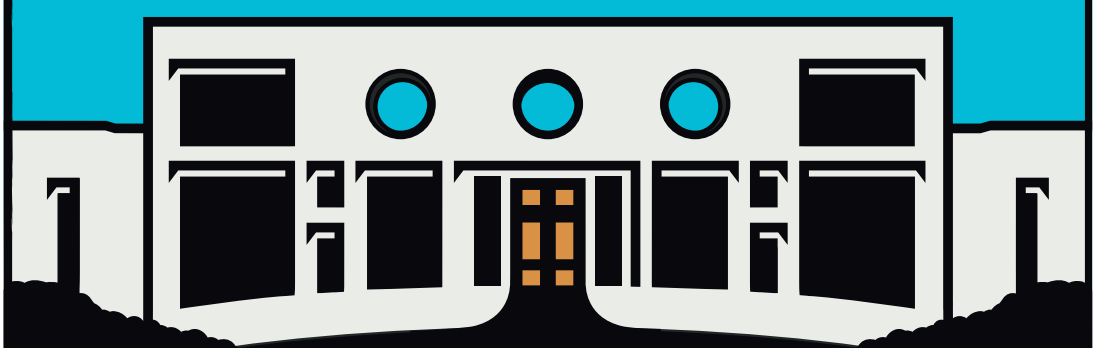
A Legacy of Fueling Inquiry-Driven Research



BURROUGHS WELLCOME FUND
1955-2015

BURROUGHS
WELLCOME
FUND

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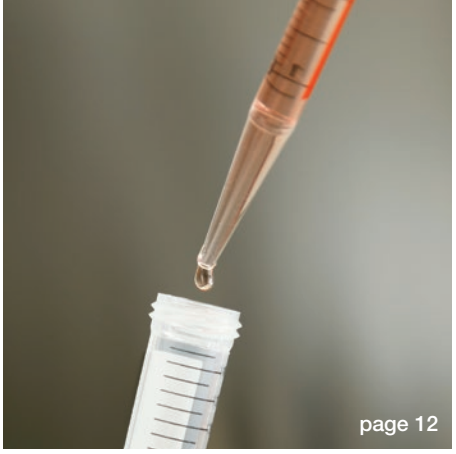
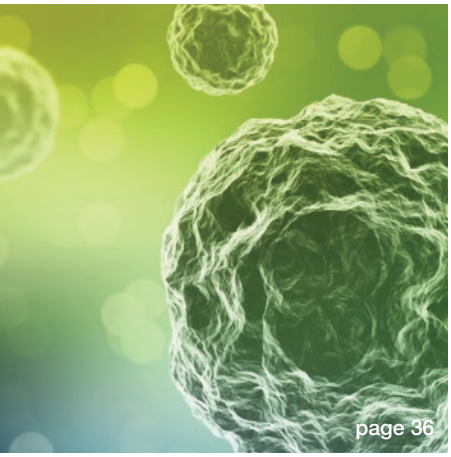
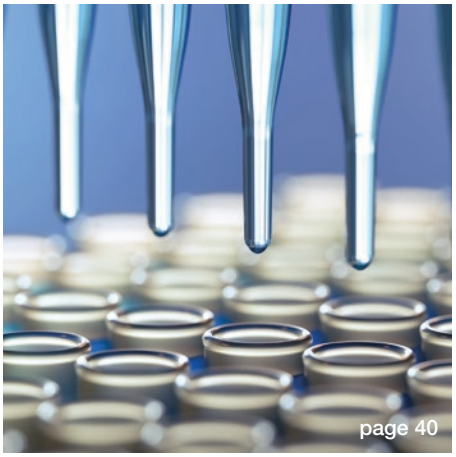
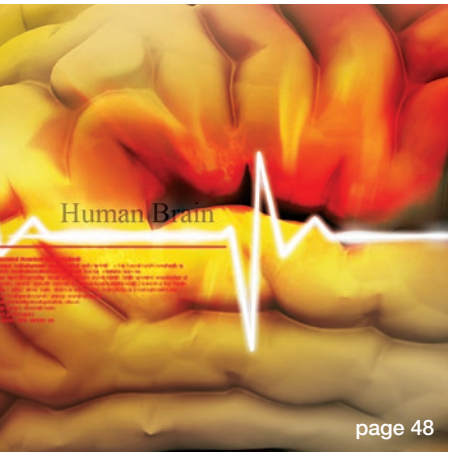








HISTORY OF THE BURROUGHS WELLCOME FUND 1955-2005

Read or download a comprehensive history of the Fund's first 50 years at *bwfund.org/history*. Email *news@bwfund.org* to order a hard copy.

INTRODUCTION

The Burroughs Wellcome Fund's mission is to advance biomedical research and since its founding in 1955, it has focused on the human capital of the research enterprise: its people. The Fund is committed to enabling curiosity-driven research and innovative education, focusing especially on areas of biomedical research that are underfunded and underserved. With that focus in mind, the Fund has made several changes within the past decade.

This volume will look at the Fund's accomplishments and vision during the decade 2005–2015, a period that has witnessed major changes not only in biomedical science, but also in the environment within which that science is being accomplished. The Fund has continued throughout these years to fund areas where it can have the most impact, primarily by supporting junior investigators.

The Burroughs Wellcome Fund's first 50 years have been reviewed in two previous volumes. The first 30 years are captured in former Executive Director Iris Evans's *Investment in Research: The Burroughs Wellcome Fund 1955–1985*. During this time, and until 1994, the Fund served as a mechanism to make philanthropic grants in biomedical research for the Burroughs Wellcome Company (USA). In 1994, with the sale of the company to Glaxo, the foundation received a $400 million endowment from The Wellcome Trust. The 2005 publication *History of the Burroughs Wellcome Fund 1955–2005* documents this period in the foundation's existence.

The following chapters offer a glimpse inside the Burroughs Wellcome Fund's progress in advancing biomedical research over the past decade. To commemorate the Fund's 60th anniversary in May of 2015, we celebrate the legacy of curiosity-driven research that drives our mission and continues the search for new scientific opportunities.

Recovering from the Market Crash

One of the most significant events the Fund experienced in the past decade was not a scientific one, but an economic one: the stock market crash of 2008. This economic downturn directly affected the Fund's ability to make awards. To add to the drama of the time, the Fund was undergoing its first major leadership change since becoming a fully independent foundation in 1994.

The leadership of President Enriqueta Bond and a series of wise and energetic members of the Board of Directors helped establish the Fund as a major player in health research funding. As detailed in *History of the Burroughs Wellcome Fund 1955–2005*, Dr. Bond and the Board helped the Fund solidify its reputation as a foundation willing to search out and fund the best and brightest researchers in areas considered valuable, yet underfunded.

Dr. Enriqueta (Queta) Bond became the Fund's first full-time president in July 1994, coming to the Fund from the Institute of Medicine, where she was the Institute's executive officer. Many of the programs in place today were founded under Dr. Bond's leadership. In 2007, Dr. Bond announced her retirement.

In July 2008, Dr. John Burris assumed the presidency. Burris came to the Fund from Beloit College in Wisconsin, where he had been president since 2000. He was no stranger to the Burroughs Wellcome Fund. He chaired the advisory committee of the Student Science Enrichment Program from 1996-2002 and during the 1990s interacted with the Fund in his role as director of the Marine Biological Laboratory in Woods Hole, Massachusetts.

When Burris assumed the presidency of the Burroughs Wellcome Fund, the stock market was already reeling from the initial effects of the global financial crisis. In September 2008, the Fund's financial team began to examine ways to retain the value of the Fund's endowment, which was already suffering large losses.

Dr. John Burris
BWF President

"Foundations can stimulate interactions, can try new areas for emphasis, and can react quickly to changing opportunities. We also remain clearly connected to each other and the human interactions that are so critical for progress."

Dr. John E. Burris, 2010 Annual Report

Dr. Enriqueta Bond
BWF President
1994-2008

In October, with the impact of the world equity market meltdown worsening, the Fund's investment committee and the Board met to consider the Fund's assets and spending in an environment of high volatility. Recognizing that measures needed to be taken to protect the endowment until the capital market crisis abated, the Board suspended most of its competitive grant programs, decreased the amount spent on ad hoc grants, reduced the number of awards, reduced expenses, and cut payouts to existing awardees by 50 percent. According to this plan, all awardees would ultimately receive the funds they had been promised; but taking these measures would give the Fund some time to avoid taking the loss from the market. Hardship requests would be managed on a case-by-case basis. By enacting these measures, the Fund was able to rebound quickly when the market recovered.

Recapturing assets allowed the Fund to soon operate at full strength. Competitive grant offerings were restored and a few newer programs were even added to the mix. Full payouts to awardees were restored as the Fund's endowment recovered.

During the financial shake up, the Fund continued focusing on strategic planning to examine its funding focus, a process it undertakes every five years. In 2010, this "terrain mapping" exercise concluded with the establishment of the Regulatory Science program and the discontinuation of the Fund's program in Translational Research, as well as a commitment to the other existing programs.

In the following chapters, we'll review the Fund's programming that enables it to help advance biomedical research.

"BWF serves best as a 'niche player,' and our Board of Directors has carefully selected areas of grantmaking in which we will support individual researchers rather than research projects or infrastructure."

Dr. Enriqueta Bond, 2005 Annual Report

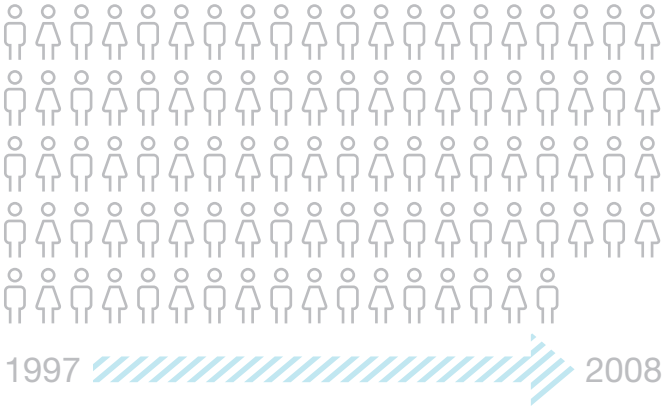
The Fund's headquarters serves as a gathering space for its award recipients to share ideas and network.

A Catalyst for Emerging Science: Translational and Regulatory Science

By 2005, the Burroughs Wellcome Fund was fully engaged in funding an emerging area of biomedical science: so-called bench-to-bedside, or translational, research aimed at moving laboratory discoveries, which may have been inspired by clinical experience, to small-scale studies in human subjects. The Burroughs Wellcome Fund was among the first organizations to lead funding efforts in translational research, through a competitive grant program called the Clinical Scientist Awards in Translational Research, or TRANS.

The Fund made its first TRANS awards in 1997 to fund associate-level physician researchers conducting research that translated laboratory findings into clinical applications. Between 1997 and 2008, TRANS invested more than $72 million, funding the bench-to-bedside research of 97 clinical professionals from a number of medical subspecialties.

The Fund's role in the emerging field of translational research helped shape and define what it meant to conduct translational research in an academic environment. By the end of the decade, other major funders had taken notice. Notably, the National Institutes of Health (NIH) in 2011 established the National Center for Advancing Translational Research. This center connected existing translational programs across several NIH institutes and created a major source of federal funding for translational research in biomedicine, the Clinical and Translational Science Awards (CTSA).



The Clinical Scientist Awards in Translational Research program invested more than

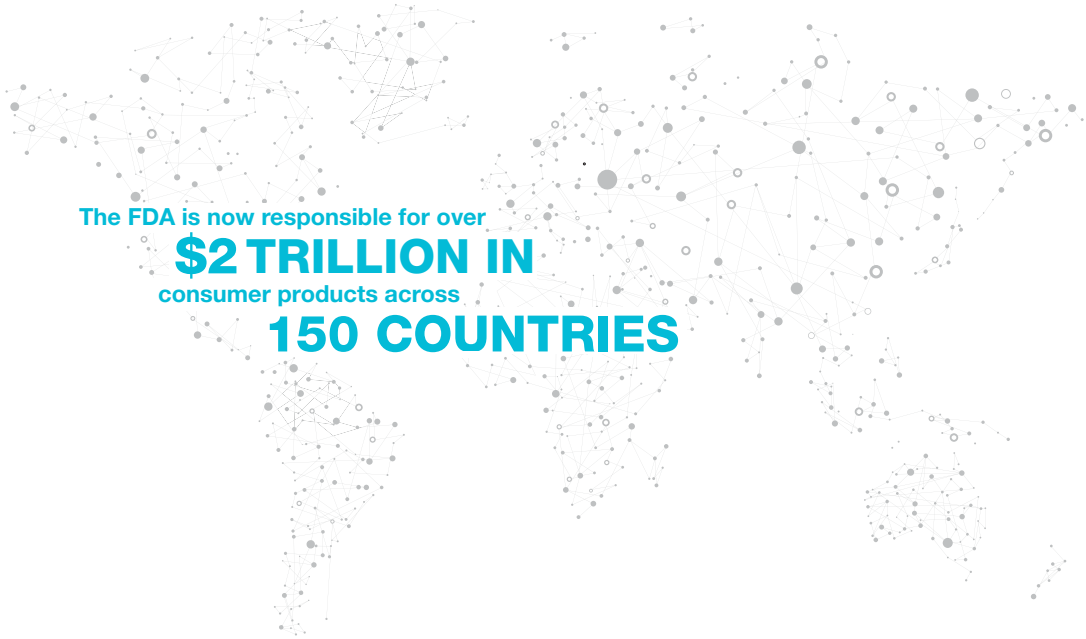
$72 million

in 97 clinical professionals from 1997-2008

The major investment in translational research by NIH and others led the Burroughs Wellcome Fund to pursue a different area that could benefit from early catalytic funding.

Over the last century, regulations governing the testing and development of drugs and medical devices have resulted in a clearer path for safe, effective therapies—as opposed to only the most aggressively marketed products—to reach the market. In recent years, however, the U.S. Food and Drug Administration (FDA), which is responsible for regulating biomedical science and technology, has become dramatically overburdened and underresourced. Now responsible for regulating over $2 trillion in consumer products across 150 countries, the agency has neither the funding nor the staffing necessary to keep up with its rising responsibility. For many researchers who aimed to translate promising lab-based innovations into effective clinical care, the time required to gain regulatory approval had become prohibitive. As a result, translational research was slowed considerably.

By 2007, it was evident that one area that clearly needed critical attention was regulatory science, which the FDA defines as the "development and use of new tools, standards, and approaches to more efficiently develop products and to more effectively evaluate product safety, efficacy, and quality." Regulatory science is essential to translational research, as turning discoveries into innovative medical treatments requires that the science of regulation keep up with advances in biomedical science and technology.



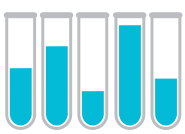
In 2011, then FDA Commissioner Margaret Hamburg made regulatory science a centerpiece of the agency's strategy for fostering innovation and called for the academic and foundation communities to take an active role in building this emerging, underfunded field. To identify areas of regulatory science where the Fund could provide strategic support, the Board began discussions with Hamburg, director of the FDA's Center for Drug Evaluation and Research (CDER) Janet Woodcock, and University of California-San Francisco Chancellor Susan Desmond-Hellman, formerly at Genentech. Initially, the Fund decided to make a few short-term, ad hoc grants focused on regulatory science to gather information about what mid- to long-term initiatives could best address this newly identified scientific need.

To bring more support for research on tools and approaches for evaluating the safety of products and treatments, the Fund ultimately decided to launch a new regulatory science-focused award initiative. The new effort, known as the Innovation in Regulatory Science Awards (IRSA) program, aimed to mimic what the Fund had accomplished in the previously underfunded area of translational research—a robust science with a secure career path. In 2012, the Fund committed

$5 million to regulatory science grant awards. Investigators funded through IRSA receive up to $500,000 over five years to help address and solve regulatory science research questions.

From the outset, the Fund defined IRSA broadly, opening the door for a diverse group of candidates. The program supports not only new cell-based *in vitro* studies and animal models of disease but also computer simulations—also known as *in silico* or "virtual human" studies that aim to stimulate new hypotheses about the molecular mechanisms responsible for people's reactions to therapies. Scientists involved with

In 2012, BWF created the Innovation in Regulatory Science Awards program. Awardees receive up to $500,000 over five years.



these model types will need a deep understanding of and ability to synthesize data from genomics and physiological, chemical, structural, pharmacodynamical, and imaging sources. The hope is that investing in diverse research models and strategies that can converge to better predict toxic outcomes will reduce the number of animals and people involved in extensive pre-clinical and clinical testing to improve predictability. The end result could be both saved money and saved time.

There's already movement in the right direction. Core competencies for regulatory science are a subset of skills associated with translational research. But for regulatory science research to advance on its own, awardees and students will need training in multiple scientific disciplines, including biostatistics, clinical pharmacology, engineering, and genetics.

INCREASING EFFICIENCY

A team of researchers, led by the Matthew Brennan, MD, MPH, received a Burroughs Wellcome Fund Innovation in Regulatory Science Award in 2014.

The BWF award dovetails with existing grants from the FDA and the NIH to evaluate the use of billing data for patient follow-up in both pragmatic clinical trials and in a national, collaborative medical device surveillance system.

The current cost of developing new drugs and medical devices is exceptionally high, and randomized clinical trials often have high operational costs and complex processes that contribute to the cost of getting new treatments to the market. The BWF award will assess whether using existing administrative claims data can help lower the costs of clinical follow-up and site monitoring, thereby increasing the efficiency of trial conduct.

From Duke Clinical Research Institute

Improving regulatory science research goes beyond revamping investigation methods, though. Clinical trial designs must also be enhanced. Consequently, the Fund supports research that applies robust biostatistical and epidemiological methods to strengthen data interpretation and boost confidence in therapeutic decision-making.

Since the program launched in 2012, the Fund has granted 11 IRSA awards. The focus varies widely, from studies of nutrition profiling and of innovations in blood transfusion to studies of organ-specific drug toxicity and of FDA policymaking.

Altering the fundamental approach to regulatory science will not be easy. Challenges exist even within academia itself. Currently, academic environments are biased toward basic biomedical research priorities and against accepting regulatory science as a field that can augment academic careers through high-impact publications and reliable funding. Through targeted funding, the Burroughs Wellcome Fund hopes to change this perception and attract awardees from many scientific disciplines that share the universal focus of impacting regulatory decision-making through research. The Fund expects that such funding will also add momentum to studies from investigators already working in regulatory science, paving the way for a well-funded academic career path that can entice talented individuals with fresh perspectives.

REGULATORY SCIENCE INNOVATION: A RATE-LIMITING STEP IN TRANSLATION
By Nancy Sung and John Burris

Read the editorial that announced the Fund's involvement in regulatory science (published in *Science Translational Medicine*, September 5, 2012) *http://stm.sciencemag.org/content/4/150/150fs35.full*

Reformulating a Flagship Program

An early focus of the Burroughs Wellcome Fund grantmaking strategy was to invest in the development of scientists at the beginning of their careers. One major focus has been "bridging" award programs (also sometimes known as hybrid, transition, or fellow-to-faculty programs) that provide support to bridge advanced postdoctoral study and the initial years of a faculty appointment—a notoriously difficult time for young scientists, who are too young to compete for major federal grants but too advanced to qualify for most postdoctoral awards.

One of the Fund's first acts after becoming an independent foundation in 1994 was to create the Career Awards for Biomedical Scientists (CABS) program, modeled after the now-discontinued Markey Charitable Trust's Scholars Program, which supported young scientists during their unstable but critical transition from postdoctoral fellows to independent, assistant-professor investigators.

From April 1995 until it was discontinued in 2006, the CABS program was the Fund's flagship program, awarding 241 early career biomedical researchers more than $100 million. Of the researchers, more than 90 percent have become tenure-track faculty members.

In 2005, responding to a report from the National Research Council (NRC) of the National Academies, the NIH began investigating the need to bolster the careers of young investigators. The NRC report, *Bridges to Independence: Fostering the Independence of New Investigators in Biomedical Research*, cited the Fund's career award programs as a model for a recommended NIH bridging award, called the Pathway to Independence, or K99/R00, award (see "A Bridging Model").

A BRIDGING MODEL

"These (NIH) awards would provide postdoctoral training support for a maximum of 2 years for the awardee to develop an independent research program and 3 or more years of support once a fully independent research position has been obtained. …Resources would provide at least partial salary support and funds for research and career development activities. …These grants would replace the current collection of K22 awards, which differ from institute to institute. The award amount and duration is similar to that of the Burroughs Wellcome Career Awards, which have shown success at fostering the independence of new investigators."

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

While the CABS program succeeded in creating independent investigators, the number of awards given during a cycle, ranging from 10 to 12, was still relatively small compared to the investment that NIH was considering bringing to the table—which, at the beginning, was estimated to be 175 postdoctoral fellows each year. NIH now funds 700 K99 awards.

With the prospect of greatly increased federal funding for bridging grants, the Fund's program staff and Board recommended that the CABS program be reformulated to focus on physician scientists working in the areas of basic biomedical research, translational research, and epidemiology. (Staff felt that physician scientists would not fare well under the requirements of the NIH awards—and, indeed they have not. Of the 700 K99 awards NIH distributed in 2012, for example, only 51 went to physician scientists, a pattern that has been consistent since the K99 program was launched in 2007.)

NIH and other funders "should substantially expand the support for the training and mentoring of physician scientists."

The FASEB Journal (2000)

With training in both clinical research and hypothesis-based research, M.D.-Ph.D.s are uniquely poised to bridge the gap between bench science and clinical practice. Unfortunately, the number of physicians performing research has long been declining. In 1979, James Wyngaarden, who later became a director of the NIH, termed physician scientists an "endangered species." The percentage of physicians engaged in research reached a high of 4.6 percent in 1985, but by 2003 the percentage had again dropped to 1.8 percent. In a 2000 report published in *The FASEB Journal*, researchers argued that in order to stabilize the early careers of the shrinking physician scientist workforce and bring more M.D.-Ph.D.s into the pipeline, NIH and other funders "should substantially expand the support for the training and mentoring of physician scientists." A 2005 article in the *Journal of the American Medical Association* suggested some indicators painted an encouraging picture, suggesting that, thanks largely to an NIH loan-repayment program instituted in 2002, the number of physician scientists was growing; however, the authors cautioned that the NIH budget would only grow modestly in the coming years, so the positive trend would need to be nurtured.

Burroughs Wellcome Fund program staff recognized that by reformulating the CABS program to focus on physician scientists and by providing support during the last years of a mentored position to enhance physician scientists' ability to compete in the research environment, the Fund could help spur more physicians to pursue careers in research. The Board of Directors approved this approach and in 2006, the Fund launched the Career Awards for Medical Scientists (CAMS) program.

To date, CAMS has undergone seven award cycles and has made 82 awards. Of the active awardees, 76 percent have transitioned to tenure-track faculty appointments; most already have assumed leadership positions at their institutions and within their research communities, an indication that the program has succeeded in keeping talented physician scientists in biomedical research.

2007 CAMS awardee Dr. Dao Nguyen converses with a fellow attendee at a physician-scientists convening in 2010.

82
CAMS awards since 2006

76% of awardees have transitioned to tenure-track faculty appointments

Encouraging Interdisciplinary Research

CAREER AWARDS AT THE SCIENTIFIC INTERFACE

Many of the most exciting questions in science today defy traditional disciplinary boundaries. Innovations in genomics, complex systems modeling, and nanotechnology are opening exciting new research landscapes for motivated young investigators who have backgrounds in physics, mathematics, computer science, and engineering and want to tackle biological questions.

Recognizing the fundamental role scientists with expertise in fields such as physics, engineering, mathematics, and computational science will play in advancing biomedical science, in 2001 the Fund launched a new program to encourage integration, or "convergence," of the biological and non-biological sciences. The Career Awards at the Scientific Interfaces (CASI) program, modeled after CABS, represents a major investment in the training and support of investigators working at the intersection of traditionally disparate fields. The five-year awards provide $500,000 to young researchers to bridge the period encompassing their advanced postdoctoral training and their first three years of faculty service. The goal of this self-nominated award is to incubate early-career development for new physical, mathematical, computational sciences, and engineering investigators as they tackle biological problems. The CASI program has so far provided grants to 111 early-career researchers.

The interdisciplinary approaches represented through the CASI program have seen phenomenal advances in the last decade, with profound implications for human health. For example, revelations in medical imaging at both the molecular and systemic levels, as well as recent developments in bioengineering, bioprinting and prosthetics, have opened up new avenues of discovery and insight.

The value of convergence is gaining prominent attention. In the preface to a 2014 National Academies workshop report addressing opportunities and challenges for convergence, University of North Carolina chemist Joseph DeSimone who chaired the convergence committee that sponsored the workshop, wrote:

> *The scientific opportunities enabled by convergence—the coming together of insights and approaches from originally distinct fields—will make fundamental contributions in our drive to provide creative solutions to the most difficult problems facing us as a society. This convergence provides power to think beyond usual paradigms and to approach issues informed by many perspectives instead of a few.*

Dr. Dan Goldman
2006 CASI awardee

SAND DUNES AND SNAKE-BOTS

Using special motion-capture cameras, Dr. Dan Goldman has studied the movement of sidewinders, applied a little math and mechanics, and found a big clue as to how they succeed where snake-bots fail.

Goldman and his team at Georgia Tech found that unlike humans and other limbed creatures, snakes do not "dig in" as they try to climb sandy slopes. Instead, they increase the area of contact with the surface as the slope angle increases, by lengthening and flattening more of their bodies against the shifting sand.

When slithering up a 10-degree slope, only a quarter of the sidewinder's body contacts the sand. This provides enough grip (or friction) to drive the snake up the slope without fear of rolling back down again.

But when scaling a 20-degree slope, the snake keeps up to half of its length in contact with the sand. This provides the grip without the slip. In other words, the extra body contact provides the extra friction needed to scale the slope, but without creating a treacherous "sand-slide," that would send the snake slipping downward.

Aside from the interest to animal physiologists and robot designers, this finding could prove invaluable in the field of rheology—the study of how liquids and "soft solids" (like sand and snow) flow as forces are applied to them. With a better understanding of the flow of granular surfaces, we might develop new tactics and technologies to prevent mudslides, avalanches and other natural disasters.

In time, a better understanding of snake locomotion could also lead to new all-terrain transports. Like jeeps or tanks with whipping, spiraling tracks—"sand-speeders" and "snow-speeders" that plow through deserts and snowdrifts with ease. Who knows—one day these could come in handy for exploring the gritty surface of Mars, or the icy wastes of some distant, snow-covered planet.

INTERFACES SHORT COURSE AWARDS

While many institutions offer formal interdisciplinary training programs, scientists with non-biological backgrounds also need introductory short courses that can immerse them in the questions and techniques of the biological sciences. To meet this need, the Fund in 2011 created the competitive Interfaces Short Course Awards (ISCA) program inviting institutions to apply for up to $200,000 per year for two years, to support the development of a new interdisciplinary biology short course.

Two institutions received ISCA grants: Princeton University, for its Biophysics and Computations in Neurons and Networks summer course; and the University of California-Santa Barbara, for a summer course series in the Santa Barbara Advanced School of Quantitative Biology.

COLLABORATIVE RESEARCH TRAVEL GRANTS

For many young investigators, finding suitable collaborators at their own institutions is difficult—and the absence of proper partnerships can cause even the best science to fall short of its goals. To help early-career investigators build the strongest research teams possible, the Fund in 2009 created the Collaborative Research Travel Grants (CRTG).

The CRTG is actually the rebirth, with a twist, of a travel grants program that ran from 1978 through 2000, the Wellcome Research Travel Grant program. The program enabled U.S. and Canadian scientists to participate in collaborative research projects for two weeks to six months in the United Kingdom or the Republic of Ireland. When the program closed in 2000, it was the longest-running program at the Fund. More than 700 travel grants were funded, and many went to researchers at institutions that otherwise would not have received a Fund grant.

Initially the CRTG grants provided up to $5000 for trainees currently working in laboratories of Burroughs Wellcome Fund awardees. In 2011, the Fund expanded the award to remove the award restrictions, providing up to $15,000 for researchers to travel to other laboratories to either learn new research techniques or develop and sustain collaborations. The funds can be used both domestically and internationally, and provide a stimulus to investigators working at the interfaces of scientific fields.

Consideration is given to applicants with a Ph.D. in mathematics, physics, chemistry, computer science, statistics, or engineering who express interest in investigating research opportunities in the biological sciences, as well as to biologists looking to partner with physical scientists, mathematicians, engineers, chemists, statisticians, or computer scientists in the effort to blend their knowledge and approaches to answer biological questions. So far, most awardees have been physical scientists or engineers who have requested travel to a biology lab.

Since its inception, the CRTG has been through three cycles, and 164 travel grants have been made.

In 2011, the Fund expanded the CRTG, providing up to $15,000 for researchers to travel to other laboratories to either learn new research techniques or develop and sustain collaborations.

Dr. Elizabeth Nance
2014 CASI awardee

A HUGE LEAP FOR TINY MEDICINE

Dr. Elizabeth Nance and her team at Johns Hopkins University work on brain diseases—especially those that appear in young children, like cerebral palsy. Brain diseases like this are difficult to diagnose and treat, due to the blood-brain barrier (BBB).

This membranous barrier—woven around every blood vessel that supplies the brain—stops large objects and molecules from passing from the bloodstream into the delicate brain cells beyond. On the plus side, this allows energy-laden sugars to pass into the brain, while keeping out dangerous blood-borne bacteria and parasites. On the downside, the barrier also prevents many diagnostic and therapeutic drugs from passing into the brain.

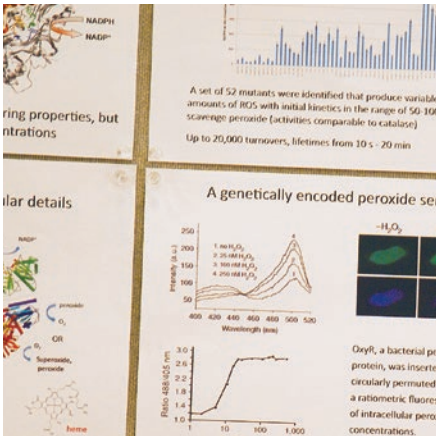
This makes it much harder to diagnose and treat brain diseases than, say, liver or heart conditions. If you want to look inside the heart or liver you can inject a patient with a type of radioactive dye, scan her with a Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) machine, and see how the bloodflow and tissues structures have been altered inside the organ. This done, doctors may then be able to perform surgery or inject medicines (like chemotherapeutic drugs) to fix the problem and restore organ function.

But because the BBB prevents most dyes (or contrast materials) from penetrating the brain, scans like these may reveal little about what's going on inside. And even when the cause is obvious, brain diseases are harder to treat because the BBB prevents drugs from getting to where they are needed.

To get around this problem, Dr. Nance and her team developed the first nanoparticles that can pass through the barrier and into the brain. With these, we can safely gather reams of information, and better understand and diagnose many types of brain disease—even in newborn babies.

Better yet, these same nanoparticles can also be used to shuttle therapeutic drugs deep into the brain. With them, Dr. Nance has already had success in treating rabbits with cerebral palsy-like brain conditions. If she can figure out more about how these nanoparticles could be used, then she may be able to treat similar conditions in humans. And not just cerebral palsy—perhaps others, such as autism and stroke, too.

Some say the 21st century will be one in which nano tech saves the world—improving our environment, our health, and our entire lives. If so, then Dr. Nance, and scientists like her, are already leading the way.



Convening activities help create a strong network of Fund award recipients.

Addressing Diversity in Science

In May 2011, the Burroughs Wellcome Fund Board of Directors discussed various ways to increase the number of underrepresented minority scientists participating in the Fund's programs. This conversation was triggered by an ongoing national debate on research showing a lack of diversity in the biomedical research community.

The Fund's Board and program staff recognized that few underrepresented minorities received Fund support. The problem is a broader one, as an article in *Science* (August 19, 2011) titled Race, Ethnicity, and NIH Research Awards observed: "… Although proposals with strong priority scores were equally likely to be funded regardless of race, we find that Asians are four percentage points and black or African-American applicants are 13 percentage points less likely to receive NIH investigator-initiated research funding compared with whites."

Although this finding was not new, it further confirmed a need to find better ways to reduce the disparity of funding success rates for underrepresented minority grant applicants and to improve how minority scientists are viewed by others, including the NIH, the largest provider of RO1 and other grants for biomedical scientists.

The Fund is known for serving as a catalyst for change in undervalued and underserved areas. Because increasing the number of underrepresented minority scientists within the biomedical and medical research and education communities align with the foundation's goals, the Fund launched its Diversity in Science program in 2012. The program's goal is to advance the careers of minority postdoctoral fellows. Toward that end, the Board approved a $1.5 million investment to fund the Postdoctoral Enrichment Program (PDEP) for three years. The grant provides $60,000 to increase opportunites among underrepresented minority postdoctoral fellows involved in biomedical research. The PDEP supports many activities to enrich these junior scientists' experiences and postdoctoral training and increase their research productivity, including funding workshops, courses, travel, collaborations, training in new techniques, and opportunities to publish.

$1.5 million was invested into PDEP, a program created to increase opportunities among underrepresented minority postdoctoral fellows involved in biomedical research

Dr. Carlos Ponce

MENTORING MAKES A DIFFERENCE TO DOCTORAL, POSTDOCTORAL STUDENTS

The distance between Harvard Medical School and Dr. Carlos Ponce's childhood home on a farm outside Mexico City can be measured in more than miles.

Obstacles abound, such as a rocky and dusty landscape, razor wire, and paperwork.

"My family moved to the United States in the late 1980s, hoping for a better life," he said. "They worked as farmers, factory workers, and waitresses. Life was better for us—the United States was then, as now, a land of opportunity—but there were clear limits to our future."

It took several years for Ponce to wade through the bureaucracy of U.S. citizenship.

Yet today, Ponce studies neuroscience, armed with an MD and a Ph.D. from Harvard. His professional goal is to determine how the brain's regions transfer and share information.

He reached this point not only through hard work, but also with plenty of guidance. Besides his family, he had mentors keeping him on course, and he believes they made the difference in his success.

"They were keen to the issues of underrepresentation and community outreach," Ponce said.

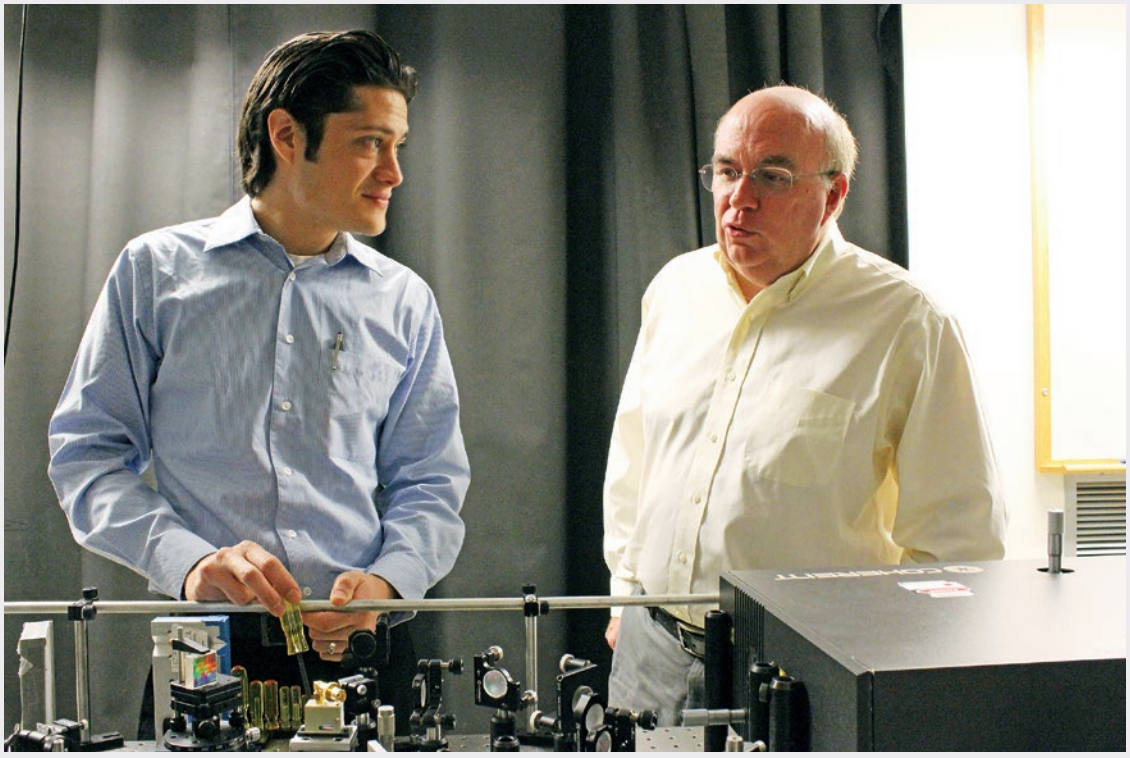
Source: Insight into Diversity *http://tinyurl.com/qx5tey3*

In addition, university mentors of PDEP fellows participate in mentoring workshops to strengthen their ability to communicate with underrepresented minority scientists. The Fund further encourages mentors to provide these scientists with university-based programs to develop or broaden peer-network systems for long-term success.

For year one of the PDEP award, the Fund partnered with the Howard Hughes Medical Institute to convene the mentors of these junior scientists to provide them with a better perspective of the issues and cultural differences that exist for underrepresented minority scientists.

VISUALIZING THE SIGNATURES OF DISEASE AT THE CELLULAR LEVEL

Dr. Francisco Robles is a postdoctoral fellow in the laboratory of Dr. Warren S. Warren, a James B. Duke Professor of Chemistry and Professor of Radiology, Biomedical Engineering, and Physics at Duke University. Robles is developing novel microscopy methods to visualize the signatures of disease at a cellular level. By creating a more detailed picture of the inner workings of healthy and diseased tissue, these methods could give insight into the origins of illness and lead to earlier and more accurate diagnoses. Robles is working with a technique called ultrafast laser spectroscopy, which enables him to probe the structure and dynamics of molecules using tailored light pulses. Typically, imaging studies in biological samples face a trade-off between spatial resolution—or the number of pixels in an image—and spectral resolution—or the ability to pick up on the different colors of fluorescent labels used to tag specific molecules in living cells. Robles is specifically addressing this challenge with a special laser that covers a large spread of wavelengths, generating a signal that can be split and analyzed two different ways to capture both spatial relationships and spectral colors. Using this method, he and his colleagues have achieved images that are true to color with a resolution of 1.2 microns, or about one thousand times smaller than a grain of sand.



Dr. Francisco Robles (left), works with Dr. Warren S. Warren, professor of chemistry at Duke University.

Catalyzing a Field: Reproductive Science and Preterm Birth

The Burroughs Wellcome Fund has long had an interest in reproductive science, viewing it as an underfunded and undervalued field. A 1992 Institute of Medicine report concluded that academic obstetrics and gynecology departments' research capabilities needed improvement and expansion. Through the 1990s, both NIH and private-sector support for reproductive science was meager. Over the past decade, the Fund has addressed these deficiencies in several ways.

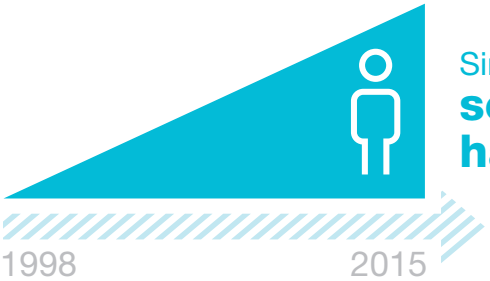
FRONTIERS IN REPRODUCTION

Since 1998, the Fund has supported the Marine Biological Laboratory's Frontiers in Reproduction (FIR) program, a six-week course that fosters reproductive scientists' career development through intensive lectures, seminars, laboratory exercises, informal discussions, and individual tutorials. The program is capped by a two-day symposium that includes presentations by FIR graduates and other distinguished speakers.

The FIR course began as a mentored-training program of the Reproductive Sciences of the Americas Network (RSANET), established in 1995 to foster career development opportunities for reproductive scientists. Its intention was to help strengthen basic conceptual knowledge and methodological skills for scientists in training. Since 1998, more than 300 young scientists—about 20 each year—have undergone FIR training.

The Fund was initially interested in the course because its focus was considered undervalued and underfunded. Today, the Fund provides support for a third of the course's annual cost.

A 2006 report on FIR participants' career outcomes, published in *Biology of Reproduction*, showed that a vast majority continue work in the reproductive sciences and demonstrate a significant increase in the "average number of articles published in highly ranked journals in the reproductive science."



Since 1998, more than **300 young scientists**—about 20 each year—**have undergone FIR training.**

FRONTIERS OF REPRODUCTION

The Frontiers of Reproduction course at Woods Hole Marine Biological Laboratory was established in 1998 to provide mentored training and professional development opportunities to reproductive scientists working in basic and clinical reproductive research. Funded by the National Institutes of Health and the Burroughs Wellcome Fund, the course also provides network opportunities for the students with visiting scientists.

REPRODUCTIVE SCIENTIST DEVELOPMENT PROGRAM

The Fund also provides supplemental support for NIH's Reproductive Scientist Development Program (RSDP), which trains OB/GYN physicians committed to careers in academic research. The program has two phases: a two-year postdoctoral phase completed in a basic science department, and a three-year faculty phase conducted in a department of obstetrics and gynecology. The majority of RSDP's support comes from a Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) grant. The Fund joined NICHD in 1998 and has funded eight scholars for the three-year faculty portion of the award, as well as providing support for an annual retreat.

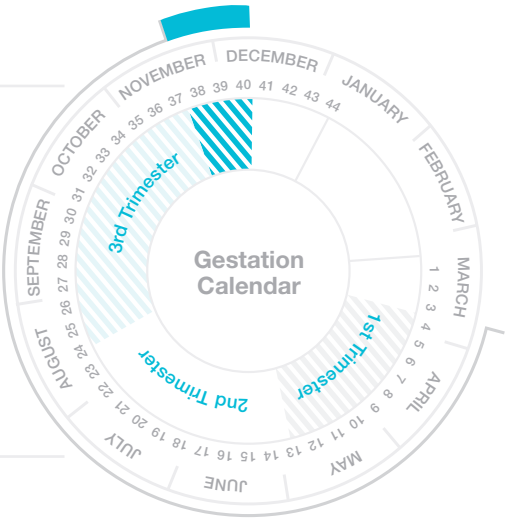
PRETERM BIRTH INITIATIVE

The Fund deepened its investment in reproductive science in 2008, when the Board approved a new program, the Preterm Birth Initiative. The initiative followed closely on the heels of a report from the Institute of Medicine's Committee on Understanding Premature Birth and Assuring Healthy Outcomes, published by the National Academies Press in 2007, which the Fund partially funded.

Although recent efforts have yielded improvements in the United States' preterm birth rate, 11.3 percent of births still occur before 37 weeks of gestation. To help reduce these early births—events responsible for many health and social problems—the Preterm Birth Initiative uses a multidisciplinary approach to expand the limited understanding of the biological mechanisms underlying childbirth and spontaneous preterm birth. The Preterm Birth Initiative competitive grant program provides five $600,000 grants in each award cycle to projects that focus on the basic biology of preterm birth and parturition.

The Fund's work with preterm birth actually began in 2007 when the Board of Directors approved a $600,000 grant to support a series of international meetings designed to enable leaders in preterm birth and childbirth to share their work with one another and to encourage and cultivate discoveries in this area. Four biannual meetings have so far been held, with the March of Dimes as a cosponsor. On average, approximately 125 individuals attend each gathering.

11.3%
of births still occur before 37 weeks of gestation



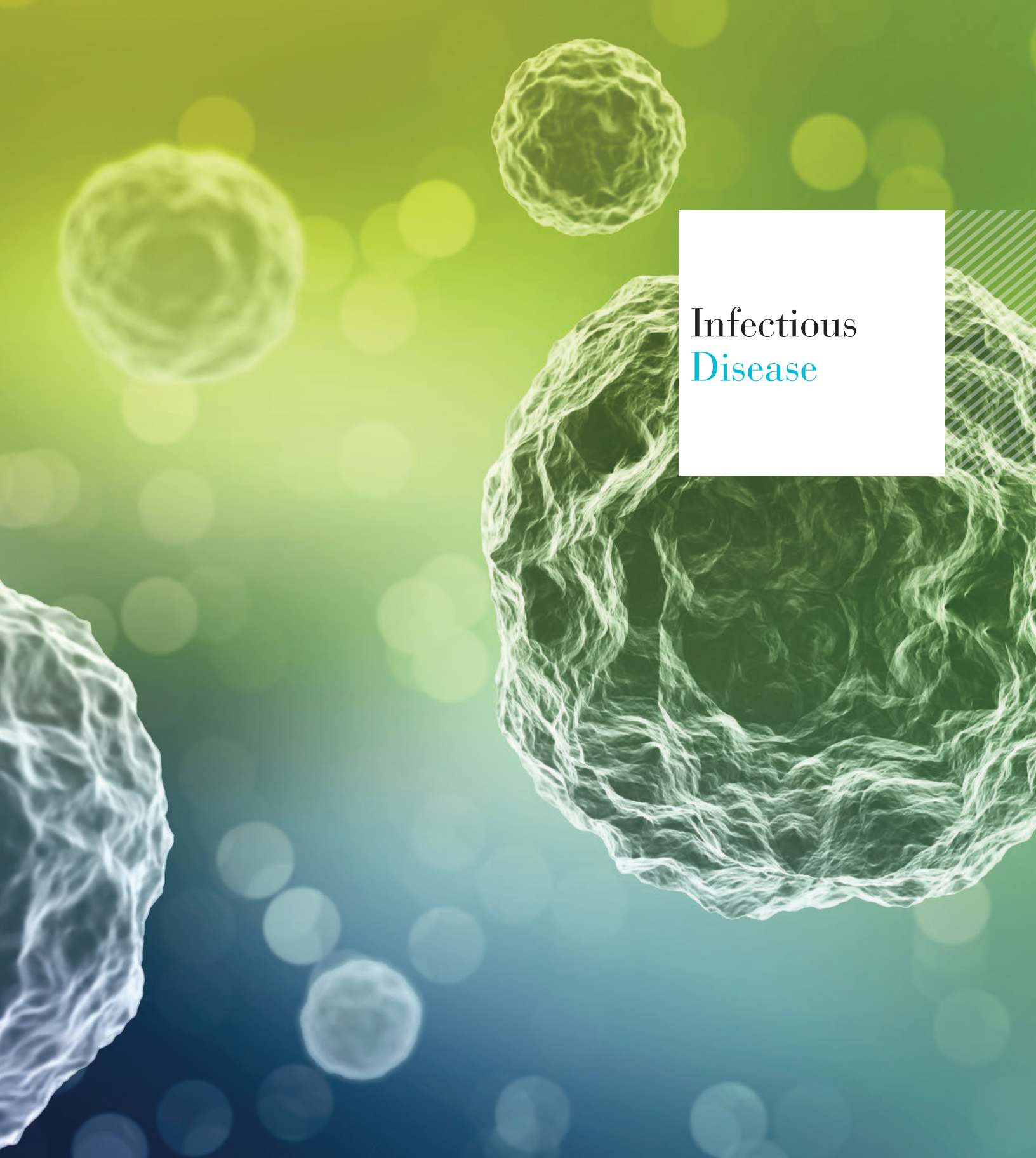
PREVENTING PREMATURITY

Beginning in 2008, the Burroughs Wellcome Fund and March of Dimes collaborated on a biannual symposium, *Preventing Prematurity: Establishing a Network of Innovation and Discovery.* The following review was published in *The New England Journal of Medicine* in 2010.

The Engima of Spontaneous Preterm Birth

The world's preterm birth rate continues to increase. In 2006, preterm births accounted for 12.8% of live births in the United States. Only about half the cases of prematurity result from identifiable causes. This review discusses the challenge of understanding the causes of premature birth and finding ways to prevent it.

The New England Journal of Medicine; 2010: 362:529-35



Infectious Disease

The Burroughs Wellcome Fund has a long history of supporting work on tough problems in the infectious diseases. We started in the early 1980s with a focus on protozoan parasites, a group of understudied organisms that cause dread diseases including malaria and African sleeping sickness, and in the mid-1990s expanded our focus across the diseases caused by eukaryotic pathogens. As we supported the development of our awardees' careers we also supported the growth of the science, helping a research community move from an era of largely descriptive explorations into today's ambitious array of basic and applied work in areas ranging from human immunology to disease eradication.

In 2000, with the launch of our Investigators in the Pathogenesis of Infectious Disease (PATH) program, we broadened our support of infectious disease research, moving away from a "bug by bug" view of infection in which a nefarious foe attacked a human victim. Instead, the program asked researchers to propose work focused on questions at the points where humans and potential pathogens intersect. What happens in the early interactions between a host and a microbe to determine how their relationship will unfold?

The PATH program provides five-year, $500,000 awards for accomplished, assistant professor-level investigators to study infectious disease pathogenesis—specifically the intersection of human and microbial biology—in multidisciplinary ways. The program's intent is to illuminate the overarching issues around how human hosts handle infectious challenges, including colonization and commensalism, and how other relationships develop at molecular or systemic levels.

Focusing on picking creative, confident researchers who will grow to lead their fields, the PATH program has raised the profile of the funded investigators and allowed them to do work they otherwise would not have been able to. The awards offer recipients freedom and flexibility to pursue new avenues of inquiry and higher-risk research projects that could significantly advance the biochemical, pharmacological, immunological, and molecular biological understanding of the interaction between infectious agents and the human body. Throughout the past decade, 108 out of 1,328 applicants (8.1%) were chosen to receive $51,900,000 in funding.

The Fund's flexible support and encouragement of early discovery has given awardees "seed corn" that has become far harder to get from other sources. Over the next decade, informatics, modeling, and high throughput approaches will advance a macroscopic view of how these complex players interact. We look forward to supporting those who will move us forward into a time when the whole natural history of a disease can be understood—how factors like insect carriers of disease, animal reservoirs, the environment, the weather, and more—integrate with the biology of humans and microbes to produce health or disease.

The annual new awardees meeting is a mechanism used to encourage interactions across scientific disciplines and questions.

Through several large grants to the American Society for Tropical Medicine and Hygiene (ASTMH), the Fund supports fellow-to-faculty bridging awards for physician scientists who will grow substantial research programs in the tropical developing world. These $130,000 awards, known as the BWF/ASTMH Fellowships, come in two parts. The first portion helps recipients develop their research projects during a clinical fellowship. The second allows them to devote significant time to the overseas project as they simultaneously work to establish themselves as young faculty.

Since 2001, the grant program has supported 32 physician BWF/ASTMH fellows. Their projects have spanned a wide gamut of topics, including the evaluation of a novel electricity-free, culture-based typhoid diagnosis in rural Nepal, the exploration of genetic diversity among Trypanosoma cruzi infections in Peru and Bolivia, and the development and evaluation of point-of-care tuberculosis diagnostics in India.

The Fund's infectious disease support reaches out to veterinarian scientists as well. In 2008, the Fund launched a career development short course, "Becoming Faculty," targeting veterinarian scientists who are preparing for academic research careers. To date, 72 D.V.M./Ph.D. participants have taken part in the course.

THE PAN-FUNGAL DATABASE

The Pan-fungal database garnered support in 2009/2010. When it launched in 2011 it included 18 organisms. An upgraded version, with more automation in data analysis, was released in Fall 2012 with 31 loaded fungal genomes and three more in progress. In addition, microarray and RNA-Seq data from five systems, including the important models *Candida albicans, Saccharomyces cerevisaie, Schizosaccharomyces pombe,* and *Neurospora crassa*, were included.

Candida albicans

THE PARASITE FIGHTER

De'Broski Herbert

As a young boy growing up in rural Mississippi, Dr. De'Broski Herbert's grandmother would tell him to avoid walking barefoot in the woods, so as not to get sick. Later, he found out she was right. Hookworm larvae generally infect the body through the skin—often through broken skin on the feet. From there, they travel through the bloodstream to the lungs, where they are coughed up, swallowed, and passed down to the intestine. There, they hook on, feed, lay eggs, and pass from the body as larvae. Seeing this all firsthand was one of the things that drove Dr. Herbert, now at the University of California, San Francisco, to study parasites in school and college.

Dr. Herbert works on one special group of proteins—called trefoil proteins—produced by goblet cells in the lining of the gut and lungs. These proteins have a special cloverleaf shape, which seems very resistant to damage by toxic chemicals. They not only protect the epithelia from damage, but also seem to help rebuild and repair tissues that have already been damaged—sealing the gaps that parasites might use to gain entry.

These proteins were discovered decades go. But until fairly recently, we didn't realize just how important they were, and not much was known about how they actually worked. Now, Dr. Herbert's team has discovered that these proteins interact with certain types of immune cell—in very specific ways—to trigger the regeneration of epithelial cells.

He hopes to find specific interface sites, or receptors, for trefoil proteins within epithelial cells and the many immune cells that interact with them. Once found, these sites could present new targets for anti-inflammatory drugs, and help fight all kinds of parasitic infection. In time, this could lead to the eradication of many parasitic diseases, and save millions of lives over the coming decades.

Check out Burroughs Wellcome Fund's YouTube channel for a video on Dr. Herbert.
www.youtube.com/user/BWFUND55

Population and Laboratory Based Sciences

Though researchers in population sciences and in basic bench sciences often have interests in common, they are typically physically separated in different schools within an institution, and students being trained from each perspective are exposed to different curricula and cultures. Through its Institutional Program Unifying Population and Laboratory Based Sciences (PUP), launched in 2007, the Fund hopes to bridge that gap, pulling together young scientists who may otherwise lack good ways to come together.

PUP is a five-year institutional award that provides graduate education programs with $500,000 annually to train Ph.D. and M.D. students in population approaches to human health and in basic biological sciences. The program's intention is to allow institutions to develop young researchers equally at home with approaches and insights generated at the molecular scale and at the population scale. Ambitious researchers trained in this way will be in a powerful position to solve problems in environmental health, infectious diseases, chronic diseases, and other areas that hold promise for bringing together epidemiological, population genetic, geospatial, and other kinds of "larger world" data with mechanistic and molecular data gained at the bench.

Students from PUP-funded programs gather at Emory University in 2013.

INSTITUTIONAL PROGRAM UNIFYING POPULATION AND LABORATORY BASED SCIENCES

Emory University's The Human Health: Molecules to Mankind program has a presence in four tracks: Predictive Health, Population Dynamics, Biomarkers, and Public Health Genomics. Each year, the program selects up to five new students. During the 2011–2012 academic year, the program boasted eight graduate students and one associate graduate student who was involved in—but not funded by—the program. By early 2013, 14 Ph.D. student associates were involved.

Students enter the program during their second year of graduate school, after being recruited from the School of Public Health and other relevant basic science programs. Of the 14 students, four have used PUP support for travel to meetings. Two bought laboratory equipment, and one traveled to an outside laboratory at St. Jude's to work.

Molecules to Mankind has hosted seminars, faculty/student socials, and research retreats where students present and discuss their research with faculty. The program maintains a core curriculum, and each track operates a separate, more specific one. The Atlanta location bolsters program efforts by offering access to many outside speakers with international insight and experience, including former Centers for Disease Control and Prevention directors and leadership from the Carter Center.

Whether their training program incorporates epidemiology, ecology, or –omics, PUP students who would have otherwise followed a traditional laboratory-based trajectory are thinking about problems through a public health lens. Likewise, students who would have otherwise trained in traditional public health approaches are exposed to the power of asking questions at the molecular or organismal level.

Since 2009, the program has award 10 PUP grants to programs whose emphasis falls into three broad groups: data science, infectious diseases and human/microbe interactions, and chronic diseases and wellness.

Changing Science Education

Since 1996, the Fund has invested more than $53 million in science education, helping to build systemic reform in science, technology, engineering, and mathematics (STEM). Much of the focus has been on reaching school-age children in North Carolina. The underlying belief is that children, whatever their future careers may be, should master basic science literacy for both their own satisfaction and interest and to become full contributors to civic life.

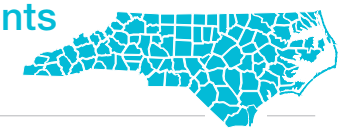
The Fund believes the most effective way to attain science literacy is to involve students in the scientific process and let them do what come naturally—asking questions and participating in hands-on activities and experiments that teach basic scientific principles. The Fund's initial science education investment was through its Student Science Enrichment Program (SSEP), begun in 1996. This initiative engages scientists and science teachers to work with primary and secondary students as part of out-of-school-time programs. So far, the Fund has invested $31.5 million in the SSEP program and reached students in all 100 North Carolina counties.

During the past 10 years, the Fund has shifted some of its focus in science education, devoting significant resources to supporting formal learning programs.

An essential component of improving students' abilities to understand STEM subjects is to produce a cadre of well-prepared teachers who have both content knowledge and the pedagogical skills to make a difference in the lives of their students and awaken their passion for STEM subjects. Since 2009, the Fund has offered career development awards to master science and mathematics teachers. Currently, there are 20 active recipients.

In 2012, the Fund also launched its Promoting Innovation in Science and Mathematics (PRISM) program, a biannual program that awards grants of up to $4,500 to teachers in North Carolina K–12 public schools to fund purchases of materials, equipment, supplies, and professional development that will allow for hands-on, inquiry-based science and mathematics projects. PRISM is also designed to improve teachers' abilities to apply for additional grant funding from other sources. To date, the Fund has invested $548,126 into PRISM awards for 171 science and mathematics teachers.

So far, the Fund has invested $31.5 million in the SSEP program and reached students in all 100 North Carolina counties.



In order to develop the careers of a cadre of highly skilled STEM teachers and to emphasize the professional nature of teaching, the Fund established the biannual Career Award for Science and Mathematics Teachers (CASMT). A partnership with the North Carolina State Board of Education and the North Carolina Department of Public Instruction, CASMT offers five-year, $175,000 awards to North Carolina public primary- and secondary-school teachers who demonstrate extensive knowledge and understanding of science and mathematics content and have exemplary performance records. Special consideration is given to teachers working in hard to staff, economically deprived classrooms. Since 2009, the Fund has invested $3.74 million in the CASMT program.

In 2011, the Fund partnered with the North Carolina State Board of Education, the Department of Public Instruction to create the Singapore Mathematics Pilot (SMP), which offers funding for teacher training; curriculum materials for students; and networking options for teachers, parents, local school boards, and other community stakeholders. The project's objective is to demonstrate how high-quality mathematics teaching and learning methods—modeled after an innovative problem-solving-based approach used in Singapore and some other countries—can produce successful students, even in North Carolina's most academically challenged schools.

Since 2011, the Fund has committed $200,700 annually to support pilot testing of the SMP program. For the 2013-2014 school year, 135 elementary school teachers were trained in SMP strategies. In 2012, the program was expanded into Durham when the SAS Institute supported a Singapore mathematics project at Y.E. Smith Elementary School in Durham.

"The Career Award from Burroughs Wellcome Fund has given me the freedom to really explore the vast amount of professional development for teachers... Without the award, I wouldn't have attended as many math, science, and Common Core conferences because of the financial burden."

FOCUS in Sound – Claudia Walker

Listen to the full podcast at:
www.bwfund.org/newsroom/awardee-profiles/focus-sound-claudia-walker

In 2007, the Fund and the University of North Carolina system developed a "fast track" to teacher certification for science and mathematics majors. The program is intended to prepare these individuals for teaching careers in North Carolina's K-12 classrooms. The Fund's Board of Directors approved a $5.4-million grant that provides $6,500 scholarships to qualifying juniors and seniors at the designated university campuses. An additional $5,000 annual salary supplement is available as a benefit to FastTrack Scholars who graduate and secure employment as a licensed science or mathematics teacher in a North Carolina public school. FastTrack partner campuses—North Carolina Central University, North Carolina State University, UNC-Asheville, and UNC-Chapel Hill—have committed to preparing 120 science and mathematics scholars. As of 2014 nearly 90 scholars have been selected. Currently, 38 FastTrack-trained teachers are employed in North Carolina public schools, instructing students in science and mathematics. More than 24 junior and senior FastTrack Scholars are now finishing their training.

In the past decade, the Fund's science education program has expanded beyond informal science education programs.

Strategies that Engage Minds®

Although science, technology, engineering, and mathematics are critical endeavors, not everyone will enter one of these fields. But it is nonetheless important to provide students with a method of thinking to enable them to problem solve, creatively explore options, and to engage innovatively.

In 2002, the Fund created the North Carolina Science, Mathematics, and Technology Education (SMT) Center to serve as a convener of all things STEM in the state. The SMT Center believes that STEM stands for more than Science, Technology, Engineering and Mathematics—it can also stand for Strategies That Engage Minds through hands-on, active involvement in STEM education.

Supporting STEM education requires first creating school conditions in which such efforts can thrive, which includes providing students with adult skills to deal with real world information and allowing them to demonstrate performance and learn to independently solve problems.

The SMT Center serves as a catalyst for innovation and change in education by developing and conducting conferences, seminars and teacher development workshops in STEM preK–12 education and distributing relevant training materials; advocating for research-based instructional programs in schools; providing tools, learning methods, and technical help to educators; and recruiting community and business leaders to encourage and promote advanced science and mathematics learning at all ages by providing a website featuring educational information in the STEM fields.

By enabling Strategies That Engage Minds, we teach our students to be independent, not dependent, learners; to be thoughtful, not thoughtless; and perhaps most importantly, to know what to do when they don't know what to do.

STRATEGIES THAT ENGAGE MINDS ADDRESSES THE 21ST CENTURY SKILL SET

- Critical thinking and problem solving
- Effective communication
- Creative and innovative thinking
- Ability to collaborate
- Contextual learning skills
- Information and media literacy skills

Dr. Samuel H. Houston Jr., President & CEO of the SMT Center, presenting at the 2013 SMT Celebration

Looking Forward

As the Burroughs Wellcome Fund enters its sixth decade, our Board and staff will continue to monitor the biomedical landscape for opportunities to champion important yet undervalued and underserved areas of research.

Building a strong community of peers is as important to the Fund's mission as any one grant. Towards that end, we provide critical opportunities, both formal and informal, for researchers we support to get to know one another, share ideas, and collaborate on research projects. As the Fund continues to evolve, we also remain committed to providing opportunities for all qualified scientists to apply for our grants, and thus are adopting a self-nomination process for all of our career award programs, freeing applicants from having to rely on the institutional nomination process.

The Fund's support for science education also continues to build in North Carolina, as we support informal STEM activities that take place outside of the traditional school day. Our investment in the North Carolina Science Festival has helped to bring permanence to that endeavor, as it brings science outreach to students and adults across the state.

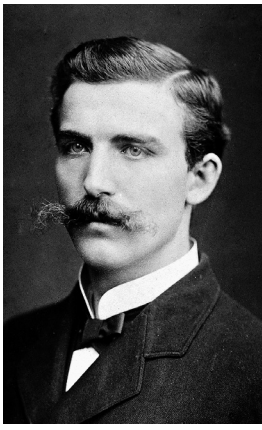
By providing career awards to science and mathematics educators, we are helping keep skilled teachers in the classroom. The Fund's support for professional development activities and other resources for public schools further strengthens STEM education in North Carolina.

Creativity is more important than ever in the lives of scientists, and the Fund has structured its programs and processes to nurture and reward innovation in young scientists. By providing flexible early-career funding, the Fund supports creative thinking and encourages young scientists to risk undertaking new research ideas. This flexibility enables innovation and empowers researchers to test these ideas and then follow up on the preliminary data that are so crucial to future funding and discoveries.

Whether at a science festival or to one's peers, science communication is a core aspect of a researcher's life. The Fund is one of the only foundations that conducts personal interviews with most of our award finalists. While this time-consuming and expensive process may seem out-of-date in a technologically driven world, it underscores the value the Fund places on being able to clearly define and communicate research goals.

It is impossible to know what new directions scientific discovery and applications will take. However, one thing is certain: Discovery will be ongoing and constant. Supporting researchers to advance biomedical science and providing resources to scientists conducting cutting-edge and risky research is something that would have made Silas Burroughs and Henry Wellcome, on whose legacy the Burroughs Wellcome Fund builds, proud.

Silas Burroughs



Sir Henry Wellcome

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21 T. W. Alexander Drive
Research Triangle Park, NC 27709
919.991.5100
www.bwfund.org