge to create solutions as well as help them in other areas of study.

One of the SMT Education Center's greatest strengths is bringing groups together to solve problems. Through a partnership with the National Science Resource Center, the SMT Education Center will offer Leadership Assistance for Science Education Reform (LASER) training for all North Carolina school districts. A LASER institute for 25 school districts will begin in the summer of 2007 at no costs to the school districts. LASER training offers strategic planning sessions, technical assistance, and assistance to superintendents, principals, and teachers developing and implementing research-based science programs in their schools.

As a complement to developing targeted and specific educational activities, improving education requires rethinking policy within state government. The SMT Education Center has worked with various organizations and agencies that influence policies that help determine what types of science and mathematics courses are taught in classrooms and how they are taught. These efforts have included working with the Center for 21st Century Skills—a public-private partnership that is redesigning preschool through undergraduate curriculum, teacher training, and student assessments in North Carolina—to develop a prototype assessment tool that will use new technologies to more accurately assess students' science knowledge.

In the past year, the SMT Education Center has partnered with the Bill & Melinda Gates Foundation to help in the development of “themed” high schools that focus on health and on science, mathematics, and technology. These schools are created when a school of 1,800 students or more is “reinvented” into several smaller independent learning communities with a specific and rigorous academic focus.

The SMT Education Center received a grant from the Golden LEAF Foundation to redesign or establish science, mathematics, and technology programs in 17 counties in the northeastern part of the state that have been most effected by the decline in tobacco farming. This effort is part of the foundation's mission to shift North Carolina counties beyond an agricultural-based economy.

Recognizing the need to move our gifted and talented students forward, a partnership involving the SMT Education Center, the North Carolina Grassroots Museum Collaborative, and the Beijing Association for Science and Technology will support N.C. students who want to compete in science competitions. This new initiative is known as the North Carolina International Science Challenge, which during the past year enabled three N.C. high school students and several state science education leaders to witness the excitement around science discovery and education in China.



REPORT ON FINANCE



The Burroughs Wellcome Fund's investments totaled \$726.8 million at August 31, 2006, the end of our fiscal year. BWF's primary financial goal is to pursue an investment strategy that will support annual spending needs and maintain a constant real level of assets over the long term. To achieve this goal, a high percentage of our investments are placed in strategies that derive the bulk of their returns from exposure to U.S. and international capital markets. Hence, fluctuations in BWF's investment results will be due largely to variability in capital market returns.

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

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

- ✿ U.S. large capitalization equity assets had a market value of \$167.5 million. The sector's target allocation was 25 percent, and actual holdings stood at 23.1 percent.
- ✿ U.S. small capitalization equity assets had a market value of \$111.9 million. The sector's target allocation was 18 percent, and actual holdings stood at 15.4 percent.
- ✿ International equity assets had a market value of \$207.4 million. The sector's target allocation was 32 percent, and actual holdings stood at 28.5 percent.
- ✿ Fixed income assets had a market value of \$120.8 million. The sector's target allocation was 22 percent, and actual holdings stood at 16.6 percent.
- ✿ Cash equivalent assets had a market value of \$14.6 million. The sector's target allocation was 3 percent, and actual holdings stood at 2.0 percent.
- ✿ Alternative assets had a market value of \$104.6 million. The sector did not have a target allocation, and actual holdings stood at 14.4 percent. The maximum permitted allocation to alternative assets stood at 20.0 percent.

The total market value of BWF's investments increased by \$36.9 million, or 5.3 percent, from the end of the previous fiscal year. This increase in assets was due primarily to strong returns in international equity markets throughout the fiscal year. U.S. stocks and bonds had positive, but somewhat muted, returns for the 12 month period. BWF's total investment return before investment management fees for the fiscal year was 10.6 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 +8.1 percent, the U.S. small capitalization equity sector had a +2.5 percent result, the international equity sector posted a return of +26.1 percent for the fiscal year, and fixed income produced a +2.6 percent result.

As of August 31, 2006, BWF employed 10 marketable securities investment managers. In the U.S. large capitalization equity sector, the managers were Independence Investment Associates; LSV Asset Management; and Enhanced Investment Technologies. 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. Barlow Partners and Winston Partners managed funds of equity oriented hedge funds. Quellos Capital Management managed a fund of absolute return strategies. Finally, Mellon Capital Management managed a global macro strategy.

FINANCIAL STATEMENTS



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, 2006 and 2005, 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 2006 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
October 20, 2006*

STATEMENTS OF FINANCIAL POSITION

AUGUST 31, 2006 AND 2005

(All dollar amounts presented in thousands)

	2006	2005
ASSETS		
Cash and cash equivalents	\$ 30,060	\$ 22,645
Marketable securities	733,955	666,144
Accrued interest and dividends receivable	1,870	1,482
Transactions receivable, net	—	603
Other assets	39	2
Property and equipment, net	11,695	12,104
Total assets	\$ 777,619	\$ 702,980
LIABILITIES AND NET ASSETS		
Transactions payable, net	\$ 39,013	\$ —
Accounts payable and other liabilities	1,101	771
Federal excise tax payable	770	372
Deferred excise tax payable	1,474	1,485
Unpaid awards	72,557	60,922
Total liabilities	114,915	63,550
Unrestricted net assets	662,704	639,430
Total liabilities and net assets	\$ 777,619	\$ 702,980

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

STATEMENTS OF ACTIVITIES

AUGUST 31, 2006 AND 2005

(All dollar amounts presented in thousands)

	2006	2005
REVENUES		
Interest and dividends, less investment expenses of \$3,842 and \$3,602 in 2006 and 2005, respectively	\$ 11,988	\$ 10,465
Net realized gain on sales of marketable securities	56,394	38,830
Total revenues	68,382	49,295
EXPENSES		
Program services	37,657	32,216
Management and general	7,286	6,551
Total expenses before net unrealized appreciation and deferred federal excise tax	44,943	38,767
Net unrealized appreciation of marketable securities, net of (benefit from) provision for deferred federal excise taxes of (\$11) and \$1,177 in 2006 and 2005, respectively	(165)	42,833
Change in net assets	23,274	53,361
Net assets at beginning of year	639,430	586,069
Net assets at end of year	\$ 662,704	\$ 639,430

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

STATEMENTS OF CASH FLOWS

AUGUST 31, 2006 AND 2005

(All dollar amounts presented in thousands)

	2006	2005
CASH FLOWS FROM OPERATING ACTIVITIES		
Change in net assets	\$ 23,274	\$ 53,361
Adjustments to reconcile change in net assets to net cash provided by operating activities:		
Depreciation	732	656
Net realized gain on sales of marketable securities	(56,394)	(38,830)
Net unrealized appreciation of marketable securities	176	(44,010)
Provision for deferred federal excise taxes	(11)	1,177
Awards granted, net of cancellations and change in unamortized discount	37,445	32,285
Award payments made	(25,810)	(24,351)
Changes in operating assets and liabilities:		
Accrued interest and dividends receivable	(388)	82
Other assets	(37)	18
Transactions payable, net	39,616	21,555
Accounts payable and other liabilities	728	(278)
Net cash provided by operating activities	19,331	1,665
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchases of marketable securities	(1,255,010)	(1,180,998)
Proceeds from sales of marketable securities	1,243,417	1,106,317
Purchase of property and equipment	(323)	(108)
Net cash (used in) investing activities	(11,916)	(74,789)
Net increase (decrease) in cash and cash equivalents	7,415	(73,124)
Cash and cash equivalents at beginning of year	22,645	95,769
Cash and cash equivalents at end of year	\$ 30,060	\$ 22,645
Supplemental disclosure of cash flow information:		
Cash paid during the year for federal excise taxes	\$ 1,050	\$ 1,212

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

NOTES TO FINANCIAL STATEMENTS

AUGUST 31, 2006 AND 2005

(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 gain (loss) on sales of marketable securities,” and the changes in market value of open contracts is included within “net unrealized appreciation 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 \$63,181 and \$10,672 at August 31, 2006 and 2005, respectively. Realized gains and losses on forward currency contracts totaled (\$369) and \$235 in 2006 and 2005, respectively. The market value of open forward currency contracts at August 31, 2006 and 2005 was \$526 and (\$80), respectively. The market value is recorded as an asset (liability) in the Fund’s financial statements. The average market value of open foreign currency contracts totaled (\$9) and (\$12) for the years ending August 31, 2006 and 2005, 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, 2006 and 2005 were \$2,764 and \$425, 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, 2006 and 2005 is the net settlement relating to these contracts of \$306 and \$120, 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 \$272 and \$0 at August 31, 2006 and 2005, respectively, which is recorded as an asset (liability) in the Fund's financial statements. The average fair value of open contracts totaled \$42 and (\$29) for the years ending August 31, 2006 and 2005. Realized gains on options totaled \$29 and \$181 for the years ending August 31, 2006 and 2005, 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 year
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 statements 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:

	2006	2005
Building	\$ 13,451	\$ 13,451
Furniture and fixtures	1,915	1,822
Computer equipment	1,009	778
	16,375	16,051
Less: accumulated depreciation	(4,680)	(3,947)
	\$ 11,695	\$ 12,104

Furniture and fixtures includes non-depreciated art work, as defined by FAS 93, of \$77 at August 31, 2006 and 2005.

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, 2006 and 2005, the Fund was in a net unrealized appreciation position; therefore, a deferred federal excise tax liability of \$1,474 and \$1,485, respectively, 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:

	2006	2005
Payable in less than one year	\$ 24,885	\$ 22,959
Payable in one to five years	50,574	38,682
	75,459	61,641
Unamortized discount	(2,902)	(719)
Total	\$ 72,557	\$ 60,922

The expected future liability to the Fund has been calculated based on discount rates ranging from 4.61 percent to 4.82 percent.

6. MARKETABLE SECURITIES

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

	2006		2005	
	<i>Cost</i>	<i>Estimated Market Value</i>	<i>Cost</i>	<i>Estimated Market Value</i>
U.S. and foreign				
governmental obligations	\$117,966	\$118,353	\$77,522	\$80,179
Corporate bonds	31,155	30,739	33,872	34,129
Common and preferred stocks	271,399	298,439	263,467	301,965
Foreign stocks and foreign				
equity funds	140,972	188,579	129,725	164,307
Option and forward foreign				
currency investments	1	272	—	—
Venture capital investments	23,749	14,939	20,976	13,616
Mutual fund	75,560	82,634	66,276	71,948
	\$660,802	\$733,955	\$591,838	\$666,144

7. EMPLOYEE BENEFIT AND RETIREMENT PLANS

The Fund provides medical insurance to all employees working at least thirty hours per week. The Fund also pays 80 percent of the cost to cover each employee's spouse and dependent children, if applicable. The expense for this employee benefit was \$205 and \$230 during fiscal 2006 and 2005, 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 \$50 and \$203 in fiscal 2006, and \$47 and \$189 in fiscal 2005, respectively.

8. CLASSIFICATION OF EXPENSES

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

	2006		2005	
	<i>Program Services</i>	<i>Management and General</i>	<i>Program Services</i>	<i>Management and General</i>
Awards granted, net of cancellations and refunds of \$2,162 and \$1,982 in 2006 and 2005, respectively	\$ 37,022	\$ -	\$ 31,856	\$ -
Federal excise tax	-	1,820	-	1,584
Salaries and other employee expenses	353	2,467	208	2,441
Depreciation expense	-	732	-	656
Travel and entertainment	120	820	21	428
Maintenance and supplies	21	677	15	658
Honoraria	-	436	-	441
Professional fees	123	157	83	139
Printing and design costs	12	44	31	98
Miscellaneous	6	133	2	106
Total expenses	\$ 37,657	\$ 7,286	\$ 32,216	\$ 6,551

9. RELATED PARTIES

The North Carolina Science, Mathematics and Technology Education Center, Inc. (the “Center”) was formed on April 24, 2002. This not-for-profit corporation solicits grants for the purpose of providing funding to improve the performance of students in science, mathematics, and technology. The Fund granted \$35 and \$2,500 to the Center during the years ended August 31, 2006 and 2005, respectively. In addition, the Fund paid \$423 and \$360 of expenses on behalf of the Center during 2006 and 2005, respectively. Expenses included salaries, travel, entertainment, maintenance, supplies, professional fees, printing cost, and other miscellaneous items.

The Health Research Alliance (“HRA”) was formed in November 2005. HRA is a public charity focusing on improving and building strategic partnerships to advance health research. The Fund paid \$212 of expenses on behalf of HRA during 2006. Expenses included salaries, travel, entertainment, maintenance, supplies, professional fees, printing cost, and other miscellaneous items.

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

SCHEDULE I: STATEMENT OF AWARD TRANSACTIONS

YEAR ENDED AUGUST 31, 2006

(All dollar amounts presented in thousands)

Unpaid awards, beginning of year	\$ 60,922
Add – Awards granted (Schedule II)	41,367
Less – Award payments made	(25,810)
Award cancellations (excluding refunds)	(1,739)
Net increase in unamortized discount	(2,183)
Unpaid awards, end of year	\$ 72,557

SCHEDULE II: STATEMENT OF AWARDS GRANTED

YEAR ENDED AUGUST 31, 2006

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. For a complete listing of all 2006 awards, please see the Grants Index on the cd found at the end of this report.

GRANTS INDEX



PROGRAM SUMMARY

	Approved	Paid	Transferred/ Cancelled*
BIOMEDICAL SCIENCES			
Career Awards in the			
Biomedical Sciences	\$13,013,837.94	\$6,537,082.95	\$828,650.00
Hitchings-Elion Fellowships	0.00	90,500.00	0.00
Reproductive Science	481,950.00	146,367.00	0.00
Other Grants	175,087.00	227,087.00	0.00
Total	\$13,670,874.94	\$7,001,036.95	\$828,650.00
INFECTIOUS DISEASE			
Investigators in Pathogenesis			
of Infectious Disease	\$ 5,600,000.00	\$2,680,000.00	\$ 0.00
Scholar Awards in			
Molecular Parasitology	0.00	85,000.00	0.00
Scholar Awards in Molecular			
Pathogenic Mycology	0.00	42,500.00	0.00
Other Grants	3,527,150.00	3,331,917.00	1,600.00
Total	\$ 9,127,150.00	\$6,139,417.00	\$ 1,600.00
INTERFACES IN SCIENCE			
Career Awards at the			
Scientific Interface	\$ 5,554,120.12	\$2,781,842.63	\$523,400.00
Interfaces Awards	0.00	1,725,000.00	0.00
Other Grants	85,000.00	165,000.00	0.00
Total	\$ 5,639,120.12	\$4,671,842.63	\$523,400.00
TRANSLATIONAL RESEARCH			
Clinical Scientist Awards			
in Translational Research	\$ 7,650,000.00	\$4,425,000.00	\$375,000.00
Other Grants	162,500.00	162,500.00	0.00
Total	\$ 7,812,500.00	\$4,587,500.00	\$375,000.00

PROGRAM SUMMARY – CONTINUED

	Approved	Paid	Transferred/ Cancelled*
SCIENCE EDUCATION			
Student Science			
Enrichment Program	\$ 2,120,614.00	\$ 1,615,296.00	\$ 0.00
Other Grants	2,667,600.00	1,414,351.00	10,000.00
Total	\$ 4,788,214.00	\$ 3,029,647.00	\$ 10,000.00
SCIENCE AND PHILANTHROPY			
Communications/			
Science Writing	\$ 47,000.00	\$ 47,000.00	\$ 0.00
General Philanthropy	189,100.00	154,100.00	0.00
Science Policy	93,000.00	93,000.00	0.00
Special Award	0.00	86,320.00	0.00
Total	\$ 329,100.00	\$ 380,420.00	\$ 0.00
GRAND TOTAL†	\$41,366,959.06	\$25,809,863.58	\$1,738,650.00

* The “Transferred/Cancelled” totals reflect grants made to award recipients who changed institutions, modified the terms of their grant at their current institution, or both changed institutions and modified their grant. In these cases, BWF’s policy has been to cancel the remaining portion of the original grant and, as necessary, approve a new grant. 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 under the Grants Index on the cd found at the end of this report, 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.

INFORMATION FOR APPLICANTS



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 2008 award series are listed on page 60.

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.

In 2005, BWF began accepting electronic applications. Now all of our programs accept electronic applications only. To obtain the most up-to-date information about our award programs, visit our website at www.bwffund.org

PROGRAM APPLICATION DEADLINES



2008 AWARD SERIES

BIOMEDICAL SCIENCES

Career Awards in the Medical Sciences October 1, 2007

INFECTIOUS DISEASE

Investigators in Pathogenesis of Infectious Disease November 1, 2007

INTERFACES IN SCIENCE

Career Awards at the Scientific Interface May 1, 2007

TRANSLATIONAL RESEARCH

Clinical Scientist Awards in Translational Research August 15, 2007

SCIENCE EDUCATION

Student Science Enrichment Program April 10, 2007

SCIENCE AND PHILANTHROPY

Received all year

COMPETITIVE AWARD PROGRAMS

BIOMEDICAL SCIENCES

Career Awards in the Medical Sciences

The Career Awards for Medical Scientists (CAMS) program is the result of the reformulation of the Career Awards in the Biomedical Sciences (CABS) program, which was instituted by the Burroughs Wellcome Fund in 1994 and ran through the 2006 award year. The awards are intended to foster the development and productivity of physician-scientists who are early in their careers and to help them make the critical transition to becoming independent investigators. CAMS provides \$700,000 over five years to bridge advanced postdoctoral/fellowship training and the early years of faculty service. Candidates should have an M.D., D.D.S., D.V.M., or equivalent clinical degree. Proposals must be in the area of biomedical, disease-oriented, translational, or in epidemiological (molecular, genetic, or pharmacological) research. Applicants submitting proposals in the area of

epidemiology should contact BWF to determine the eligibility of the proposal. Proposals in health services research or involving large-scale clinical trials are ineligible. During the postdoctoral/fellowship period, awardees may train at degree-granting institutions in the United States or Canada. All faculty positions must be taken at U.S. or Canadian degree-granting institutions. During the award period, at least 75 percent of the awardee's time must be devoted to research-related activities. Researchers who hold a faculty appointment as an assistant professor or the equivalent, or who know they will hold such an appointment within a year of the application deadline, are not eligible.

INFECTIOUS DISEASE

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 14 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 12 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. Degree-granting institutions may nominate up to three 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 10 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. Candidates must hold a current license to practice medicine in the U.S. or Canada. 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 \$2.16 million annually for this program, and grants provide up to \$60,000 per year for three years. Approximately 12 awards are expected to be awarded annually. 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.

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 BWF'S INVESTMENT POLICIES. THIS COMMITTEE IS APPOINTED BY AND REPORTS TO THE BOARD OF DIRECTORS.

CAREER AWARDS IN THE BIOMEDICAL SCIENCES

Aravinda Chakravarti, Ph.D.

Henry J. Knott Professor and Director
McKusick-Nathans Institute
of Genetic Medicine
Dept. of Medicine, Pediatrics,
Molecular Biology and Genetics
Johns Hopkins University School
of Medicine

Thomas M. Jessell, Ph.D.

Investigator, Howard Hughes
Medical Institute
Professor of Biochemistry
and Molecular Biophysiology
Columbia University

George M. Langford, Ph.D.

Dean of Natural Sciences
and Mathematics
University of Massachusetts-Amherst

J. Anthony Morshon, Ph.D.

Silver Professor
New York University

Cecil B. Pickett, Ph.D.

President, Research & Development
Biogen IDEC

Matthew R. Redinbo, Ph.D.

Associate Professor of Chemistry,
Biochemistry and Biophysics
University of North Carolina-
Chapel Hill
(BWF Career Awardee in the
Biomedical Sciences – 1999)

David Tank, Ph.D.

Professor of Molecular Biology
Lewis-Sigler Institute
for Integrative Genomics
Princeton University

John York, Ph.D.

Assistant Investigator, Howard Hughes
Medical Institute
Associate Professor
Duke University Medical Center
(BWF Career Awardee in the
Biomedical Sciences – 1995)

**CAREER AWARDS IN THE
MEDICAL SCIENCES**

Jack Antel, M.D.

Professor of Neurology
and Neurosurgery
McGill University

Shelton H. Earp, M.D.

Professor and Director, Lineberger
Comprehensive Cancer Center
University of North Carolina-
Chapel Hill School of Medicine

Laurie Glimcher, M.D.

Irene Heinz Given Professor
of Immunology
Harvard School of Public Health

Piet de Groen, M.D.

Professor
Mayo Clinic College of Medicine

Margaret K. Hostetter, M.D. (cochair)

Jean McLean Wallace Professor
of Pediatrics
Professor of Microbial Pathogenesis
Chair, Department of Pediatrics
Yale University School of Medicine

Martin M. Matzuk, M.D., Ph.D. (cochair)

Stuart A. Wallace Professor of Pathology
Baylor College of Medicine

Roderick R. McInnes, M.D., Ph.D.

University Professor
Anne and Max Tanenbaum Chair
in Molecular Medicine
Professor of Pediatrics and Molecular
and Medical Genetics
Senior Scientist, Hospital for Sick
Children, University of Toronto
Scientific Director, Institute of Genetics,
Canadian Institutes of Health Research

Louis J. Muglia, M.D., Ph.D.

Professor, Department of Pediatrics
Director, Division of Pediatric
Endocrinology and Diabetes
(BWF Career Awardee in the
Biomedical Sciences – 1995)

Jeffrey A. Whitsett, M.D.

Chief, Section of Neonatology,
Perinatal and Pulmonary Biology
University of Cincinnati
Children's Hospital

J. Lindsay Whitton, M.D., Ph.D.

Professor
Scripps Research Institute

**INVESTIGATORS IN PATHOGENESIS
OF INFECTIOUS DISEASE**

Arturo Casadevall, M.D., Ph.D.

Professor of Medicine and Microbiology
and Immunology
Albert Einstein College of Medicine

Terence S. Dermody, M.D.

Professor of Pediatrics and Microbiology
and Immunology
Director, Elizabeth B. Lamb Center
for Pediatric Research
Vanderbilt University School
of Medicine

William E. Goldman, Ph.D.

Professor of Molecular Microbiology
Washington University School
of Medicine

Philippe Gros, Ph.D.

Professor of Biochemistry
McGill University Faculty of Medicine

Stephen L. Hajduk, Ph.D. (chair)

Director, Global Infectious
Disease Laboratory
Marine Biological Laboratory

Kasturi Haldar, Ph.D.

Charles E. and Emma H. Morrison
Professor of Pathology and
Microbiology-Immunology
Northwestern University Feinberg
School of Medicine

Anne Moscona, M.D.

Vice Chair for Research of Pediatrics
Professor of Pediatrics, Microbiology
and Immunology
Weill Medical College
of Cornell University

David G. Russell, Ph.D.

Professor and Chair of Microbiology
and Immunology
Cornell University College
of Veterinary Medicine

Alan Sher, Ph.D.

Head, Immunobiology Section
National Institute of Allergy
and Infectious Diseases

Joseph W. St. Geme III, M.D.

Professor and Chair of Pediatrics
Professor of Molecular Genetics
and Microbiology
Duke University Medical Center

INTERFACES IN SCIENCE

Laurence F. Abbott, Ph.D.

Professor
Center for Neurobiology and Behavior
Columbia University

James B. Bassingthwaite, M.D., Ph.D. *(chair)*

Professor of Bioengineering
and Radiology
University of Washington

Bonnie Bassler, Ph.D.

Investigator, Howard Hughes
Medical Institute
Professor of Molecular Biology
Princeton University

Emery N. Brown, M.D., Ph.D.

Professor of Computational Neuroscience
and Health Sciences and Technology
MIT-Harvard Division of Health Science
and Technology
Massachusetts Institute of Technology
Associate Professor of Anaesthesia
Harvard Medical School

Julio M. Fernandez, Ph.D.

Professor of Biological Sciences
Columbia University

Wendell Lim, Ph.D.

Professor
Department of Cellular and Molecular
Pharmacology
Department of Biochemistry
and Biophysics
University of California-San Francisco

Erin O'Shea, Ph.D.

Investigator, Howard Hughes
Medical Institute
Professor of Molecular
and Cellular Biology
Harvard University

Susan R. Pfeffer, Ph.D.

Professor and Chair
Department of Biochemistry
Stanford University

Michael C. Reed, Ph.D.

Professor of Mathematics
Duke University

Eric Siggia, Ph.D.

Professor of Physics
Rockefeller University

Susan S. Taylor, Ph.D.

Investigator, Howard Hughes
Medical Institute
Professor of Chemistry and Biochemistry
University of California-San Diego
School of Medicine

*Note: Additional members will be added to
the committee. Check www.bufund.org for the
latest information.*

**CLINICAL SCIENTIST AWARDS
IN TRANSLATIONAL RESEARCH**

Andrea Dunaif, M.D. (cochair)

Charles F. Kettering Professor
of Medicine
Chief, Division of Endocrinology,
Metabolism, and Molecular Medicine
Northwestern University Feinberg
School of Medicine

John W. Griffin, M.D.

Professor of Neurology, Neuroscience,
and Pathology
Director, Department of Neurology
Johns Hopkins University
School of Medicine

Gail Jarvik, M.D., Ph.D.

Professor of Medicine
University of Washington Medical Center

Shannon C. Kenney, M.D.

Kenan Distinguished Professor
of Medicine and Microbiology
University of North Carolina-
Chapel Hill School of Medicine

Alan M. Krensky, M.D.

Shelagh Galligan Professor of Pediatrics
Chief, Division of Immunology
and Transplantation Biology
Stanford University School of Medicine

H. Kim Lyerly, M.D.

Director, Duke Comprehensive
Cancer Center
George Barth Geller Professor
for Research in Cancer
Duke Medical Center

Beverly S. Mitchell, M.D. (cochair)

George E. Beckman Professor
of Medicine
Deputy Director, Comprehensive
Cancer Center
Stanford University School of Medicine

Jennifer M. Puck, M.D.

Professor, Department of Pediatrics
University of California-San Francisco

Steven S. Rosenfeld, M.D., Ph.D.

Professor of Neurology
Director, Division of Neuro-Oncology
Columbia University

Christine E. Seidman, M.D.

Investigator, Howard Hughes
Medical Institute
Professor of Medicine and Genetics
Harvard Medical School

Michael J. Welsh, M.D.

Investigator, Howard Hughes
Medical Institute
Professor, Departments of Internal
Medicine, Physiology, and Biophysics
University of Iowa Carver College
of Medicine

Wayne M. Yokoyama, M.D.

Investigator, Howard Hughes
Medical Institute
Chief, Rheumatology Division
Department of Internal Medicine
Washington University School
of Medicine

*Note: Two members will be added to the
committee. Check www.bwfund.org for the
latest information.*

**STUDENT SCIENCE
ENRICHMENT PROGRAM**

Julia V. Clark, Ph.D.

Program Director
Division of Elementary, Secondary,
and Informal Education
National Science Foundation

G. Thomas Houlihan, Ed.D.

Executive Director
Council of Chief State School Officers

Marian Johnson-Thompson, Ph.D. (chair)

Director, Education and Biomedical
Research Development
National Institute of Environmental
Health Sciences

The Honorable Jeanne H. Lucas

Senator
North Carolina General Assembly

Willie Pearson Jr., Ph.D.

Professor of Sociology and Chair
School of History, Technology,
and Society
Georgia Institute of Technology

Sylvia Sanders, Ph.D.

Elementary Educator
Palo Alto, California

Brenda Shumate Wojnowski, Ed.D.

Program Officer
T. Stem Initiatives

Terri L. Woods, Ph.D.

Associate Professor of Geology
East Carolina University

Margaret M. Young, Ph.D.

Assistant Professor
Department of Biology
Elizabeth City State University

Note: An additional member will be added to the committee. Check www.bwfund.org for the latest information.

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

James Hirschmann

Legg Mason Inc.

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.

Investigator, Howard Hughes
Medical Institute
Luis Alvarez Professor
of Molecular and Cell Biology
University of California-Berkeley



Gail H. Cassell, Ph.D.

Vice President, Scientific Affairs
and Distinguished Lilly Research
Scholar for Infectious Diseases
Eli Lilly and Company
Lilly Corporate Center



Stephen D. Corman

Founder and former Chair
and Chief Executive Officer
PharmaLink Inc.



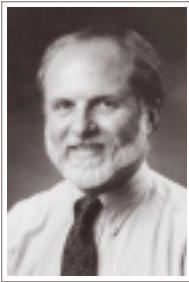
Marye Anne Fox, Ph.D.

Chancellor
University of California-San Diego



Phil Gold, M.D., Ph.D. (chair)

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



Mary-Lou Pardue, Ph.D.

Boris Magasanik Professor of Biology
Massachusetts Institute of Technology

Jerome F. Strauss II, M.D., Ph.D.

Dean, School of Medicine
Executive Vice President for Medical Affairs
Virginia Commonwealth University

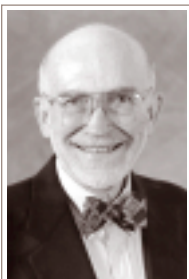


Judith Swain, M.D.

Executive Director, Singapore Institute
for Clinical Sciences (A*STAR)
Professor of Medicine,
National University of Singapore
Adjunct Professor of Medicine,
University of California-San Diego

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

STAFF



EXECUTIVE

Left to right:

Enriqueta C. Bond, Ph.D., President

Scott G. Schoedler, Vice President, Finance



ADMINISTRATION, FINANCE, MEETINGS, AND TECHNOLOGY

Sitting, left to right: Wendell Jones, Technology Coordinator; Glenda Oxendine, Programs Assistant and Document/Web Specialist; Sam Caraballo, Systems and Web Engineer; Brent Epps, Administrative Assistant

Standing, left to right: Barbara Evans, Administrative Meeting Assistant; Martie Nolan, Senior Manager, Facility and Administrative Services; Ken Browndorf, Senior Asset and Accounting Manager; Jennifer Caraballo, Accountant; Betsy Stewart, Secretary; Catherine Voron, Meeting Professional



PROGRAMS AND COMMUNICATIONS

Sitting, left to right: Debra Vought, Senior Program Associate; Debra Holmes, Program Associate; Jean Kramarik, Senior Program Associate; Carr Thompson, Senior Program and Communications Officer

Standing, left to right: Russ Campbell, Communications Officer; Melanie Scott, Senior Program Associate and Database Specialist; Rolly Simpson Jr., Program Officer; Nancy Sung, Ph.D., Senior Program Officer; Victoria McGovern, Ph.D., Senior Program Officer

CONTACT INFORMATION



BIOMEDICAL SCIENCES

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Program Officer

Debra Holmes
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Program Associate

INFECTIOUS DISEASE

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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

COMMUNICATIONS/MEDIA CONTACT

Russ Campbell
news@bwfund.org
Communications Officer

TO OBTAIN INFORMATION ABOUT PROGRAMS

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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FINANCIAL STATEMENTS
AND GRANTS INDEX

