

## Physician-Scientists Receive \$7.5 Million in Awards

The Burroughs Wellcome Fund has awarded Clinical Scientist Awards in Translational Research to 10 researchers who will help bridge the gap between the laboratory bench and patient care.

Made as part of BWF's 2000 award series, the awards each provide \$750,000 over a period of five years and will begin on July 1.

The awards are intended to foster the development and productivity of midcareer physician-scientists who will strengthen translational research—the two-way transfer between basic research and the treatment of patients—through their own studies as well as their mentoring of the next generation of physician investigators.

"Although recent years have seen an explosion of fundamental insights into the mechanisms of disease, transferring this knowledge into practical advances in health care has moved more slowly," says BWF President Enriqueta C. Bond, Ph.D. "The National Institutes of Health and other public and private organizations support a significant amount of basic biomedical research, while industry supports the commercial development of medicines and medical products—yet the vital bridge between these areas remains underserved."

BWF's awards will enable recipients to explore important scientific questions, to apply the resulting knowledge at the bedside, and to bring insights from the clinical setting back to the laboratory for further exploration. These efforts, it is hoped, will lead to a better understanding of the mechanisms of disease, as well as to new methods of diagnosing, treating, and preventing disease.

Among funded projects, the awardees will be studying methods to activate "killer cells" that specifically target cancers, to induce immunity in the cells of persons exposed to the AIDS virus, and to reduce the threat of atherosclerosis by modulating the body's metabolism of certain fats.

**Translational Awards** (Continued on page 7)

## Growing up Together—BWF and Me

By Martha G. Peck, BWF Vice President of Programs

In June 2000, I will leave the Burroughs Wellcome Fund, after 19 years of what I've come to regard as a "once-in-a-lifetime" experience. For me, BWF has not been merely a "job." Rather, it has provided an opportunity to *serve* the scientific and educational communities, to support the careers of hundreds of young scientists, and to help foster cutting-edge research in underfunded areas. And undoubtedly, the most rewarding part of my work at BWF has been the interactions with so many wonderful people.

The anticipated question comes: Martha, what could possibly induce you to leave your job? I reply unhesitatingly: the realization of a long-held dream and another unique opportunity. This fall, I enter the class of 2000 at the University of North Carolina-Chapel Hill School of Medicine. (A fitting start to my own millennium!)

BWF today is vastly changed from the foundation I joined in 1981. And I derive considerable satisfaction in knowing I had the fortunate opportunity to participate in its historic transformation. In this article, I'd like to reminisce a bit about "growing up" with BWF and to describe the Fund's remarkable growth along the way.

"Our long-time foundation director, Iris Evans, is retiring. Would you consider coming back to Burroughs Wellcome Co.," asked Dr. Win Singleton, vice president of the company's medical division. At the time, I was serving as coordinator of clinical

pharmacy services at Wake Medical Center (in Raleigh, North Carolina), having recently returned to pharmacy practice after spending several years as a clinical research scientist in the neurology section of BW Co.'s medical division. My departure from the company 10 months prior had been prompted purely by the practical realization that my job as a clinical research scientist required almost full-time travel to monitor clinical trials, a situation not conducive to nurturing a new marriage or contemplating a future family.

Greeting me on my first day as the newly appointed executive director of the Burroughs Wellcome Fund (October 1, 1981) was BWF President Dr. George Hitchings. "Just call me George," said the retired vice president of research, development, and medical at BW Co., and a Nobel Laureate-to-be. Thus began the start of my lifelong friendship with, and mentoring by, this remarkable scientist and humanitarian. (Later, I was to add George's collaborator and fellow Nobel Laureate, Dr. Gertrude Elion, to the list of special people—a list that also includes the other members of BWF's Board of Directors—who have mentored me during their service with the Fund.)

Competition for the position had been keen, and I later asked George how a relative "greenhorn" just turning 30 had been selected over more senior applicants.

**BWF and Me** (Continued on page 2)

### We've Moved!

BWF has moved into our permanent headquarters building.

Our new particulars are:

21 T. W. Alexander Drive  
Post Office Box 13901  
Research Triangle Park, NC 27709-3901  
Telephone (919) 991-5100  
Fax (919) 991-5160

[www.bwffund.org](http://www.bwffund.org)

**BWF and Me** (Continued from page 1)

"You were the one candidate who seemed more interested in what you could do for BWF than in how BWF might enhance your own career," he replied. And, indeed, I've attempted to keep this focus in my daily activities. For I believe that foundations, as tax-exempt organizations, have a public responsibility not only to be good



Martha Peck

stewards of our resources, but also to put our *primary* focus on responding to needs in our targeted communities and to building constructive relationships with our grantees. BWF has

long strived to promote the "personal touch" in our grant-making. This includes fostering the career development of awardees and building a "wellcome family" among those we support.

In these days of increasing mobility, people generally don't spend nearly two decades with the same organization. But the fact is, I've really worked for two distinct organizations bearing the same name. When I came to BWF, it was a corporate foundation, supported entirely by the pharmaceutical firm known as Burroughs Wellcome Co.-USA. BWF was a modest foundation with assets of just under \$8 million and only one other staff member, Carr Agyapong (who is still with the Fund, as senior program and communications officer). And that's how it stayed for my first six years!

Together, Carr and I handled our competitive award programs, ad hoc grants, meetings, etc. And always George Hitchings was there for inspiration and advice. He called himself the "valve turner"—a label he readily embodied. George not only was an innovative scientist, but as well a creative philanthropist. We both were action-oriented, and we agreed that the size of BWF's awards was not nearly as important as the research prowess of the recipients and the catalytic potential of small but well-placed grants.

In 1991, when George retired and Dr. Howard Schaeffer took over BWF's helm, the Fund's endowment had grown to \$24 million. During the decade since my

arrival, BWF's grants portfolio had enjoyed modest expansion, and our staff had grown to a total of five. Beyond Howard's succeeding George as president, I had little reason to anticipate that an even greater transition was soon to occur.

At a company gathering in early 1992, I recall John Robb, then chief executive officer of the Wellcome Foundation Ltd. (our parent company in the United Kingdom) discreetly asking me what it might take to fully endow BWF. "We'd

need about \$100 million to maintain our current level of grantmaking," I replied. Several months later, Howard Schaeffer returned from a visit to the Wellcome Trust, in London, with news (overwhelming!) that the Trust was considering making a \$400 million gift to BWF.

An agreement was reached in January 1993, and shortly thereafter BWF received the first of five \$80 million annual install-

**BWF and Me** (Continued on page 3)**Why Medicine? Why Now?**

*Some answers are revealed in the essay Martha Peck submitted with her application to medical school. With Martha's permission—given only over her usual sense of modesty—excerpts follow:*

I stare intently at the corpse as the pathologist begins his autopsy of study patient #9. What was to have been a routine site visit to monitor the Phase II clinical trial of BW122U, an experimental antiepileptic, has been changed radically by the sudden death of a patient. A myriad questions flash through my head—relationship to the study drug? patient compliance? IRB reporting? ethics in treating other patients? And to these unknowns, I add another: what am I doing in the autopsy room at 8 p.m.?

The truth be known, however, I am *not* ill at ease. I have always reveled in the sights, sounds, and smells of medicine. Hospital volunteering and working summers in a physician's office provided early familiarity, while my nurse mother, pharmacist neighbor, and doctor mentors mirrored the day-to-day realities of health professionals. My pharmacy experiences assuredly were nontraditional—administering medications to patients at Duke University, serving as the "roving" pharmacist at three mountain clinics, accompanying physicians on ward rounds at the University of North Carolina and local county hospitals, monitoring therapies, and reporting adverse drug reactions. My graduate thesis on medication compliance in geriatric hypertensive patients kindled an ongoing interest in chronic diseases and polypharmacy, as well as provided "firsthand" experience with the statistics—up to 60 percent of outpatients are non-compliant to their chronic medication regimes....

So why medicine? Why now? I believe my unique combination of pharmacy, pharmaceutical, and foundation experience provides substantial opportunity to contribute to medicine, particularly in the area of geriatrics, which has long held my passion and interest. The statistics are well known: by 2015, one in five Americans will be over the age of 65. The health system must gird itself for delivering high-quality, cost-effective care to a graying population.

But the pool of practitioners is not expanding as fast as the geriatric pool. Physicians trained in the problems of aging, who relate well to this population, and who bring additional skills in management, policy, and advocacy have crucial roles to play. Leaders are needed within managed care organizations, residential care facilities, clinical research organizations, the pharmaceutical industry, and interdisciplinary gerontology centers. As a physician, I would be well equipped to fill such a role.

In due course, if my career should be autopsied like the corpse I examined that night, I hope the final report will state: she deferred an M.D. to midcareer, all the while displaying an ongoing predilection for medicine. Her broad knowledge, diverse experience, and proclivity for leadership had substantial impact upon geriatric practice and policy.

**BWF and Me** (Continued from page 2)

ments. This gift resulted, in large measure, from the Trust's sale of its holdings in the Wellcome pharmaceutical enterprise. The sale significantly expanded the Trust's endowment and enabled the Trust to provide a generous gift to its sister foundation in the United States.

The gift brought growth, change—and the creation of a *new* BWF. We had outgrown our space at the company, and the only way to add needed staff was to move off site. So we did—and finding and out-fitting suitable office space became an added job responsibility. Then, driven largely by U.K. tax laws and the Trust's desire that BWF become independent from the company, I was asked to begin the process of completely separating the Fund from BW Co.

After legal consultation to revise our By-laws and Articles of Incorporation, a new and entirely separate private foundation, still bearing the name "Burroughs Wellcome Fund," was born on September 1, 1994. With this came the installation of a new payroll system, benefits, and numerous other services that previously had been provided by the company.

Concurrently with these activities, Howard and the BWF Board of Directors decided that the Fund needed to recruit an individual from the outside to serve as full-time president. Many individuals expressed interest in the position, but Dr. Enriqueta Bond, then executive officer of the Institute of Medicine, brought the requisite knowledge, management experience, and communication and interpersonal skills. Both the board and BWF's staff immediately recognized this "right match," and Queta came to the Fund on July 1, 1994.

BWF has blossomed since Queta's arrival. She and I enjoy a collegial and mutually supportive working relationship and have jointly tackled many of the challenges of expanding BWF staff, programs, and other activities. I'm indebted to her for the freedom she has given me, as well as the personal growth she has helped foster.

I leave BWF a much changed foundation from when I joined it—though our mission to advance the biomedical sciences through

research and education has remained intact. Given that the essence of foundations is their grants, perhaps the most notable change has been the dramatic increase in our grantmaking. In 1981, BWF (with assets of \$7.7 million) made 58 grants totaling approximately \$2.3 million, and the average grant was for roughly \$40,000. In fiscal 1999, BWF (with assets of \$695 million) made 340 grants totaling approximately \$47.4 million, and the average grant was for roughly \$139,000. Due to our greatly expanded assets, I've seen more money

going to more awardees—resulting in more advances in the medical sciences.

I also leave BWF a much-changed person from the experiences of my 19 years of serving philanthropy. Of course, I couldn't take my leave without thanking the awardees, advisers, board members, staff, and numerous others with whom I have had the good fortune to interact. I cannot name all of you, but I do want to convey my sincerest thanks for your help, words of advice, encouragement, support, and so much else. You've been colleagues, mentors, and friends!

## Program Application Deadlines

*For 2001 award series*

### Career Development of Scientists

|  |  |
|--|--|
| Career Awards in the Biomedical Sciences | October 1, 2000                        |
| Life Sciences Research Fellowships       | October 1, 2000                        |
| BWF Research Travel Grants               | March 1/July 1/November 1 of each year |

### Emerging Infectious Diseases

|   |                  |
|---|------------------|
| Scholar Awards and New Investigator Awards in Molecular Parasitology        | January 15, 2001 |
| Scholar Awards and New Investigator Awards in Molecular Pathogenic Mycology | January 15, 2001 |
| New Initiatives in Malaria Research   | January 15, 2001 |

### Therapeutic Sciences

|  |                   |
|--|-------------------|
| Clinical Scientist Awards in Translational Research                      | September 1, 2000 |
| New Investigator Awards in the Pharmacological or Toxicological Sciences | November 1, 2000  |

### Reproductive Science

|  |                 |
|--|-----------------|
| Career Awards in the Biomedical Sciences                   | October 1, 2000 |
| Obstetrics and Gynecology Research Fellowships             | October 1, 2000 |
| Reproductive Scientist Development Program Research Grants | October 1, 2000 |

### Interfaces in Science

|   |                   |
|---|-------------------|
| Interfaces between the Physical/Chemical/Computational Sciences and the Biological Sciences | To be announced*  |
| Innovation Awards in Functional Genomics  | To be announced** |

### Science Education

|   |                  |
|---|------------------|
| Student Science Enrichment Program                          | October 15, 2000 |
| BWF Visiting Professorships in the Basic Medical Sciences   | March 1, 2001    |
| BWF Visiting Professorships in the Microbiological Sciences | March 1, 2001    |

### Environment for Science

Received all year

\* It is anticipated that these awards will be made approximately every two years. The deadline for the 2000 award series was April 10, 2000.

\*\* BWF is evaluating this program to determine its future direction. More information will be available by August 2000.

Note: If a date falls on a weekend or holiday, the deadline is the next business day.

## More Than \$1 Million Awarded for Science Education

Thousands of middle school and high school students across North Carolina are digging into a variety of science activities, thanks to nearly \$1.1 million in new BWF awards.

The students are learning firsthand about science and the excitement of research. Among their activities, the students are using methods of art and design to create three-dimensional working models of biological systems, exploring freshwater and wildlife environments, and working alongside computer experts to sharpen their understanding of computational science.

BWF made Student Science Enrichment Program (SSEP) awards to eight nonprofit educational and community organizations statewide. Made as part of BWF's 2000 award series, the awards each provide up to \$180,000 over three years.

"These science-enrichment projects enable students to participate in a variety of hands-on, inquiry-based avenues of exploration—an educational approach that we believe to be an effective way to increase students' understanding of science," says BWF President Enriqueta C. Bond, Ph.D. "We hope the projects will nurture students' enthusiasm about science, expose them to the excitement of scientific discovery, and interest them in pursuing careers in research or other science-related areas."

The new awards bring to almost \$6 million the total that BWF has invested through our science-enrichment program (which is limited to North Carolina) during the past five years. We've supported 46 projects, which have reached more than 20,000 middle school and high school students.

The 2000 award recipients and their projects are:

**Duke University**  
Design to Learn

**Johnson C. Smith University**  
Intensive Summer Science Camp

**North Carolina State University**  
Science and Mathematics Colloquies at the Science House

**Pines of Carolina Girl Scout Council**  
Healthy START UP: Science and Technology around Research Triangle Park

**Shaw University**  
Mentoring and Encouraging the Science Skills of Youth

**Shodor Education Foundation**  
Stimulating Understanding of Computational Science through Collaboration, Exploration, Experiment, and Discovery

**Swain County High School**  
Swain County Students Involved and Experiencing Nature, Careers in Science, and Environmental Awareness

**Wilmington Children's Museum**  
Middle School Docent Program

Through our SSEP awards, BWF seeks to encourage the widespread use of creative inquiry-based science education and to foster the development of effective materials and methods for teaching science.

"BWF's resources are not sufficient to change the nation, but we feel these enrichment projects can produce measurable results on a smaller scale—our home state—that will directly and immediately affect real students in real schools," says Carr Agyapong, BWF senior program and communications officer. "Our broader goal is to see the lessons learned from

these projects incorporated into nationwide efforts to improve science, mathematics, and technology education—at all levels, in all schools, and beyond classroom doors."

One of BWF's measures of the program's success is the response we receive from student participants. In a recent survey, 88 percent of the students who responded said they liked the program, and 81 percent said they would recommend the program to a friend.

We are continuing to investigate ways to measure the effect of the SSEP activities on the students' educational choices, such as whether they choose to take science courses in high school or choose to pursue a science degree in college.

Additional information about the Student Science Enrichment Program is available online at <http://ssep.bwffund.org>. Developed and maintained by students in a SSEP project conducted by the Durham-based Shodor Foundation, this Web site provides students with interactive science activities; promotes communication among program award recipients; and provides information on experiential science programs to students, parents, educators, and community leaders.

The application deadline for the 2001 series of awards is October 16, 2000. For more information, visit BWF's Web site at [www.bwffund.org](http://www.bwffund.org), or contact Melanie B. Scott, programs and database specialist, at (919) 991-5107 or [mscott@bwffund.org](mailto:mscott@bwffund.org).

## Bringing "One-Stop Shopping" to Malaria Researchers

With a \$1 million grant from BWF, an international group of researchers is developing a comprehensive and easy-to-use database containing information about the genetic makeup of *Plasmodium falciparum*, the organism responsible for much of the world's burden of human malaria.

The *Plasmodium* Genome Database, or PlasmoDB, will help speed the transfer of genomic information, now flooding from a number of laboratories, into the hands of malaria researchers worldwide, say its developers. The project is led by David Roos and Chris Overton, of the University

of Pennsylvania, and by Ross Coppel, of Monash University, in Australia.

"In particular," the researchers say, "effective dissemination of genomic information should accelerate the development of new therapeutics and vaccines."

The grant, announced in February 2000, builds on BWF's support for malaria research.

Since 1996, BWF has helped support the Malaria Genome Project, an international effort to determine the complete sequence of the DNA of *P. falciparum*. The other funders are the Department of Defense

**Malaria Research** (Continued on page 5)



## **Malaria Research** *(Continued from page 4)*

and the National Institute of Allergy and Infectious Diseases, in the United States, and the Wellcome Trust, our sister philanthropy, in the United Kingdom.

Progress has been steady. Scientists have completed the sequencing of several of the organism's 14 chromosomes (the thin strands of DNA contained in the nucleus of cells) and are forging ahead on the others.

"With such success, there has come growing recognition among malaria researchers that mining this genetic wealth most effectively will require making the information widely available," says BWF Program Officer Victoria McGovern, Ph.D. "This is where PlasmoDB comes in."

By serving as a single, reliable, searchable source that integrates and catalogues the

latest genetics information, the database will offer what its developers call "one-stop shopping" to malaria researchers.

Users will be able to access PlasmoDB by the World Wide Web, by e-mail, or by requesting the data on CD-ROM. Thus, it will be easily available to all parties, regardless of geographic location.

Of critical importance, say its developers, PlasmoDB will be easy to use. It will feature a "user-friendly" interface, and assistance will be available through on-line help desks, as well as through such activities as tutorials and workshops.

In developing PlasmoDB, the group will assemble the computer hardware and software, gather data from the genome sequencing centers and other laboratories, and serve as the system's curators, among

other activities. Along the way, the group will consult with an advisory committee composed of experts in malaria research, as well as in bioinformatics and database design.

The group plans to have the first stages of PlasmoDB operating by the end of 2000, with extensive additions and upgrades to follow, most likely during the next two years.

"Supporting this project represents what we think philanthropies are best suited to do," Dr. McGovern says. "By making such a timely, targeted grant in an area where funding traditionally has been inadequate, BWF is catalyzing work that promises to fill an important scientific gap—and, we hope, to advance efforts to control this devastating disease."

## **New Awards Target Tropical Infectious Diseases: BWF Adds to Support**

Scientists in both developed and developing nations are joining together as equal partners in the fight against tropical infectious diseases, thanks to roughly \$19 million in new awards from BWF and the Wellcome Trust, our sister philanthropy in the United Kingdom.

This first-of-its-kind award program, called the Wellcome Trust-Burroughs Wellcome Fund Infectious Diseases Initiative, is intended to help build the research capacity of tropical developing countries as well as to help reduce the toll that infectious diseases take in these regions.

Launched in 1998, the initiative requires that research teams must include scientists from the United States or Canada, from the United Kingdom, and from the tropical developing nations themselves. Although proposals may originate from any of the geographic areas involved, scientists from developing countries must play a pivotal role in the research, and, in most cases, the main research must be conducted in tropical locations where infectious diseases are causing significant morbidity and mortality.

In the initiative's first round of awards, made in late 1999, funding went to seven programs that will conduct research in Africa, Central America, and South America.

The programs will target some of the major killers of the developing world, including tuberculosis, measles, hepatitis C, and sexually transmitted diseases.

Most of the awards provide on the order of \$2 million to \$4 million (U.S. currency) over a period of five years.

The programs, along with the names and affiliations of the principal investigators, are:

### **Evaluation of protective, disease-associated and therapeutic immunity to hepatitis C virus infection**

*Main location of research: Egypt*

G. Thomas Strickland  
University of Maryland-Baltimore

### **Population pathogenesis of tuberculosis**

*Main location of research: Mexico*

Peter Small  
Stanford University

### **Strategies for the control of blinding trachoma**

*Main location of research: Gambia and Tanzania*

David Mabey  
London School of Hygiene  
and Tropical Medicine

### **Childhood tuberculosis: identification of the molecular immunological basis of susceptibility and resistance to mycobacterial infection**

*Main location of research: South Africa*

Michael Levin  
Imperial College School of Medicine  
(London)

### **Impact of HIV on measles and measles immunization**

*Main location of research: Zambia*

Felicity Cutts  
London School of Hygiene  
and Tropical Medicine

### **Urban community randomization trial of sexually transmitted diseases**

*Main location of research: Peru*

King Holmes  
University of Washington-Seattle

### **Clinical response and resistance to antimonial drugs in *Leishmania***

*Main location of research: Colombia*

Nancy Saravia  
International Center for Medical Training  
and Investigation  
(Cali, Colombia)

**Infectious Diseases** *(Continued on page 8)*

## More Than \$2.3 Million Awarded in Pharmacology and Toxicology

BWF has made New Investigator Awards in the Pharmacological or Toxicological Sciences to 11 scientists who hold promise for bringing new ways of thinking and new experimental approaches to their fields.

Made as part of BWF's 2000 award series, the awards each provide \$210,000 over a period of three years and will begin on July 1.

Among funded projects, one awardee in the pharmacological sciences will probe the molecular and cellular mechanisms of learning and other cognitive functions in the mammalian brain, with an eye toward identifying potential molecular treatments for memory disorders in humans.

In the toxicological sciences, one awardee will study the basic development of mitochondria, critical energy-producing structures within cells, with a goal of learning how to avoid or reduce mitochondrial malfunction that now can lead to disease.

The awards are intended to foster the development and productivity of scientists who are at the beginning stages of their faculty careers, and to enable them to pursue research projects that have higher-risk but also the potential for moving their fields in significant new directions.

"We believe that supporting the career development of tomorrow's leading scientists offers an effective way to strengthen and expand interactions between the pharmacology and toxicology communities," says BWF President Enriqueta C. Bond, Ph.D. "These fields share much in common: both are inherently multidisciplinary, and both are well-positioned to capitalize on the new ideas and experimental approaches emerging from such frontiers of investigation as the computational sciences, animal models, and molecular genetics."

These awards flow naturally from BWF's goal of leveraging scientific investigation and knowledge, promoting creative interaction among scientists, as well as among disciplines, for the benefit of all.

The awardees, along with their institutions and research projects, are:

### PHARMACOLOGICAL SCIENCES

#### **Pehr A. B. Harbury, Ph.D.**

Stanford University School of Medicine  
DNA display: in vitro evolution of small molecules

#### **Neil L. Kelleher, Ph.D.**

University of Illinois at Urbana-Champaign  
Genome-proteome correlations in respiratory pathogens: an experimental approach for identification of new pharmacological targets

#### **Carla Mattos, Ph.D.**

North Carolina State University  
The surface features of the Ral GTPase obtained from the multiple solvent crystal structures and from its complex with RalBP1 and calmodulin

#### **Erik J. Sontheimer, Ph.D.**

Northwestern University  
Reversible control of RNA structure with small biarsenical ligands

#### **Joseph Tsien, Ph.D.**

Princeton University  
Novel pharmacogenetic approach to neuronal signaling

#### **Hongtao Yu, Ph.D.**

University of Texas Southwestern Medical Center-Dallas  
Molecular investigation of transitions and checkpoints in mitosis

### TOXICOLOGICAL SCIENCES

#### **Raffi V. Aroian, Ph.D.**

University of California-San Diego  
*Bacillus thuringiensis* toxicity and resistance in nematodes

#### **Virginia W. Cornish, Ph.D.**

Columbia University  
An in vivo screen for enzymatic activity

#### **Bevin P. Engleward, Sc.D.**

Massachusetts Institute of Technology  
Fluorescent detection of loss of heterozygosity in mammals

#### **James M. Ford, M.D.**

Stanford University School of Medicine  
Transcriptional regulation of damage-inducible DNA repair genes

#### **Carla M. Koehler, Ph.D.**

University of California-Los Angeles  
Mitochondrial biogenesis in health and disease: assembly of the mitochondrial inner membrane

The application deadline for the 2001 series of awards is November 1, 2000.

Candidates must be U.S. or Canadian citizens or permanent residents. They must have an M.D. or Ph.D. degree and be independent investigators appointed within three years of the application deadline to a tenure-track position as an assistant professor or its equivalent.

BWF encourages candidates to define these fields in the broadest terms, so long as the research has application to either the pharmacological or toxicological sciences.

Candidates need not hold appointments in established programs in pharmacology or toxicology; BWF encourages applications from researchers in such diverse departments and fields as biochemistry, genetics, molecular biology, and the physical and computational sciences. Professionals in clinical and veterinary departments who are engaged in fundamental research also are eligible.

For more information, visit BWF's Web site or contact Jean A. Kramarik, program associate, at (919) 991-5122 or [jkramarik@bwfund.org](mailto:jkramarik@bwfund.org).

[www.bwfund.org](http://www.bwfund.org)

Check out our new look! BWF's Web site has been redesigned. The site contains complete descriptions of our award programs and lists the most recent award recipients.

You also can access BWF's annual reports, the latest directory of recipients of our competitive scientific awards, previous newsletters, and much more.

**Translational Awards** (Continued from page 1)

The 2000 award recipients, along with their institutions and research projects, are:

**Robert B. Darnell, M.D., Ph.D.**

Rockefeller University  
Detection and activation of tumor-specific killer cells in animal models and cancer patients

**Brian J. Druker, M.D.**

Oregon Health Sciences University  
Mechanism-based therapy for chronic myelogenous leukemia

**Thomas F. Gajewski, M.D., Ph.D.**

University of Chicago Pritzker School of Medicine  
Development of a second generation melanoma vaccine

**Daniel C. Javitt, M.D., Ph.D.**

New York University School of Medicine  
NMDA-based treatment development for schizophrenia

**Joseph M. McCune, M.D., Ph.D.**

University of California-San Francisco School of Medicine  
Gladstone Institute of Virology and Immunology  
Regulation of human thymic function in vivo

**M. Juliana McElrath, M.D., Ph.D.**

University of Washington School of Medicine  
Fred Hutchinson Cancer Research Center  
Induction of cellular immunity in HIV-1 exposed seronegative individuals

**Mark R. Philips, M.D.**

New York University School of Medicine  
Endomembrane trafficking of Ras: novel molecular targets for anticancer agents

**Daniel J. Rader, M.D.**

University of Pennsylvania School of Medicine  
Novel therapeutic approach to atherosclerosis through modulation of HDL metabolism

**Don C. Rockey, M.D.**

Duke University Medical Center  
The cellular and molecular basis of portal hypertension: an endothelialopathy in cirrhosis

**Matthew L. Warman, M.D.**

Case Western Reserve University School of Medicine  
Delineating the proteins and pathways that maintain human joints and their potential for treating heritable and acquired forms of arthritis

BWF's translational research award program addresses a pressing national need. A number of factors, perhaps most notably the growth of managed health care, have increased the pressure on academic medical centers, which historically have been at the forefront of both basic and clinical

**Translational Awards** (Continued on page 8)

**Fighting Free Radicals**

Atherosclerosis, many neurodegenerative diseases, and the paralyzing aftereffects that follow a stroke are all linked to a powerful biological process known as oxidant stress.

"Oxidant stress, or oxidative injury, is a term that refers to the presence in the body of too many free radicals—that is, a kind of molecule that is derived from oxygen and is very unstable," says Jason Morrow, M.D., a 1999 recipient of a BWF Clinical Scientist Award in Translational Research.

Free radicals have the potential to damage important biomolecules, including proteins, lipids, and DNA, by modifying them chemically, destroying their ability to function.

"The human body has developed an inordinate number of mechanisms to repair or control oxidative stress," says Dr. Morrow, who specializes in this field as a professor of medicine and pharmacology at Vanderbilt University Medical Center.

His research focuses on a family of molecules called the isoprostanes, which form spontaneously in the body in response to oxidative stress. "The chemical reaction of oxygen with arachidonic acid [a major component of all cell membranes] gives rise to a number of molecules, one of which is the isoprostanes," Dr. Morrow explains.

He has been able to determine that isoprostane formation occurs very predictably and consistently in this way—so much so that spectrometric measurements of isoprostane formation have become the "gold standard" for assessing oxidative injury in vivo. Previous methods had performed well in the test tube but fallen short in their application to living humans.

"There had been a translational gap there, no doubt about it," says Dr. Morrow, who has received three patents for this new means of assessing oxidative injury.

But his investigations don't end there. Dr. Morrow now is looking more closely at the process of isoprostane formation, as well as at the metabolism and biological activity of these compounds once formed. He also uses mass spectrometry to study certain compounds that inhibit isoprostane formation—notably, vitamins E and C—to try to see how they achieve this protective effect.

Another of his endeavors is fostering an interest in clinical research among new medical students. In this regard, Vanderbilt University, with its strong tradition as a research-oriented medical school, has proved an ideal setting.

Several years ago, Dr. Morrow was asked to launch the Medical Scholars Program, in which five medical students are given the opportunity (with stipend) to add one year of intensive research to their curriculum. "Some 200 faculty members are available as mentors through this program, so the choices for research area range from molecular to clinical to epidemiological," he says.

On completion of the research year, each scholar gives a formal presentation, and publications are encouraged as well. "In 1998, with five scholars, we had eight publications. That's a lot," Dr. Morrow says proudly.

But his plans for the future are bigger still: Vanderbilt has applied to the National Institutes of Health to fund three additional medical scholar positions—and these three will be designated specifically for translational research.

**Translational Awards** (Continued from page 7)

research, to invest their faculty's time more in patient care and less in research.

"Our awards are intended to relieve some of this pressure for individuals whose research promises to contribute significantly to medical knowledge," says BWF Program Officer Nancy Sung, Ph.D. "The awards 'buy time' from other duties, enabling truly outstanding researchers to continue doing what they do best—which includes providing critical guidance for up-and-coming physician-scientists."

A recent survey of current awardees in the translational research program illustrates the importance of mentoring.

"Since these are people who already are successful, with their careers well established, we wanted to get at the question of what went into their success," says Dr. Sung. "Three common factors have emerged."

One factor is the awardees' relative lack of debt at the time of graduation from medical school, a finding that might be expected, given the financial squeeze that pushes many newly minted M.D.s toward clinically oriented jobs that offer a higher immediate payoff.

The second factor is the awardees' early exposure to research—in most cases, significant exposure while they were still in medical school.

The third factor is that the awardees typically had mentors who conveyed enthusiasm for research itself. Even more important than their specific guidance or help, the mentors' clear validation and enjoyment of the day-to-day work of scientific investigation seemed to plant an interest among their young associates that later would bear scientific fruit.

Dr. Sung emphasizes that this is a "small, informal, retrospective" study. But the information, she says, may be informative for other funding organizations.

"Clearly," she says, "funding that would lower the debt load for medical graduates, and programs that would draw medical students into research and put them in contact with active physician-scientists as mentors, could each contribute toward improving the picture for translational research."

BWF's translational award program is described in more detail in our 1999 annual report, which is available in printed form or on our Web site at [www.bwfund.org](http://www.bwfund.org).

The application deadline for the 2001 series of awards is September 1, 2000.

Candidates must be U.S. or Canadian citizens or permanent residents. Candidates generally must be affiliated with a medical school; scientists at other types of degree-granting institutions (including schools of veterinary medicine, public health, and pharmacy) will be considered only if they can coordinate with institutions that provide the patient connection essential for translational research.

Candidates must have an M.D. or M.D.-Ph.D. degree and hold an appointment or joint appointment in a subspecialty of clinical medicine. In exceptional circumstances, non-M.D. candidates will be considered if their work is likely to contribute significantly to the clinical enterprise; these candidates should hold an appointment or joint appointment in a clinical department.

Candidates must be academic investigators at the late assistant professor level or the associate professor level, holding a tenure-track or equivalent position, and they already must have established an independent research career.

For more information, visit BWF's Web site at [www.bwfund.org](http://www.bwfund.org), or contact Debra Linkous, program associate, at (919) 991-5116 or [dlinkous@bwfund.org](mailto:dlinkous@bwfund.org).

# FOCUS

This newsletter is published quarterly by the Burroughs Wellcome Fund, an independent private foundation dedicated to advancing the medical sciences by supporting research and other scientific and educational activities.

Send comments to:

FOCUS editor  
Burroughs Wellcome Fund  
Post Office Box 13901  
Research Triangle Park, NC 27709-3901  
Telephone (919) 991-5119  
Fax (919) 991-5160  
E-mail: [khede@bwfund.org](mailto:khede@bwfund.org)

Information about BWF and our award programs is available on the World Wide Web at [www.bwfund.org](http://www.bwfund.org).

**Infectious Diseases** (Continued from page 5)

"This exciting program brings together the firsthand knowledge and experience of researchers working in developing countries and the complementary expertise of U.K. and North American researchers in both laboratory and long-term field studies," says Dr. Richard Lane, program director for the Wellcome Trust's Tropical Initiatives. "It offers new scope for researchers to tackle some of these very persistent health problems."

"It is increasingly clear that forming global partnerships, effectively multiplying the strengths of each of the participants, is a key step toward reducing the health toll of infectious diseases in the tropics," says BWF President Dr. Enriqueta C. Bond. "Moreover, given the insidious potential of these diseases to spread beyond national boundaries, working now to understand both the diseases themselves and the eco-

nomic, social, and public health conditions that let them thrive may prove an important investment in the long-term health of the world."

The initiative initially committed \$25 million, provided by the Wellcome Trust, to supporting collaborative research programs. BWF helps administer the initiative. In response to the level of researcher interest—more than 250 groups applied for the first round of awards—BWF in March 2000 committed an additional \$1 million to the initiative.

The initiative now is evaluating a second round of proposals, and the awardees are expected to be announced later this year.

Details about the initiative and its awards are available on the Wellcome Trust's Web site ([www.wellcome.ac.uk](http://www.wellcome.ac.uk)) and BWF's Web site ([www.bwfund.org](http://www.bwfund.org)).