









Advancing the

Biomedical Sciences

. Evans as an Incorporator

HISTORY of the BURROUGHS WELLCOME FUND 1955-2005

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Book Design: Generate Design

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- * 1955 BWF established as a corporate foundation in Tuckahoe, New York
- 1955 William N. Creasy appointed first president and board chair
- 1959 First advisory committee appointed, on clinical pharmacology
- 1959 First competitive award program launched—Clinical Pharmacology Scholar Awards
- 1970 BWF moves to Research Triangle Park, North Carolina (with Burroughs Wellcome Co.)
- 1971 Dr. George H. Hitchings becomes president
- 1974 Iris B. Evans appointed first executive director
- > 1978 BWF grantmaking reaches \$1 million annually
- 1979 Toxicology Scholar Awards program launched
- > 1981 Martha Peck appointed executive director
- 1981 Molecular Parasitology Scholar Awards program launched
- 1983 Pharmacoepidemiology Scholar Awards program launched
- 1985 Immunopharmacology of Allergic Diseases Awards launched
- 1987 Hitchings Awards for Innovative Methods in Drug Design and Discovery launched
- ▶ 1988 First newsletter (FOCUS) published
- 1988 President George H. Hitchings receives Nobel Prize in Physiology or Medicine, along with Dr. Gertrude Elion and Sir James Black
- 1990 Dr. Howard J. Schaeffer appointed president
- 1991 First female member appointed to the board—Dr. Gertrude Elion
- 1991 First non-Wellcome representative appointed to the board—Dr. Samuel Katz
- 1993 BWF receives \$400 million endowment from the Wellcome Trust
- 1993 BWF becomes independent private foundation
- 1994 Dr. Enriqueta Bond becomes first full-time president
- 1994 Dr. Howard Schaeffer appointed board chair

FOREWORD

The Burroughs Wellcome Fund, or BWF as it has become known, is now 50 years old. During the past half century, BWF has transformed itself from a small corporate foundation, with assets of \$160,000 and awards totaling \$5,800 in 1955, to a major independent private foundation, with assets in excess of \$650 million and annual awards of more than \$25 million in 2005. In the past decade alone, BWF has made approximately \$250 million in grants.

Through strong, farsighted leadership over the years, BWF has played a significant role in the biomedical sciences by supporting research and education. Two key strategies have guided BWF's grantmaking process—supporting the career development of young scientists and sustaining investigators in underfunded or undervalued areas of science. BWF invests in talented, innovative researchers who conduct leading-edge research and in model science-related programs that can be replicated. Many BWF award recipients have gone on to win additional major research funding and to make noteworthy contributions to human health and the treatment of disease. Several BWF programs have been adopted by government and other foundations with larger endowments.

During the years of its transformation, BWF has grown from a one-person staff to a staff of 24 and moved into permanent headquarters that serve as a convening center for scientists, science educators, health research funders, and most importantly, its own award recipients. BWF's Board of Directors has evolved from one of corporate members to one comprising top national and international scientists; and its award programs have evolved to meet the needs of a changing research environment.

With funds contributed by the N.C. headquarters of Burroughs Wellcome Co., BWF created a program to support science education in grades pre K-12 in North Carolina, recognizing that a good education enriched by hands-on, inquiry-based science instruction would benefit the state—by preparing tomorrow's workforce for jobs in an increasingly technology-driven economy. To date, BWF has contributed more than \$10 million to innovative science enrichment programs throughout the state, engaging nearly 24,000 students, and has partnered with other organizations, such as science museums, universities, and policymaking groups, to improve the environment for teaching and learning the sciences. In 2002, BWF created the North Carolina Science, Mathematics, and Technology Education Center to coordinate the state's numerous science education initiatives and to push forward the crucial work of improving student performance in the sciences and of attracting more students into science and technology careers.

From the pharmaceutical company that Silas M. Burroughs and Henry S. Wellcome founded in 1880 has grown a vibrant philanthropy that has acted upon the directives in Wellcome's will—that the funds be used for "the advancement of research work...which may conduce to the improvement of the physical conditions of mankind"—and moved beyond it to areas that even such a visionary as Sir Henry Wellcome could not have foreseen.

Career Awards in the Biomedical 1994 Sciences program launched BWF conducts first terrain mapping 1995 (strategic planning) exercise Interfaces in Science program 1995 launched Molecular Pathogenic Mycology 1995 Awards program launched New Initiatives in Malaria Research 1996 Awards program launched Student Science Enrichment 1996 Program launched International Malaria Genome 1996 Project launched, with BWF support First BWF website launched 1996 North Carolina Institute for 1996 Education Policymakers formalized Clinical Scientist Awards 1997 in Translational Research program launched First directory of BWF award 1997 recipients published **BWF-Wellcome Trust Infectious** 1998 Diseases Collaboration launched Ground broken for permanent 1998 BWF headquarters building (April 17) North Carolina Grassroots Science 1999 Museum Collaborative formalized Dedication ceremony for BWF's new 2000 headquarters (May 24-25) BWF conducts second terrain mapping 2000 exercise, which focuses core programs on five areas: basic biomedical sciences, infectious diseases, interfaces in science, translational research, and science education Pathogenesis of Infectious Disease 2000 program launched Career Awards at the Scientific 2001 Interface program launched North Carolina Science, 2003 Mathematics, and Technology Education Center formalized Health Research Alliance formalized, 2005 with BWF support BWF conducts third terrain 2005 mapping exercise BWF celebrates 50th anniversary 2005 (May 25)



CHAPTER 1

Sir Henry Wellcome's Legacy

Beside County Highway J in central Wisconsin, about a half mile south of the village of Almond, surrounded by potato fields and Indian burial mounds, is a tiny plaque marking the humble origins of the man who was to help revolutionize the pharmaceutical industry, build an international business empire, and leave a legacy that to this day galvanizes biomedical research.

Henry Solomon Wellcome was born on August 21, 1853, the second son of Solomon Cummings Wellcome, a poor Maine farmer who had settled in Almond after a grueling 1,000-mile journey west by covered wagon, and his wife, Mary Curtis. At the time of their marriage, Mary, who with her family also had moved west from Maine, owned a 13-acre farm in Almond. The devoutly religious pair worked hard. But Solomon was frail and Almond a harsh place, with poor soil and short growing season, and neither the farm nor the family prospered.

Among Henry's most vivid memories of his childhood in Almond was finding an ancient arrowhead—and the lesson that came with it. The occasion is reported in *Henry Wellcome*, a biography published in 1995 by Robert Rhodes James that provides much of the background presented here. Henry's father explained to the young discoverer that to the early people who had made it, the arrowhead represented a greater advance than did the invention of the telegraph to the contemporary populace. Henry later recalled that this event "stimulated a babyish interest [in history] that lasted through my life."

In 1861, Solomon moved his family farther west to Garden City, Minnesota, where his elder brother, Jacob, was a busy and skilled physician and surgeon who also owned a drugstore. Blessed with fertile soil and a mild climate, Garden City was a thriving settlement.

Facing page: Sir Henry S. Wellcome, portrait photograph, 1879.



In November 1996, Sir Robert Rhodes James, Wellcome's biographer (center), Dr. Enriqueta Bond, Fund president, and Dr. Martin Ionescu-Pioggia, Fund senior program officer, dedicated the historic marker at Sir Henry Wellcome's boyhood home in Almond, Wisconsin.

Young Henry was blissfully happy; he learned to ride and to shoot and, taught by friendly Winnebago Indians, to canoe on river waters. In his uncle, Henry also found a hero and a mentor. A year after the Wellcomes' arrival, Sioux Indians, outraged by broken treaties and white settlers overrunning their lands, attacked the town, along with other towns in the region. Henry, not yet nine years old, directed the team of boys casting

lead bullets for the defenders and assisted Jacob in treating the wounded. (The U.S. Army eventually quelled the Sioux uprisings.) The episode made a lasting impression on Henry, evoking sympathy rather than hate for the Indians and their plight, and inspiring a lifelong concern for the welfare of indigenous peoples.

In 1866, Solomon took over his brother's drugstore and achieved a middling success, though he soon found his true calling as a traveling preacher. Thirteen-year-old Henry, influenced by Uncle Jacob, took a serious interest in the work and became proficient

in compounding medicines. Support for Henry's leanings came as well from a friend and colleague of Jacob's, the eminent physician William Mayo, who lived in the neighboring town of Rochester. Mayo's sons, who became Henry's lifelong friends, would go on to found the famed Mayo Clinic. Henry also was influenced by an English pharmacist, H. J. Barton, who settled in Garden City and gave him lessons in chemistry. Henry proved an apt and ambitious pupil, conducting experiments



Commemorative sign erected by the Minnesota town where Henry Wellcome spent much of his boyhood.



Burroughs and Wellcome debuted their product line at the International Medical Show in 1881.

with, among other things, explosive powders and firecrackers. At 16, he manufactured his first product: Wellcome's Magic Ink. He also produced his first advertisement, placed in a local newspaper and touting the new ink as "The Greatest Wonder of the Age! Write with quill or golden pen on white paper. No trace is visible until held to the fire, when it becomes very black."

Garden City became too limited a stage for Wellcome's gifts and drive and,

at age 17, he left home and headed to Rochester. Henry had little money, but he carried a letter of reference, signed by Garden City's leading physicians, pharmacists, lawyers, and merchants, describing him as "a worthy young man...trustworthy in every respect...honest as the day is long, and no bad habits of character about him." On William Mayo's recommendation, he took a post with a firm of pharmaceutical chemists. Wellcome worked from six in the morning to ten at night, for a pitifully low wage, from which he paid for his board and clothing and sent the rest home to support his family.

Impressed by Henry's hard work, Mayo further advised the young man that he needed to get a professional education in order to reach his full potential. In 1872, Wellcome enrolled in the Chicago College of Pharmacy, but switched the next year to the Philadelphia College of Pharmacy. He paid for the lectures and supported himself with part-time jobs and graduated in 1874, after turning in an impressive thesis on urethral suppositories. His thesis demonstrated that the current suppositories were poorly manufactured, bulky, brittle, irritating, and often ejected. To solve these problems, Wellcome devised a mold that would produce uniform, smooth, tapered suppositories that could be more easily inserted and were less likely to be rejected. Showing a flair for marketing, Wellcome also proposed that the medication be offered in cotton-lined boxes. "The observance of these points," he wrote, "should be carried out by all those who appreciate the reputation of neat dispenses of pharmaceutical preparations."



Silas Mainville Burroughs (1880 photo) started his career as a pharmaceutical sales representative in Philadelphia and moved to London in 1878 as an agent for a U.S. drug firm.

It was in Philadelphia that Wellcome met the man who would become his business partner. Silas Mainville Burroughs, the son of a U.S. congressman, was born in 1846 in Medina, New York, and finished his early schooling there. Seven years Wellcome's senior, Burroughs worked for a number of pharmacists, beginning in 1866, before joining the firm of Wyeth & Brothers in Philadelphia in 1869. While employed at Wyeth, he also enrolled at

the Philadelphia College of Pharmacy, after Wellcome had graduated.

Burroughs proved a popular and outstanding student. His 1877 graduation thesis was as striking as Wellcome's. The subject: compressed medicines, tablets made by compressing powders that were beginning to attract the attention of pharmaceutical manufacturers. The new manufacturing method promised to produce drugs in standardized, reproducible doses, making the dispensing of medication safer and more effective and obviating the need for pharmacists to make up pills, potions, and powders individually. Drugs could be massproduced and packaged for wide distribution. In his thesis, Burroughs summarized the benefits that his tests revealed, declaring



Henry Wellcome enrolled in the Chicago College of Pharmacy in 1872 and finished his education at the Philadelphia College of Pharmacy, where he met Silas Burroughs.

that "the compressed form of powder, by reason of speedy disintegration, decreased bulk, the ease with which it may be swallowed, and the comparative freedom from taste, constitutes it a benefit to the patient, a valuable aid to the druggist, and to the physician an advantage over former expedients in the administration of medicines."

Both Burroughs and Wellcome left Philadelphia fairly soon after their respective graduations, but they kept up a friendly correspondence. Wellcome moved to New York City, joining the firm of Caswell Hazard and Co. His two years there gave him experience in a major pharmaceutical company. In particular, he exhibited a lively interest in plants, from which all remedies then derived, and corresponded with people in the East Indies, Sierra Leone, Turkey, and elsewhere, seeking clues to native medical practices. In a letter to his parents, Wellcome noted, "My stay in New York is not for the purpose of making money, but for cultivating my knowledge of business as can only be learned by practical business in a house such as this." At the same time, however, money was never too far from his mind. He bluntly laid out his goal to become wealthy in another letter to his parents, on his 21st birthday, in which he offered the quotation, "He that striveth not for earthly blessings is not wise," but then tempered it by adding, "I want to live a life devoted to the true God and to mankind."

In 1876, Wellcome accepted an offer from the prominent New York-based pharmaceutical firm of McKesson and Robbins to introduce gelatin-coated pills to physicians and druggists. His pay was a paltry \$16 dollars a week, but he was able to travel widely in



Burroughs and Wellcome signed partnership papers in 1880 and within a year had opened businesses around the world. Wellcome himself designed the interior of the head offices in London.

the United States, as well as in Central and South America. One of his more significant trips was through the wild mountainous countryside of Peru and Ecuador by mule in search of cinchona bark, then the only source of quinine, which was becoming increasingly important in the treatment of malaria. He returned with tree bark and other botanical specimens, as well as a collection of native surgical instruments. Wellcome's observations, published in the *Proceedings of the American Pharmaceutical Association* and in the *Pharmaceutical Journal of Great Britain*, drew wide attention and marked him as an up-and-comer.

For his part, Burroughs moved to London early in 1878 as a sales representative for Wyeth & Brother. He soon started his own small company and gained the rights to act as sole European agent for Wyeth. His dynamism, combined with the increasingly recognized benefits of compressed medicines, drove the business forward. To continue to grow the company, Burroughs decided to ask Wellcome to join him as a partner and so began corresponding with his friend from Philadelphia in early 1879. Wellcome was cautious and took his time making a decision, finally sailing for England in April 1880, with a personal contract from McKesson and Robbins in hand, giving him exclusive rights to market the firm's preparations

in Europe, as well as Asia, Africa, the East Indies, and Australia. Burroughs and Wellcome signed partnership papers in September 1880, contributing to the venture $\pounds 1,200$ and $\pounds 800$, respectively.

Burroughs Wellcome & Co. quickly made its mark. By informal agreement, the fanatically organized and detail-oriented Wellcome assumed the task of administering the rapidly growing business and cultivating markets in England, while the sociable and sophisticated Burroughs trotted the globe in search of other markets. Starting in 1881, Burroughs traveled for two and a half



Burroughs Wellcome & Co. packaged its Tabloids and other products into compact travel cases to serve as first-aid kits for motorists, explorers, and adventurers.

years straight, visiting Spain, Portugal, Turkey, Egypt, India, Australia, New Zealand, and the United States. For his part, Wellcome stayed busy selecting staff; searching out equipment advances; establishing new manufacturing plants near London, in order to avoid the stiff import duties placed on U.S. products; and designing a new company headquarters. Opened in 1883, the lavish new offices boasted electric lights, Moorish motifs, and a replica of the Statue of Liberty. (The building was destroyed in 1941 by German bombs.)

Wellcome also worked hard at drumming up new business. A publicity genius, he introduced a system of regular mailings to physicians and pharmacists, trained pharmacists to serve as sales representatives, and issued "directions for use" circulars in three languages— English, French, and Italian. Most famously, he coined a catchy new term for compressed medicines—Tabloid—and registered it as a company trademark. (The term later was adopted for newspapers that delivered compressed news.) Wellcome was a fixture on the London social scene as well. He entertained widely, attracting writers, artists, actors, politicians, diplomats, and businesspeople to opulent parties.

In 1885, however, Wellcome's health began to fail. (His disease would go undiagnosed for 13 years, until finally described as ulcerative colitis.) When his condition worsened in 1886, his physician ordered him to rest and recuperate. Wellcome returned to the United States, where he spent months in the forests of Maine, canoeing, camping, hunting, and fishing. During that time, he wrote a book, The Story of Metlakahtla, about an Indian tribe in British Columbia with which his friend Father William Duncan had been involved as a missionary. Although not a critical or scholarly success, the book quickly sold out three editions, with profits going to benefit the Indian community.



Burroughs Wellcome & Co.'s Tabloid First-Aid kits accompanied the first explorers to reach both the North Pole and South Pole.



Following a trip to Egypt in 1901, Wellcome founded the Wellcome Tropical Research Laboratories at Khartoum for the study of tropical diseases, particularly malaria. He is shown here with the laboratory staff in Khartoum.

Returning to England, a recovered Wellcome took up the administrative reins of Burroughs Wellcome & Co. with renewed fervor. He expanded the company's manufacturing capacity. And in 1894, he took the bold step of establishing an in-house laboratory devoted to physiological research. The first of its kind in the pharmaceutical industry, the laboratory was intended not only to develop new commercial products but also to work on basic biomedical problems.

Wellcome's unprecedented actions revolutionized the pharmaceutical industry; until then, firms invested no money in basic research, which promised no foreseeable profit. A visionary, Wellcome saw basic research as key to a company's growth and success, as well as to the eradication of the medical scourges that inflicted pain and misery on millions of people.

In 1895, the partnership of Silas Burroughs and Henry Wellcome abruptly ended when Burroughs, on a visit to the Italian Riviera, contracted pneumonia and died. He was 49 years old. Wellcome, then 42, was left to oversee the company alone. "I regard our business as in its infancy," he said, and with characteristic zeal, he plunged into growing it further and faster. He established in 1896 the Wellcome Chemical Research Laboratories, also charged with the dual goals of fostering product development and basic research. (That same year, its companion facility was renamed the Wellcome Physiological Research Laboratories.) Wellcome's tenet, "Freedom of Research—Liberty to Publish," attracted to the laboratories some of the most talented scientists of the day.

On the commercial side, Wellcome expanded the company's geographic reach. As a result, in part, of Burroughs's initial globetrotting, the company had established an "associated house" in Australia in 1886. In the first dozen years of the new century, Wellcome



In 1907, Wellcome converted a barge into a floating research laboratory on the Upper Nile to study infectious diseases.

opened new subsidiaries in South Africa, Italy, the United States, Canada, China, Argentina, and India. Among other efforts to promote products and boost sales, Wellcome erected booths at trade exhibitions and splashed pages of advertisements in professional journals. He also packaged Tabloids into compact medicine cases to serve as first-aid kits for motorists and adventurers alike. Admiral Peary, the first person to reach the North Pole, and Captain Amundsen, the first to reach the South Pole, carried and subsequently paid tribute to their Burroughs Wellcome & Co. medicine cases.

As business boomed, Wellcome's energies turned increasingly to philanthropic pursuits. Following a trip to Egypt and the Sudan, he established in 1902 the first Wellcome Tropical Research Laboratories, located in the city of Khartoum, at the junction of the White Nile and Blue Nile rivers. The laboratory, devoted to the study of tropical diseases, particularly malaria, was directed by Andrew Balfour, who subsequently became a giant in



Wellcome's long-standing interest in archaeology led to his financing the excavation of a prehistoric site, Jebel Moya, in the Sudan.

the field of tropical medicine. To assist the researchers, Wellcome provided them in 1907 with a floating laboratory, believed to be the first of its kind in the world. A converted barge, the laboratory could be towed into the otherwise inaccessible upper reaches of the Nile to collect, study, and analyze materials on the spot. After meeting the explorer and journalist Sir Henry M. Stanley, Wellcome developed a profound interest in Africa and, in 1905, he founded a medical hospital dispensary in Uganda. In 1908, he established a fund to translate standard medical and scientific texts into Chinese and make them available at prices that local physicians and students in China could afford.

Wellcome also indulged his long-standing interest in archaeology. He financed an expedition to Palestine, which yielded historically significant pottery fragments that carried inscriptions describing events mentioned in the Old Testament, and he financed, organized, and personally directed a four-year expedition to the Sudan. The Sudanese project focused on a region called Jebel Moya, located in rugged terrain some 15 miles west of the Blue



Interior of Wellcome's floating laboratory, believed to be the first of its kind in the world.



In 1932, King George V knighted Wellcome, who had been a British citizen since 1910.

Nile, where Wellcome believed there to be several prehistoric settlements. The project combined archaeology with social engineering: The local chieftains opposed the excavation, and potential workers lacked both the skills and work habits that would make for an efficient dig. Wellcome decided to offer prizes for finding objects and for practicing productive work habits, such as forsaking the potent local alcoholic brew. To reward the men who remained sober, he ceremoniously presented them with a peacock feather. Two thousand workers ultimately won recognition, and peacocks had to be ferried from England to provide enough feathers.

Wellcome's passion for medical history yielded richer returns. He collected hundreds of thousands of books, manuscripts, prints, and letters, and almost an equal number of

objects, including surgical implements, medicine chests, specimen jars, early microscopes, and ancient amulets and charms. At his direction, a sampling of his vast collection was transformed, over several years of painstaking effort, into a historical medical exhibition that would debut in 1913 at the International Medical Congress in London. Following the meeting, Wellcome announced that the exhibit and its accompanying library would be made permanent as the Wellcome Historical Medical Museum, with himself as director. Over the years, it has proved a valuable source for scientific and historical investigations.

In 1924, Wellcome placed his myriad enterprises—businesses, museums, libraries, laboratories, and research projects—under one umbrella, The Wellcome Foundation Limited. (The term "foundation" actually is something of a misnomer, since the organization was still a business entity.) Honors began pouring in. Most notably, in 1932, King George V knighted Wellcome, a British citizen since 1910. The coat of arms created for him was inscribed *Floreat Scientia*—"Let knowledge grow!"—a motto he certainly lived up to. That same year, Sir Henry also was elected an Honorary Fellow of the Royal College of Surgeons, a distinction bestowed on few people without a medical degree.

His remarkable life was drawing to a close, however. In 1935, while visiting the United States, Wellcome took ill and, in a poignant twist, received treatment over a period of months at the Mayo Clinic. He returned to England in 1936, where his condition worsened. He underwent an operation, but died of bladder cancer, on July 25. He was 83 years old.

Wellcome's will proved as innovative as his other deeds. He dictated that all shares in the Wellcome Foundation were to be vested in five Trustees. Further, he directed the Trustees to dedicate all profits from what came to be known as The Wellcome Trust to support scientific and biomedical research, medical history, and related educational activities. Today, the Trust remains one of the largest charitable foundations in the world—and it stands as Sir Henry Wellcome's legacy to the world.



Sir Henry Wellcome died in England in 1936 at the age of 83.



CHAPTER 2

In the Beginning

Sir Henry Wellcome's philanthropic wishes were carried out solely by the Wellcome Trust until 1955, when a parallel U.S. foundation, the Burroughs Wellcome Fund, was created. William Neville Creasy, head of the U.S. subsidiary of the Wellcome enterprise, kindled the idea for the Fund.

Born in England and educated in Canada, Creasy joined the U.S. subsidiary, Burroughs Wellcome Co., in 1929 as a professional service representative and ascended to the presidency and chairmanship in 1945. The company, started in 1906 in New York City, was in rickety financial shape directly after World War II, having dedicated itself during the war years to providing drugs at low cost to the military. Under Creasy's charismatic and energetic leadership, the company turned around and flourished, developing and introducing a multiplicity of new drugs, including vital anesthetics, an immunosuppressive agent critical to successful organ transplants, the antibiotic Neosporin, the decongestant Sudafed, and the antihistamine Actifed. Burroughs



William N. Creasy, first Fund president and board chair.

Wellcome Co. grew so much and so fast that in 1947, it moved from New York City to bigger quarters in more rural Tuckahoe, New York.

By 1954, the company was so prosperous that Creasy, a keen admirer of

Facing page: Dr. George H. Hitchings and Dr. Trudy Elion. The 1988 Nobel laureates autographed this photograph to help encourage a young student interested in pursuing a career in science.

Wellcome's philosophy, broached the question of setting up in the United States a sister organization to the Trust. Fairness and sentiment favored the idea. The U.S. firm had become the largest contributor to the Wellcome empire, with some estimates suggesting that it was doing 40 percent of the total business and generating 60 percent to 70 percent of the overall profits. However, because of Britain's tight restrictions on currency transfers, the Trust sent little of that money back to the United States. The inequity could be redressed, Creasy suggested, by having the U.S. company give a portion of its profits directly to a U.S. entity that could carry out Henry Wellcome's directives. Fortuitously, a recently enacted U.S. law permitted corporations to deduct a portion of taxable income spent for charitable causes. And from a grander perspective, a U.S. foundation would be a natural tribute to Henry Wellcome, recognizing the land of his birth.

Creasy found enthusiastic support for the idea in Sir Michael Perrin, chairman of the Wellcome Foundation, and even more importantly in Sir Henry Dale, chairman of the Wellcome Trust and recipient of the 1936 Nobel Prize in Physiology or Medicine for his studies of the chemical transmission of nerve impulses. After World War II, Creasy and Dale had developed a strong relationship, nurtured by transatlantic visits and the discovery that Creasy's grandparents, who had run a bed and breakfast in Devon, England, had been frequent hosts to Dale's vacationing parents. Indeed, Sir Henry Dale and William Creasy's

CERTIFICATE OF APPROVAL rt of the Rinth Judicial District, de 20 . 1955. Les Supress Court 133256 at New Pert cial seal of the Depa London

The Burroughs Wellcome Fund's incorporation paper, May 24, 1955.

fathers had played together as children at the seaside resort.

The Burroughs Wellcome Fund became operational on May 25, 1955, at the Fund's first Board of Directors meeting. The minutes of that meeting also recorded Creasy as the Fund's president and chair of its board, which was drawn from the scientific and business leaders of Burroughs Wellcome Co., the Wellcome Trust, and the Wellcome Foundation. Although the Fund was a corporate-financed foundation, its bylaws made clear that the money given was not to be determined in any way by company interests. The Fund, the bylaws stressed, "is not organized for pecuniary profit....It is organized and will be operated exclusively for charitable, scientific and education purposes."

The Fund started small, quartered in found space within the company, with a start-up sum of just \$30,000 and a single full-time staff member. The company increased its contributions steadily, but the Fund remained a modest operation for more than two decades. Seeking the biggest bang for the Fund's small bucks, its directors resolved that the major mission would be to champion promising young researchers in the United States who were working in key medical disciplines that lacked significant recognition and financial support. Put succinctly, the Fund's goal was to "catalyze the career and fertilize the field."

That policy was implemented in an improvised way during the Fund's early years. Outside scientists, often acquainted with board members, typically solicited financial support for a biomedical researcher or endeavor, and the directors voted modest sums, to be funneled through institutions, to individual scientists. The early grants, ranging typically from \$400 to \$6,000, went to scientists working in diverse biomedical areas, such as anesthetics, arteriosclerosis, and eye viruses; other small grants supported researchers traveling to major conferences, and training programs for minority students.

Gradually a more structured approach evolved, as the Fund established advisory committees of eminent



Sir Henry Dale, chairman of the Wellcome Trust, partnered with William Creasy to establish the Burroughs Wellcome Fund.

scientists to help focus its areas of interest and select awardees. For the Fund's first major program, the directors chose the fledgling field of clinical pharmacology, the study of the effects of drugs in humans. Following World War II, advances in biochemistry triggered an explosive production of compounds with medicinal potential—the "therapeutic revolution." Useful evaluation of these substances lagged, however. Compounds were tested in the laboratory on animals, not at the bedside with humans. A handful of physician-scientists were pioneering a new interdisciplinary specialty that bridged the gap between basic research and clinical practice. Their aims were two-fold and two-way: to rigorously assess new compounds coming out of the laboratory for safety and efficacy in humans, and to spark creation of better therapeutic agents by taking clinical discoveries of natural and disease processes back to the laboratory. Recognizing the urgent need for more such clinical pharmacologists, the Fund decided to support the training of physicians in the principles and tools of pharmacology and scientific investigation. Enlisted to help develop the funding program was Dr. A. McGehee Harvey, physician-in-chief at Johns Hopkins Hospital, who had studied under Sir Henry Dale and been a consultant to the Fund since its founding.

In 1959, the Fund announced its first major competitive grant program, the Clinical Pharmacology Scholar Awards program, which provided awards of \$75,000 paid out over five years. (Award amounts increased in later years.) With the help of an advisory committee led by Dr. Harvey, the Fund's directors chose two recipients in the first round of awards, given in 1961: Kenneth R. Crispell, M.D., of the University of Virginia, and Leon I. Goldberg, M.D., Ph.D., of Emory University. Dr. Goldberg, who died in 1988, noted the award's profound influence on his work and the discipline: "The award," he said, "freed me, at a critical stage of my career, to undertake the research on dopamine that I wanted to do." His groundbreaking studies of the neurotransmitter led to its use in shock and heart failure.



Dr. Leon Goldberg, from Medical World News "New Breed at the Bedside," 1965.

More broadly, the new award program inspired universities and medical schools to recruit and train clinical pharmacologists. "At that time, clinical pharmacology was almost in the prenatal state, and people in academic medicine could not even define it," noted Dr. Goldberg, who went on to become head of clinical pharmacology at the University of Chicago Pritzker School of Medicine. "I believe that without the Fund's support and encouragement, the discipline could have been wiped out."

In total, the Fund contributed more than \$8 million in support of 49 scholars,

many of whom went on to become leading clinical pharmacologists in academia, business, and government. As the field and its needs evolved, the Fund restructured its funding priorities and, in 1990, launched the Experimental Therapeutics Scholar Awards program, open to researchers working in many medical specialties as well as to scientists formally identified as clinical pharmacologists. The focus remained the same: to support outstanding scientists in their efforts to apply basic knowledge of drugs and drug mechanisms to clinical medicine. This program evolution underscores the Fund's commitment to keep pace with the changing needs of the biomedical research community.

The clinical pharmacology scholar Dr. Goldberg also noted a hallmark of the Fund: its personalized style. "Mr. Creasy visited me after I received the award," he recalled, observing that Creasy "possessed great warmth and sympathetic understanding for people....As the years passed, we would telephone each other to discuss matters concerning the field and those of personal concern. He could always be reached easily and took an interest also in my career and in my family."

Indeed, the Fund has centered on people from its inception. The tone reflected the personality not only of Creasy, but also of Iris B. Evans, who handled the day-to-day running of the foundation. Evans, who was born in Belfast,

Northern Ireland, and reared in Canada and the United States, was the Fund's first administrator. After a stint as advertising manager with Burroughs Wellcome Co. in Montreal, she returned to the United States to become assistant to the president of the company. During that time, she worked with William F. Dowling, Burroughs Wellcome Co.'s corporate counsel and later chair of the Fund's board.

"We wanted to not only give a grant, but to invest in the person," Evans says. "We wanted to get to know them, to establish a relationship with them." Admiring Fund officers remarked on her success, one noting that "her ability and



Iris B. Evans, first executive director of the Fund.

personal warmth created just the right image for the Fund." With her expansive knowledge of the Fund, Evans also was the perfect person to write its first history, *Investment in Research*, which chronicled the Fund's birth and activities through 1985, and which provides much of the information given here.

William Creasy retired from the Fund in 1971. George H. Hitchings, former head of research at Burroughs Wellcome Co. and a member of the Fund's board since 1968, became its new president. Dr. Hitchings took the helm soon after the company, having outgrown its New York home, moved to expansive new headquarters in Research Triangle Park, North Carolina. The move was dictated not only by the need for more space, but also by the insight of Fred A. Coe Jr., Creasy's successor as head of Burroughs Wellcome Co. and a board member since the Fund's beginning. Besides land and building costs being low, Research Triangle Park, with its location near three major universities and its requirement that all companies within its boundaries be research-based, promised to be an area of scientific and intellectual ferment. To design its new headquarters and research laboratories, the company chose acclaimed architect Paul Rudolph. With soaring inner spaces and a dramatic exterior, the building became a local landmark and a symbol not only of the company's futuristic vision but also of the high-technology park itself.

During the 1970s, the Fund remained a limited operation. Evans, who was named executive director in 1974, continued as the only full-time staffer, thanks in part to the Fund's frugal board. "One of the directors once said to me, 'I don't see why we have to spend money to give money away," Evans recalls. "I was like a one-woman band. We had not had a great deal of publicity for the Fund, and I tried to make it bigger than it was by sending out lots of announcements and putting together the first annual report in 1971 and writing up news releases for awards that we made."

Help arrived in 1977, when Deborah Carr Thompson joined the Fund as Evans's assistant. Still at the Fund today, Thompson now serves as a senior program and communications officer, overseeing its science education and communications activities. "My professional growth at the Fund reflects the leadership's mindset to grow human capital," she says. "We strive to give opportunities to individuals who are committed to doing the best job possible. When I joined Burroughs Wellcome Co., I had no idea that the foundation existed." Her unfamiliarity with the Fund echoed that of most scientists. "We spent many hours responding to inquiries about who we were and what we did," Thompson recalls. "The typical letter was, 'We want funding for our project. Do you do this sort of thing?' And we would respond sympathetically, even if we couldn't fund the project, with a nice turndown letter."

When Iris Evans retired in 1981, Martha G. Peck became executive director. Trained as a pharmacist, she had worked at Burroughs Wellcome Co., and she, too, had never heard of the Fund before being asked if she would like to work there. Peck became a respected figure in the Fund's history, noted for her intelligence, hard work, and nurturing nature—and for a critical conversation that she was to have with the chief executive officer of the Wellcome Foundation, the British holding company, a conversation that was to transform the Fund.

By 1980, the Fund had amassed assets of approximately \$7 million, and Dr. Hitchings, as president, was eager to extend its reach. Dr. Hitchings was a scientific



Martha G. Peck, M.D., appointed executive director of the Fund in 1981.

luminary and a fervent believer in basic research. For 31 years at Burroughs Wellcome Co., he collaborated with fellow biochemist Dr. Gertrude B. Elion in pioneering a more rational approach to drug discovery and testing by delineating the link between compound structure and biological effect. "My own years in research have given me the conviction that science and its applications are an indivisible whole," Dr. Hitchings once said, explaining the Fund's policy. "Often seemingly untargeted, innovative studies have led, some indirectly, to many of the important discoveries in medicine of this century. How exciting to be the backers of some of those discoveries!"

Under Dr. Hitchings's leadership, the Fund added major new competitive award programs in three scientific areas that its advisors and directors determined were vitally



Dr. George H. Hitchings served as president of the Fund from 1971 to 1990.

important but overlooked and underfunded: toxicology, molecular parasitology, and pharmacoepidemiology. Awards in each of these areas provided \$250,000 paid out over five years, a substantial sum for the day. Among its other programs, the Fund began to offer research travel grants to foster the speedy exchange of scientific information and training; visiting professorships in the basic biomedical sciences and in microbiology; and research fellowships (frequently in conjunction with professional societies) in a number of fields, such as anesthesiology, ophthalmology, and the life sciences.

The Toxicology Scholar Awards program, announced in 1979, was stimulated by growing concern over the potential health hazards of the surging numbers and concentrations of chemicals in the environment, including pesticides and fertilizers, food additives, and industrial wastes. The idea for the award program came from Dr. Tom Miya, a respected toxicologist who was then dean of the University of North Carolina-Chapel Hill School of Pharmacy. Toxicology, which focuses on better understanding the interactions of chemicals with biological systems, was at a threshold. Scientists, once limited in how deeply they could probe fundamental toxicological questions, were gaining access to new research tools for investigating biochemical changes within cells, and even within genes, that occurred with chemical exposure. The field, then, seemed primed for advances.

And, indeed, the Fund's support proved an effective catalyst. As a case in point, Alan P. Poland, M.D., of the University of Wisconsin Medical School, received the first Toxicology Scholar Award in 1981. His work established that dioxin, once considered a harmless byproduct of pesticide production, waste incineration, and paper bleaching, is a potent carcinogen that does injury by binding to a specific cellular receptor protein. Dr. Poland's work spurred changes in industrial practices in order to curb production of this hazardous chemical. Over the years, the Fund provided more than \$7 million in support of 23 scholars, comprising a cadre of key researchers who helped shape the landscape of the toxicological sciences. As in clinical pharmacology, the Fund's goals in toxicology changed over time to meet changing scientific needs. In the early 1990s, the Fund decided to place less emphasis on increasing the sheer number of researchers in the field and more emphasis on attracting investigators from other disciplines. In this way, a diverse group of researchers would gain skills and experience in applying a toxicological perspective to their own work. For example, Debra L. Laskin, Ph.D., of the Rutgers University College of Pharmacy, used her 1993 scholar award to study the intricate interplay between nitric oxide and the immune system. Nitric oxide is not only a toxic component of air pollution, but also is a molecule that is produced in the body and serves several important physiological functions. Her award, she said, gave her "the time to learn new techniques and the resources to pursue new ideas and directions."

The Fund announced its new Molecular Parasitology Scholar Awards program in 1981, following a number of smaller grants made over the years for projects to improve tropical medicine. The program was inspired by the abiding interest of Henry Wellcome in matters of tropical health, and, more immediately, by the reasoned encouragement of Dr. Paul Talalay, a professor of molecular pharmacology at the Johns Hopkins University School of Medicine. The awards aimed to foster a cadre of researchers who would take advantage of molecular biology's innovative and powerful tools to increase understanding of parasitic diseases. These diseases—malaria, trypanosomiasis (also known as sleeping sickness), leishmaniasis, and schistosomiasis, among others—have long exacted enormous tolls on the health and economies of peoples in the developing world. Even today, they afflict more than 850 million people worldwide and kill 2 million to 3 million people annually.

Collectively, the Fund's awards are widely recognized as having played a major role in revitalizing parasitology, once a largely observational science, into a vibrant and modern enterprise. Several grant recipients were interested in the parasites that cause trypanosomiasis. Paul T. Englund, Ph.D., of the Johns Hopkins University School of Medicine, named in 1982 as the program's first scholar, worked to understand how the parasites evade the body's immune system by periodically shedding their coat of surface proteins. The 1984 scholar, Nina M. Agabian, Ph.D., took another approach. Her work demonstrated that the parasites must splice segments from two different genes—not one, as scientific dogma held—to build a genetic molecule called mRNA that is critical in growth and development. The discovery suggested that blocking this process might be an effective strategy for interrupting the parasites' endless replication without damaging the human host. Dr. Agabian, who received the award while at the University of California-Berkeley School of Public Health, now heads the Molecular Parasitology Laboratory at the University of California-San Francisco.

In total, the Fund provided nearly \$15 million to support 37 scholars. In 1989, the Fund launched a complementary program, the New Investigator Awards in Molecular Parasitology program, designed to support younger scientists who would bring innovative thinking and new experimental approaches to the study of parasitic diseases. Many awardees in both programs went on to become leaders in the field. Based largely on the work of these awardees, a number of research institutions established centers for molecular parasitology, drawing students and faculty into the field. "The people who received these awards really have been the major contributors in the field," says Dr. Englund. "The Fund has an outstanding success rate in picking the best people, and the award has had a tremendous impact on people's careers."

Dr. Hugh Tilson, then director of Product Surveillance and Drug Epidemiology at Burroughs Wellcome Co., championed the Fund's Pharmacoepidemiology Scholar Awards program, launched in 1983. What was needed, Dr. Tilson said, was a more rigorous and systematic method of assessing the risks and benefits of medicines and continued monitoring of drugs on the market for unexpected or delayed effects, both good and bad. Armed with such information, physicians could make better treatment decisions for patients. The advent of computers, which could collect and crunch data on large populations, made these tasks feasible. "Unfortunately," Dr. Tilson argued, "a background in epidemiologic methods is not part of the specialty training in clinical pharmacology or in the teaching of drug development procedures." The Fund's directors agreed, declaring "the present state of pharmacoepidemiology is analogous to that of clinical pharmacology in the early 1960s when the Fund had a significant impact through its scholar awards." The first scholar awards came in 1984. Craig R. Smith, M.D., of the Johns Hopkins University School of Medicine, used his award to pursue several lines of investigation, including studies to decipher the particular effects of drugs in elderly people. "The elderly," he noted, "seem to have a high susceptibility to adverse drug reactions and drug failures." As his research progressed, Dr. Smith noted that the program "is helping to bridge the disciplines of epidemiology and clinical pharmacology, for which there is a need. For me," he added, "the award is having a major and fortuitous impact on my career." The scholar awards provided more than \$2 million to 10 scientists. Following the 1990 awards, the Fund determined that the field had achieved a critical mass of researchers and that its support could be directed to other pressing areas.

At the beginning of the 1990s, the Fund offered several new awards, including Immunopharmacology of Allergic Diseases Awards and Hitchings Awards for Innovative Methods in Drug Design and Discovery. Steadily, the Fund's profile grew higher as its impact was felt across a range of biomedical research. The Fund gained further luster with the awarding of the 1988 Nobel Prize in Physiology or Medicine to Dr. Hitchings and Dr. Elion. Although the Nobel was tied to their research at Burroughs Wellcome Co., "Dr. Hitchings always acknowledged his role as president of the Burroughs Wellcome Fund," says Fund staffer Carr Thompson. "That helped spread the word about the foundation, what we did, and why we did it. It made us special."



CHAPTER 3

Bigger and Better

As special as the Burroughs Wellcome Fund was coming to be perceived within the biomedical research arena, it nevertheless was a corporate foundation, albeit different from most. "The Fund was started to further biomedical research in areas in which the company might have an interest, but its aims were really separate from the company's," says Martha Peck, who had been named the Fund's executive director in 1981. "And the Fund had put into place safeguards, including peer review by outside advisory committees to recommend and review applications for awards."

Still, the Fund was totally dependent on money contributed by Burroughs Wellcome Co., and the Fund's Board of Directors was wholly drawn from the company and the larger Wellcome enterprise. The sums given were not huge, about \$5 million to \$7 million annually in the 1980s. Nor were they guaranteed; they depended on the company's profits, and in some years no money at all was given. "We never knew how much we were getting, and so we really couldn't plan very far in advance," Peck says.

The Fund's leaders had greater ambitions, however, and with the advent of the 1990s, it began a profound transformation. Dr. Hitchings retired as the Fund's president in 1990 (he remained a board member) and his mantle was picked up by Howard J. Schaeffer, Ph.D., a pharmaceutical chemist who had been vice president of Research, Development and Medical at Burroughs Wellcome Co. and a Fund board member since 1985. Under Dr. Schaeffer's calm and thoughtful leadership, the board in 1991 made historic changes, acquiring its first female director, the extraordinary Dr. Gertrude Elion, and its first director from outside the Wellcome enterprise, Samuel L. Katz, M.D., an eminent professor of pediatrics at nearby Duke University. Dr. Katz went on to serve as chair of the Fund's Board of Directors from 1995 to 1999.


Dr. Samuel Katz and Dr. Gertrude Elion joined the Fund's board in 1991.

But it was an informal conversation in mid-1992 between Martha Peck and John Robb, then the chief executive officer of the parent Wellcome Foundation that would trigger the Fund's biggest transformation. "It really was a strange thing," Peck recalls. "We were talking about the Fund, and I said that we could use more money to make grants. And he asked me, 'What would it take to endow the foundation?' At the time, we were giving grants totaling roughly \$5 million per year, and I thought it would take \$100 million to endow us." The first step on the road to independence had been taken. Fund President Dr. Schaeffer built on Peck's suggestion and, equipped with a brief proposal for increased support, traveled to London to meet with officials at the Wellcome Trust. Dr. Schaeffer and his proposal were well received. His long-term friendship with officials at the Trust, especially with its chairman, Sir Roger Gibbs, undoubtedly smoothed the way, as did the many scientific advances, and their commercial rewards, that scientists at the U.S. company, including the powerhouse team of Drs. Hitchings and Elion, had made over the years.



Fund President Dr. Schaeffer (right) and Sir Roger Gibbs, chairman of the Wellcome Trust, were instrumental in bringing about the Fund's major endowment by the Trust.

Dr. Schaeffer's visit had come at an opportune moment. Directors of the Trust for some time had been concerned that Henry Wellcome's intentions to maximize income for his beneficiaries were not being fully realized, and they had asked for an interpretation of Sir Henry's will. They were told, to their surprise, that it was their duty to diversify. "The Trust had 100 percent of its holdings in

Wellcome stock, and that's not good fiduciary responsibility for any foundation," Peck says. In 1986, the Trust had made its first public offering of Wellcome Foundation stock to diversify its resources. In July 1992, just before Dr. Schaeffer's visit, the Trust made a second offering, raising approximately \$4.4 billion dollars. "Our immediate thought was what would Henry Wellcome want us to do," said the Trust's Sir Roger Gibbs, "and we were all convinced we should do something for medical research in the country of his birth."

Dr. Schaeffer came back from England excited. "He said to me, whispering, 'I think they're going to give us \$500 million. *\$500 million!*'," Peck remembers. "And he went on, 'They have certain questions for us, like, 'How would you use this increased amount of funding?' And 'How would you separate from Burroughs Wellcome Co.?' Because of British tax regulations, the Trust wanted to avoid any appearance that it was giving money to an entity that could be perceived as part of the company."

Ultimately, the Trust decided to give the Fund \$400 million, to be distributed in \$80 million annual installments over five years, and the gift was announced officially in April 1993. At the time, the Fund's assets stood at approximately \$35 million. The gift catapulted the Fund from a small foundation to one of the top 50 in the United States. (Today, with the creation of a number of new large foundations, the Fund ranks in the top 100.) "The Trust's gift is especially important in light of government reductions in research funding,"

Dr. Schaeffer commented at the time. "Foundations such as the Burroughs Wellcome Fund can play a key role in furthering the career development of researchers and in strengthening support for biomedical research."

The momentous occasion went unheralded, however. The Fund had made plans for a ceremony announcing the endowment. "We had press kits ready and press conferences lined up," says Thompson. "However, Burroughs Wellcome Co. was then involved in litigation over one of its products, and we got a call from the company's legal department telling us that we were not allowed to generate any publicity that would put the company's name in the media. The judge had issued a gag order and we could not announce our \$400 million gift. We were floored!"

Separating from Burroughs Wellcome Co. was the immediate challenge facing the Fund. As required by the Trust, the Fund had to establish itself not only as an independent private foundation but also as an independent operation responsible for its own everyday activities. The task was daunting. "We had depended on the company for paying our



Early Fund staff: (from left) Anne Alderson, Catherine Voron, Martha Peck, Martie Nolan, and Carr Thompson.

employees, for all of our health benefits, life insurance, retirement savings, office furniture, and office space," Peck says. In July 1993, the Fund took the plunge, renting space in a nearby office complex and moving in its staff, which now numbered seven. In addition to Peck and Thompson, there were controller Anne Alderson and her assistant, Anne McGrath; programs assistant Catherine Voron; secretary Martie Nolan; and clerk Lisa Izzell. The company helped during the transition, setting up the Fund's computer system and providing mail delivery.

Other changes followed. In order to further its emergence as an independent foundation, the Fund enlarged and recast its board by adding three more directors from outside the Wellcome enterprise: Mary Ellen Avery, M.D., professor of pediatrics at Harvard Medical School; Joseph S. Pagano, M.D., professor of cancer research at the University of North Carolina-Chapel Hill; and Jerry L. Whitten, Ph.D., professor of chemistry at North Carolina State University.

As one of its first tasks, the newly constituted board embarked on a search for a Fund president. "As the Fund now was a larger enterprise, we needed a new full-time president—the position had been part-time—who would



Dr. Joseph Pagano joined the Fund's board in 1993.

have significant scientific credentials and could represent the Fund to the scientific world and as well would have organizational skills and some vision for the Fund," says Dr. Pagano. The board found a new leader in Enriqueta "Queta" C. Bond, Ph.D., who was then the executive officer of the Institute of Medicine in Washington, D.C., which is part of the National Academy of Sciences and charted by Congress to advise the federal government on issues of medical care, research, and education. In her nearly 20 years at the institute, she had supervised the work of eight divisions and been responsible for executing the policies of the organization, managing and developing programs, and securing outside funding.

Dr. Bond emerged as a candidate to head the Fund in roundabout fashion. "I was a member of the search committee," says Dr. Katz, "and I wrote to Queta and asked

her to suggest a few people. I knew from past meetings that she knew everyone, usually on a first-name basis, and would have all sorts of people in mind who might serve the position well. She wrote back a very thoughtful letter with a number of names, and then appended a little script note that said, 'Would I be a possibility?' I jumped at that instantly and submitted her name. We interviewed three or four other people, but it was clear: she was the one. Identifying Queta was probably my biggest contribution to the Fund."

"The thing that appealed to me about the Fund," Dr. Bond says, "was its focus on making awards in the area of biomedical sciences. That was my area. I am trained as a molecular biologist, and I had been director of the Division of Health Sciences Policy at the Institute of Medicine before I became the executive officer. That division dealt with issues relating to the resource and infrastructure needs in research, as well as policy issues relating to the health sciences. So it was an area I knew a lot about. I'd also been in the fundraising business for many years, as a result of being an academic in earlier life and then through my duties at the National Academy of Sciences, and the mission was very attractive to me." Dr. Bond also had unusual scope. "Health is a global issue," she says, and her background made her especially attuned to that fact. Born



Dr. Enriqueta Bond brought a wealth of management experience to the Fund when she took the reins as president in July 1994.

in Argentina, the daughter of an international banker, Dr. Bond grew up in Latin America as well as in the United States. "Spanish is my first language actually," she says. She also is a pilot. "The pilot part of me is due partially to who I married. He was a pilot, and his father ran an airline in China."

Dr. Bond joined the Fund in July 1994 and grasped the reins quickly. "I've rarely seen anybody in such a short time take hold of an enterprise, shape it, mold it, make it move the way she did," says Dr. Pagano. "She had this all-encompassing understanding of what we're about, how to set goals, how to emerge as an elite national fund. It used to be that the board really ran the Fund, and I like to say that when Queta came to the Fund, she first worked for us. Then we began to recognize that we were going to work with Queta, and finally we realized that we were working for Queta. It's a remarkable achievement and she's done it with tremendous yet quiet self assurance."

Martha Peck, who had been serving as executive director, became the Fund's vice president for programs. She continued her usual high level of activity and dedication in developing and administering the Fund's programs and staff. "Martha was tireless in her efforts to help both me and the Fund," Dr. Bond says. "When it came to the Fund's everyday activities, Martha set the tone for professionalism and made sure that everything operated with utmost efficiency. She also continued to work actively with people and organizations outside the Fund, forming collaborations and networks to serve the needs of the larger biomedical and philanthropic communities. In so many ways, Martha remained an absolutely key part of the Fund's operations." In pursuit of a lifelong dream of being a physician, Peck left the Fund in 2000 to enroll at the University of North Carolina-Chapel Hill School of Medicine and earned her M.D. in 2004.

In order to better protect and develop the Fund's financial assets, Dr. Bond hired Scott Schoedler to serve as its first chief financial officer (the title later changed to vice president for finance). He came from the Rockefeller Foundation, where he had gained experience in managing the investments of a large philanthropy. At the Fund, he quickly moved to establish an Investment Committee, comprising members from outside organizations and the Fund's board, to help develop a sound investment strategy and review its implementation. "When you go from being a \$35 million foundation—a small corporate foundation—to being a more than \$400 million independent foundation, the investment program has to change," Schoedler says. "You have to become more sophisticated and more diversified.



Scott Schoedler, current Fund vice president for finance.

The Fund had been following a conservative money strategy; its portfolio comprised 60 percent U.S. stocks and 40 percent bonds. We started a new investment policy. We went into the international equity market, did some venture capital investing, and made forays into other types of innovative investing.

"The objective of all this is not to make a profit," he stresses. "Rather, we operate by giving away money for beneficial purposes. In that, we're more like a pension plan or a college endowment. We manage a pool of money with the goal of getting some rate of return over time that enables accomplishing the organization's goals while minimizing the volatility of that return. Smoothing out the return stream is especially important since the Fund's grant programs are mostly multiyear. Volatility wouldn't matter as much if we were making just one-year grants, but our programs are geared to long-term awards. You need to be able to rely on the money being there. With a very diversified portfolio, you're more assured that when one part of it is lagging, another part is doing well."

An equally important goal of the Fund's investment strategy is to keep its endowment intact. Under Internal Revenue Service regulations, a charitable enterprise must disburse at least 5 percent of its assets annually, and the Fund has set as its standard paying out 5.5 percent each year. "We want to make back whatever we give out, plus a bit more to counter inflation," Schoedler says. "Making more and growing the Fund is a bonus, not a goal, though of course we want it to happen." Since becoming independent, the Fund's assets have fluctuated, going as high as \$780 million in 2000, just before the U.S. stock market bubble burst, to as low as \$490 million in 2003. That drop forced the Fund to suspend new grants in three of its programs for a year. "We didn't want to spend 7 percent of our assets in a given year, as we would have needed to do to keep all the programs at full strength, because then we'd be sacrificing the future to fund the present," says Schoedler. Today, the Fund's resources hover around \$650 million, and all of its programs are up and running.

With the Trust's gift swelling the coffers, the Fund's biggest question became how best to put its resources to work. There was general agreement that the core mission should remain unaltered—to support and advance biomedical research. But how to accomplish that most effectively required critical rethinking. Rather than simply ramping up awards, giving more money to more scientists in more areas, Dr. Bond believed in a targeted approach. "Remember that in comparison to the National Institutes of Health, which has a budget of some \$30 billion annually, the Fund is quite small," she says. "We give away about \$30 million each year. But science is expensive, and the amount we award, though needed, can't go very far in the large picture. So we knew in those early days that we had to pick niche areas in which our limited dollars could make a real difference. To help us identify such promising areas, we used a process of 'terrain mapping.' This is a term I became familiar with at the Institute of Medicine. It was coined by Dr. David Hamburg, who was the institute's president from 1975 to 1980, because he knew that many scientists have allergic reactions to the very idea of 'strategic planning.' Engaging in terrain mapping, then, gets the concepts of strategic planning through the back door."

The Fund began mapping its terrain in early 1995, taking a broad approach. Recalls Dr. Bond: "We did surveys. We wrote to friends of the Fund and others to get their input on what they thought were promising areas where we could make a difference. We researched the literature and brought together a lot of the research agendas and lists of underserved areas



Dr. David Kipnis chaired the Fund's board from 2000 to 2002.

that had been identified by policy groups at the Institute of Medicine, the National Academy of Sciences, and elsewhere. And then we used our Board of Directors to go through the process of thinking about the issues and identifying areas that needed more attention." By then, the board had gained two additional members: David M. Kipnis, M.D., professor of medicine at the Washington University School of Medicine, and Daniel Nathans, M.D., professor of molecular biology and genetics at the Johns Hopkins University School of Medicine, interim president of the university, and recipient of the 1978 Nobel Prize in Physiology or Medicine. Dr. Kipnis maintained a 25-year relationship with the Fund, serving on a number of advisory committees and chairing its board from 2000 to 2002. "What we came up with," Dr. Bond says, "reflected a lot of the same thinking that our own George Hitchings, who once led the Fund, had done—that we were going to support people. We would focus on the 'human capital' component of the biomedical research system, not on funding such things as buildings, general operations, or development campaigns." The Fund's primary strategy would be to foster the development and productivity of career scientists, especially those working in scientific fields that historically have been underfunded. By supporting scientists at strategic points in their careers, the Fund would help build a cadre of highly trained researchers and scholars who could advance biomedical research and help train future generations of scientists.

With its "people first" philosophy in mind, the Fund decided to offer its award programs to researchers in Canada as well as in the United States. The Fund took this step because it recognized the increasingly international nature of science and the long-standing partnership between Canada and the United Kingdom, Sir Henry's adopted country. To begin building a bridge to Canada, the Fund added to its board Henry G. Friesen, M.D., then president of the Medical Research Council of Canada. (A majority of board members now represented organizations outside the Wellcome enterprise.) "Dr. Friesen was the equivalent

in Canada of the director of the National Institutes of Health," says Dr. Katz, who in April 1995 had been elected to chair the Fund's board. "He spoke for medical science in his country. With him on board, we would be better able to cultivate and seek applications from Canadian scientists. The Fund made a definite effort to encourage and fund these scholars, and we set up special programs that would help Canadian medical science."

To ensure that a sufficient supply of young scientists were in the educational pipeline, the Fund also determined that science education needed more attention. Again, the challenge would be to target the Fund's resources in a way that was ambitious yet realistic in scope. Board



Dr. Henry Friesen was the first Canadian member of the Fund's board.



Board members Philip Tracy (left) and Stephen Corman were early champions of supporting science education in North Carolina.

members Philip R. Tracy and Stephen D. Corman—respectively, president and chief financial officer of Burroughs Wellcome Co.—championed the idea of supporting science education in the Fund's home state of North Carolina. As in the Fund's research-oriented programs, the primary goal would be building human capital. This could best be achieved by supporting programs that provide students with inquiry-based, hands-on educational activities that not only impart scientific knowledge but also generate enthusiasm for scientific discovery. "We felt it important for the Fund to invest in science education with the money it had received from its parent company," Tracy recalls. "Focusing on science enrichment for primary and secondary students in North Carolina would be an effective and achievable way to attract more students into the sciences and get them thinking about pursuing science careers."

The Fund was moving forward on a number of carefully chosen fronts, but something was missing—a permanent home of its own. "We needed a place where the Fund could convene meetings of our board, advisory committees, and awardees," Dr. Bond says, "and provide a secure environment for employees, a signature building like that of Burroughs Wellcome Co. We needed a place that said, 'This is the Burroughs Wellcome Fund."

The Fund Builds a Home

The Burroughs Wellcome Fund and its staff led a vagabond existence for more than four of its five decades. During its years as a corporate foundation, it trailed along behind Burroughs Wellcome Co., squeezing into space at the firm's headquarters in New York and then in North Carolina. After the Fund became a private independent foundation in 1994, it rented space in the Research Triangle area. Then in 1996, talk started about building a permanent home. Although some board members were initially reluctantconstructing a building would divert a sizeable amount of money that perhaps should be spent on grants-they were quickly won over by the merits of a home for the Fund. The chief argument: A freestanding headquarters would firmly establish the Fund as an independent entity and provide meeting space for convening award recipients, as well as the Fund's board and advisory committees.

Perkins and Will of Charlotte, North Carolina, the architecture firm selected in a bid process, designed the Fund's new headquarters in the tradition of Italian Renaissance buildings. The basic plan, at once simple and monumental, features a central courtyard surrounded by clean geometrical forms. To design the blueprint, the architects surveyed the staff. "It was a long process," says vice president for finance Scott Schoedler. "They wanted to know everything from the intangible, 'Give me some adjectives,' to the specific, 'What kind of features do you want to have?""

Among the heeded requests were lots of light and windows that open. "Everyone wanted the windows," says program officer Dr. Martin IonescuPioggia. "So if the power goes down, we can still work. We're probably the only power-proof building around here." Dr. Ionescu-Pioggia also plugged for working fireplaces in the formal loggia and a fountain in the courtyard. "We got them, but the fountain was a struggle with Scott. He didn't want one because fountains always break and you've got to fix them."

"As the finance guy, I'm the designated Dr. No," says Schoedler, laughing. 'No, you can't do that; it costs too much money.' Well, I tried to say no to everything, and I lost every time except for one thing: underground parking. It really wasn't worth it."

In 1998, the Fund finally broke ground, and one year later the staff moved into its permanent home. The 43,000-square-foot building of tan and rose-colored Indiana sandstone is light and airy with 12- to 18-foot high ceilings, French doors, and gleaming Brazilian cherry floors. It boasts a large library, a multipurpose loggia, three conference rooms, and 34 offices. "As a building, it's not luxurious, but solid and impressive, just like the Fund," says Dr. Ionescu-Pioggia.



Remembering the Fund's Origins







Although the Burroughs Wellcome Fund is an independent private foundation, it does not forget its origins, and mementos of Sir Henry Wellcome and Burroughs Wellcome Co. are prominently displayed at the Fund's headquarters. In the entrance sits the nearly three-foot tall sculpture of a unicorn, the logo of Burroughs Wellcome Co. that once graced the lobby of the now defunct pharmaceutical firm. In the formal loggia is a bust of Sir Henry Wellcome from the firm's boardroom.

Flanking the entrance are two large glass cases that contain more company souvenirs, including such early product samples as firstaid kits and pill boxes. The cases also hold reminders of two Burroughs Wellcome Co. and Fund stalwarts, Drs. George Hitchings and Gertrude Elion.

Among the Fund's most prized display items are medically related artifacts acquired by Sir Henry Wellcome himself and loaned to the Fund by the Wellcome Trust. An exhaustive collector, Sir Henry amassed hundreds of the same object: Roman votives, mortars and pestles, statuettes of bloodletting, and enema kits.









CHAPTER 4

Fulfilling the Promise

Having reaffirmed its core mission—advancing the medical sciences by supporting research and other scientific and educational activities—the Burroughs Wellcome Fund entered an era of both opportunity and challenge. The mid-1990s saw a decline in the number of dollars available for research. Federal support of basic science was leveling off with the end of the Cold War, and patient revenues—used to subsidize research and education at academic health centers and medical schools—were dropping with the advent of managed care. At the same time, fields such as molecular biology and genetics were poised for major discoveries, but there was a shortage of researchers who could translate the new knowledge into patient care.

BUILDING AWARD PROGRAMS

From its terrain-mapping exercise, the Fund had charted a path that it believed would make the best use of its grantmaking resources and fill some of the gaps in research funding. In 1995, the Fund made the first round of Career Awards in the Biomedical Sciences (CABS), a set of awards that would become its flagship program. The CABS provide postdoctoral researchers with a financial bridge between their late postdoctoral years and their first years as faculty members. Unlike most other career development awards, which offer a year or two of postdoctoral training or new faculty support, the five-year CABS awards are intended to enable scientists to develop innovative and independent research programs. "This period spanning the late postdoctoral years and junior faculty years is traditionally one of the most difficult times for obtaining adequate research support," says Dr. Bond. "Researchers at these stages of their careers are too new to compete effectively for grants

Facing page: Burroughs Wellcome Fund's headquarters, dedicated in May 2000.

from the National Institutes of Health and other federal funding agencies, but too advanced to qualify for standard postdoctoral fellowships. Our career awards are intended to boost promising researchers over this hump and get them firmly established in the research enterprise."



CAREER AWARD IN THE BIOMEDICAL SCIENCES

Sarah A. Tishkoff, Ph.D., of the University of Maryland-College Park, has combined genetics, archaeology, and history to study how infectious disease can shape the human genome and human evolution. By tracing the genetic histories of people in Africa, the Middle East, and the Mediterranean with variations of a gene mutation that confers resistance to malaria, Dr. Tishkoff and an international team discovered that the mutations occurred about the same time that the disease became prevalent in those areas. Dr. Tishkoff argues that the parallel development of malaria

and genetic resistance to it is not an accident, but the result of genetic adaptation to a threat. Dr. Tishkoff is using a similar strategy to study tuberculosis. The hope is that understanding how nature deals with these devastating diseases will lead to more effective treatments.

Other award programs supported study and exchange of information between the United States and the United Kingdom. (Canadian scientists later became eligible.) Hitchings-Elion Fellowships provided support for postdoctoral scientists to train in U.K. laboratories for two years, often working with mentors supported by the Wellcome Trust, and then to return to the United States for an additional year of training. Wellcome Research Travel Grants, offered jointly with the Wellcome Trust, were designed to send established researchers to the United Kingdom where they could spend up to six months exchanging scientific information with their U.K. colleagues or learning new research techniques. The Fund also continued its fellowships (administered in partnership with the Life Sciences Research Foundation) for postdoctoral scientists pursuing careers in the life sciences.

Emerging infectious diseases was targeted as another area deserving major program support. Infectious diseases—some known for years; some newly emerging or reemerging after periods of quiescence—constitute a leading cause of death worldwide, yet the basic science of many of them is poorly understood. Two decades earlier, the Fund had singled out parasitic diseases for attention, and it now continued its award programs supporting mid-career and early-career scientists working in molecular parasitology. To build on that foundation, the Fund in 1995 launched a new program concentrated specifically on malaria, a widespread and often deadly parasitic disease, and announced the first New Initiatives in Malaria Research Awards. These awards were designed to encourage investigators to bring new ideas and approaches to malaria research, to foster collaborations among scientists, and to enable investigators to connect their laboratory work with field stations in regions where the disease is endemic.



SCHOLAR AWARD IN MOLECULAR PARASITOLOGY

Worldwide, parasitic worms afflict an estimated one in four people, many of them children. In the tropics, helminthic infections rank second only to malaria in injuring health. Helminthes do their damage steadily for years by evading the body's immune system. **Edward J. Pearce, Ph.D.**, of the University of Pennsylvania School of Veterinary Medicine, is exploring just how helminthes go under the radar, in particular *Schistosoma mansoni*. This worm, after burrowing into the body and riding along the bloodstream for two or three weeks, sets up resi-

dence in the veins leading from the intestine to the liver. How does the worm know it has arrived at its resting place? Dr. Pearce has discovered that *S. mansoni* has a specific chemical receptor on the surface of its body that detects when the worm has arrived at the right veins. Dr. Pearce's work could lead to more effective treatments against worm infection. Equally important, it could yield new ways of enhancing organ transplant acceptance that do not depend on taking massive doses of antirejection drugs.

Noting that diseases caused by fungi were a serious problem in the United States and the world—especially for people whose immune systems were impaired by disease or drug therapy—the Fund launched two programs in 1995: Scholar Awards in Molecular Pathogenic Mycology and New Investigator Awards in Molecular Pathogenic Mycology. The aim of the two programs was to encourage outstanding scientists to work on basic studies of virulent fungi, pursuing challenging and riskier research projects, which could potentially offer significant rewards.



SCHOLAR AWARD IN MOLECULAR PATHOGENIC MYCOLOGY

William E. Goldman, Ph.D., of the Washington University School of Medicine in St. Louis, is probing the way respiratory pathogens take over the host's cellular defense mechanisms. In histoplasmosis, *Histoplasma capsulatum* parasitizes macrophages, a first line of defense in the lungs. Unlike most microorganisms, *H. capsulatum* is able to survive and multiply inside the sac-like cell compartment where intruding microbes are sequestered and chewed up by macrophages. The

fungus accomplishes this by secreting a calcium-binding protein (CBP) that maintains the compartment at a near neutral pH, deactivating the immune system army and leaving the fungus free to maraud. Dr. Goldman is con ducting experiments to unravel the structure of CBP and identify other genes that may contribute to *H. capsulatum* infection.

The therapeutic sciences also came under the Fund's umbrella, continuing a tradition of supporting researchers in pharmacology, toxicology, and experimental therapeutics. To meet changing needs in these areas, the Fund modified its programs and in 1995 announced the New Investigator Awards in the Basic Pharmacological Sciences and New Investigator Awards in Toxicology. Beginning with the 1998 award cycle, the two programs were combined into the New Investigator Awards in the Pharmacological or Toxicological Sciences.

"We now offered new investigator awards in pharmacology and toxicology, parasitology, and mycology," says Dr. Bond. "These programs reflect the importance that the Fund places on bringing 'new blood' into the sciences. The awards would give promising investigators at the beginning of their independent research careers the freedom and flexibility to apply novel approaches and to engage in higher-risk and longer-term studies. Not only would their work advance the sciences, but the awardees would be well prepared to pursue other fruitful lines of investigation throughout their research careers."

To address the nation's growing shortage of investigators skilled in both medicine and research, the Fund launched a program for physician-scientists—those who are comfortable moving between the laboratory and the patient's room and play a critical role in translating basic research discoveries into patient care. Consequently, in 1997, the Fund recast its experimental therapeutics program as the Clinical Scientist Awards in Translational Research. The first of these awards were made in 1998. The goal is to provide mid-career physician-scientists with the freedom to pursue research and to serve as mentors for the next generation of physician-scientists, rather than having to focus primarily on treating patients in order to bring in revenue for their institutions.



CLINICAL SCIENTIST AWARD IN TRANSLATIONAL RESEARCH

Nina Bhardwaj, M.D., Ph.D., is working on a new way to boost the immune system's ability to ward off viruses and cancers by creating vaccines using dendritic cells. Named for their fingerlike projections, these cells play a critical role in priming T-cells, the attack dogs of the body's immune system, to recognize and strike foreign invaders or tumor cells. Dr. Bhardwaj, of the New York University School of Medicine, is conducting trials of dendritic cell vaccines in patients with HIV and melanoma.

During the last decade of the 20th century, some of the most exciting discoveries in biomedicine resulted from the insights and skills of investigators with strong backgrounds in physics, chemistry, mathematics, the computational sciences, and engineering. Yet academic institutions generally lacked interdisciplinary training programs to equip advanced students with the skills needed to cross the boundaries between the quantitative sciences and the biological sciences.

To help close the gap between the disciplines, the Fund in 1995 launched the Interfaces between the Physical/Chemical/Computational Sciences and the Biological Sciences program, and the first round of awards were made in September 1996. Three members of the Fund's Board of Directors—Dr. David Kipnis, Dr. Daniel Nathans, and Dr. Jerry Whitten championed the new program, which made awards to degree-granting institutions (or groups of institutions) of up to \$500,000 per year for five years to create new interdisciplinary training programs at the graduate and postdoctoral levels. "Our goal was not simply to introduce more students into the research system," Dr. Bond says. "Rather, we wanted to promote an entirely different kind of training that breaks down traditional institutional barriers and produces researchers who are ready, willing, and able to bring innovative approaches and new ways of thinking into the biomedical arena."



Board members Dr. Jerry Whitten (left) and Dr. Daniel Nathans (right) joined with fellow board member Dr. David Kipnis to champion the Interfaces in Science Program.

Another neglected research area was reproductive science; there were knowledge gaps in such areas as the immunology of pregnancy and the causes of premature birth. Board member Dr. Mary Ellen Avery, an eminent pediatrician whose research centered on newborn

infants' respiratory problems, argued persuasively that this area was woefully under funded and deserving of the Fund's attention. The Fund channeled its support for reproductive science in several ways: by allocating at least one Career Award in the Biomedical Sciences each year to researchers proposing to work in reproductive health; by underwriting each year a postdoctoral research fellowship in obstetrics and gynecology, administered by the American Association of Obstetricians and Gynecologists Foundation; and by funding each year a research grant for a faculty-level scientist through the Reproductive Scientist Development Program, which is administered by a consortium of government and private



Dr. Mary Ellen Avery served on the Fund's board from 1993 to 2001.

organizations.

SUPPORTING SCIENCE EDUCATION

Science education has been part of the Fund's mission for a long time. For a number of years, the Fund sponsored visiting professorships in the basic medical sciences and in microbiology. With the Fund's support, dozens of colleges and universities could invite distinguished scientists from around the world each year to teach and collaborate with faculty and students. But emerging educational challenges called for more.

The Fund recognized that without getting young students excited about science and mathematics, the supply of talent for future science careers could dry up. Even students who choose other career paths will need more skills in science and mathematics to succeed in a technology-driven marketplace. Accordingly, the Fund in 1996 launched the Student Science Enrichment Program to support innovative science education activities, outside the classroom, for middle- and high school students in North Carolina.

"Our goal," says Dr. Bond, "is to catalyze the development of programs within communities that use creative ways to introduce students, and especially young women and members of minority groups, to science and excite them about careers in research." The Fund makes awards to well-thought-out projects that give students hands-on experience with science and encourage a sense of exploration and discovery. Students involved in some of the projects have done everything from building robots and model roller coasters to studying the human chest and abdomen in a medical school lab and monitoring oysters and collecting



Students gain hands-on experience in the discovery process through the Fund's science education programs.

water samples in a project to restore water quality to a coastal bay.

BUILDING THE COMMUNITIES OF SCIENTISTS AND HEALTH RESEARCH FUNDERS, AND FOSTERING COLLABORATION

Beyond its competitive award programs, the Fund convened meetings of program awardees, Fund board members, advisory committees, and leading scientists to identify and discuss issues of common concern. In 1997, the Fund brought together CABS recipients and Hitchings-Elion Fellowship recipients for a two-day meeting to discuss the challenges scientists face early in their careers. The group targeted three key concerns about developing their careers: seeking and negotiating a faculty position, setting up and managing a laboratory, and facilitating academic-industrial collaborations. The Fund took note of these concerns and through a number of projects connected scientists with resources, or created new resources, to help them advance their careers.

In 1998 and 1999, the Association of American Medical Colleges and the American Medical Association convened the National Clinical Research Summit to examine issues important to the success of the clinical research enterprise. Building on the summit's recommendations, the Fund gave the Institute of Medicine a three-year grant to establish the Clinical Research Roundtable, created to promote mutual understanding of clinical research within the scientific community and the general public and to encourage the public's participation in clinical studies.

The Fund's vision has been broad enough to encompass the health of the U.S. research enterprise itself, and the health of the research enterprise is closely tied to its funding sources. Working with three other private philanthropies—the Pew Charitable Trusts, the Howard Hughes Medical Institute, and the American Cancer Society—the Fund and its partners convened a special meeting on the role of private funders in the health research enterprise. Held in 1998, the meeting was the first of its kind—designed to enable philanthropies to exchange ideas on boosting health research and training in the United States. The Fund also helped draft a summary of the meeting, *Strengthening Health Research in America: Philanthropy's Role*, which laid out needs and opportunities and suggestions for moving forward.

The Fund's scope has covered support of cutting-edge scientific initiatives, which has included leading an international collaboration to sequence the genome—the complete set of genetic material—of *Plasmodium falciparum*, the most dangerous form of the

parasite that causes malaria. The Fund collaborated with the Wellcome Trust, the World Health Organization, and the U.S. National Institute of Allergy and Infectious Diseases and Department of Defense on this project. The research team announced its breakthrough success in 2002. With this vital genetic blueprint in hand, scientists will be able to develop new drugs or vaccines to treat or prevent this killer disease.

Frontiers in Reproduction, an innovative training course offered yearly at the Marine Biological Laboratory, is a another initiative the Fund has supported to buttress research in reproductive science and bring scientists together; the hands-on, laboratory-based course, attended by scientists throughout the world, is led by a faculty of prominent basic and clinical scientists and provides comprehensive training in research strategies and state-of-the-art laboratory methods.

The 21st century ushered in two more rounds of terrain mapping that have honored the Fund's core mission while at the same time have kept pace with the progress of the U.S. research endeavor and consequently, its shifting needs. In 2000 and 2005, the Fund would grapple with which of its programs to sustain and which needed to change.



CHAPTER 5

Burroughs Wellcome Fund Today

Through years of experience, the Burroughs Wellcome Fund—now commonly known as BWF—has honed its ability to target the right program areas at the right time. BWF now focuses on five core areas: basic biomedical sciences, infectious diseases, interfaces in science, translational research, and science education. Within these areas, BWF offers competitive awards to foster the development of early-career scientists, of mid-career scientists who can serve as mentors to those early in their careers, and of tomorrow's scientists—students in primary and secondary schools who may have an interest in science and the aptitude to pursue it. Program evaluation is a key part of all BWF's funding activities, to ensure that its programs are doing what they were designed to do and to provide data for any needed changes.

Each program area is directed by a senior program officer and a program associate, who are as dedicated in their mission as are the awardees they serve. They embody BWF's spirit and are the best guides to its programs. The following sections describe BWF's current programs, through the program officers' own words.

BASIC BIOMEDICAL SCIENCES

-Dr. Martin Ionescu-Pioggia:

I came to BWF in 1994 from Burroughs Wellcome Co., where I was doing research and marketing work related to the company's psychiatric drugs. I also was continuing my research affiliation with McLean Hospital-Harvard Medical School. My Ph.D. is in clinical psychology with a research concentration in clinical psychopharmacology. As an academic and industry researcher, I had long been interested in the Fund, so when I saw a "help



Basic Biomedical Sciences: Martin Ionescu-Pioggia, Ph.D., senior program officer (right), and Rolly L. Simpson Jr., senior program associate.

wanted" ad on the company bulletin board, I applied at once, believing that working with the Fund offered an opportunity to have an important influence on the scientific profession. At the same time, I could meet my need to work in an organization with a charitable component, enabling me to do something I love rather than just earn a living working in industry.

The Career Awards in the Biomedical Sciences (CABS) program that I manage is BWF's flagship program. The grants—\$500,000 over five years—support young scientists making the critical transition from advanced postdoctoral training to faculty service and independent research. To date, we've given out 215 awards for a total of approximately \$105 million. About a quarter of the recipients are in the neurosciences, a field that is making rapid advances and is the nexus for many disciplines.

The career awards are made in honor of George Hitchings and Gertrude Elion, two pioneering scientists who played major roles in BWF's history. In developing the CABS program, BWF took a lesson from the Lucille P. Markey Charitable Trust, which was offering grants to help young scientists get faculty positions and become independent investigators. But the Markey Trust had elected to disperse all of its money, rather than act as an endowment, and was scheduled to close shop in 1997. BWF staff brought the concept of the Markey program to the attention of our Board of Directors, and the rest, as they say, is history. Jean Wilson, who was the program's first advisory committee chair and now chairs the Fund's board, was instrumental in helping us develop the CABS program. Former advisory committee members Paul Berg and Mike Bishop, both Nobel laureates, also played important roles in the program's development. The board recognized that such awards would meet a terrific need within the biomedical community and would fall well within the Fund's mission statement.

In the early 1990s, there was a large group of postdoctoral fellows who could not obtain faculty positions because of the economic woes at universities, and there also was

a large influx of postdoctoral fellows coming to the United States from foreign countries. Many of these postdocs left the sciences, and many others wound up sitting in a postdoc limbo while trying to find a faculty position and become independent researchers. Since scientists tend to do their most innovative work when they're young, sitting in limbo can cost them their best years. The Fund's career awards were intended to get promising postdocs into faculty positions as quickly as possible. And they've worked. We've found that the awards have been effective in helping people get great job offers and bridge to faculty posts. There are other relatively new bridging awards, but they are few in number, less flexible, and do not offer the vital ancillary career support that BWF's awards provide.



Dr. Jean Wilson, current chair of the Fund's Board of Directors.

BWF is now in the process of assessing the program's overall impact on awardees' careers and the quality of their science. We've completed the first part of the evaluation: a study that tracked the career paths of award recipients. The study found that 98 percent of recipients have gotten tenure-track or equivalent faculty positions, and they have received laboratory start-up packages averaging approximately \$400,000, which are well above national averages. In the second part of the evaluation, we're comparing the scientific achievements of award recipients to unfunded applicants. Preliminary results from this study, which is nearly complete, suggest that awardees are more successful in obtaining appointments at top-ranked academic research institutions, obtaining federal research support, and publishing in leading professional journals. As further evidence of the success that our awardees have achieved, a number of them have gone on to be named Howard Hughes Medical Institute (HHMI) investigators and to receive support from other major foundations. One awardee has won a no-strings-attached "genius grant" from the John D. and Catherine T. MacArthur Foundation.

One of the strengths of the CABS program is that we're attentive to the needs of our awardees. Rolly Simpson, the senior program associate, likes to say that we have "pastoral responsibilities" to our flock. To that end, we're very flexible. We will tailor the award to individual circumstances. It's not a one-size-fits-all, jump-through-the-hoops award with rigid requirements and rules, as is so often the case with grants.

Perhaps the most important way we tend our flock is by convening our awardees on a regular basis. These meetings bring together awardees with members of our board, advisory committees, and staff, as well as with leading scientists from outside the Fund, to identify and discuss issues of concern. Awardees receive needed career-development training and mentoring, and they develop valuable networks among themselves and other senior scientists. Just as importantly, the meetings serve to develop a sense of "family" among our awardees and make it clear that the Fund is an advocate and partner in their scientific growth and career progression.

We also solicit feedback from our awardees in a variety of other ways, including telephone interviews and annual surveys. We ask them questions: "What do you need? What are the major problems you face in science, and what do you need to overcome them? How does your award deal with those issues? What changes would you make to the award?" And often, we implement the requested changes.

Some of their responses have pointed us to systemic issues that can't be resolved by individual awards. BWF is one of the first foundations to recognize that there are things that all young scientists need to know that they are not taught in graduate school or during postdoc training. For example, they need to how to negotiate for faculty positions and how to get their papers published, and we have sponsored workshops on these and other topics. Out of those experiences, Rolly and I began keeping an eye out for articles dealing with career development issues. Such articles usually are buried in the backs of professional journals, so they can be easily overlooked; if a journal is out of a scientist's area, it usually isn't seen. We published an annotated bibliography of these articles dealing with such concerns as time management, how to establish collaborations, negotiating for laboratory space, and handling the tenure process. This publication was one of the first career-development resources available for young scientists. We've since produced many other types of materials, which we've distributed in a variety of ways: we've handed them out at BWF's annual awardee meetings and at gatherings of BWF awardees at professional society meetings, and we've distributed them more broadly in print form and via BWF's website and other electronic outlets.

Our early research on these career resources underscored the dramatic need for training in other areas that support science and prompted our initial collaboration with the Howard Hughes Medical Institute. We worked with HHMI to develop and co-fund *Science* magazine's Career Development Center, a Web-based free access career resource for postdocs and new faculty worldwide (http://nextwave.sciencemag.org/).

In direct response to feedback from our awardees, we also have worked with HHMI to create a laboratory management training course, the first ever of its kind. Postdocs don't get such training during their fellowships, and when they move to faculty appointments and try to set up their labs, they're beset by new demands to teach, submit research grants, and do administrative work. Setting up a lab is the equivalent of running a business: newly minted faculty members have to hire people, buy equipment, and prepare budgets. Most of them simply aren't ready.

So BWF and HHMI developed this three-and-a-half day training course to teach postdocs the basics of laboratory management, and also to help our awardees who already have established labs run them more effectively. The course debuted in July 2002 and had nearly 130 participants—who uniformly gave it great reviews. (A revised version of the course is scheduled for summer 2005.) We also have converted the course into a 240-page book, *Making the Right Moves: A Practical Guide to Scientific Management for Postdocs and New Faculty*, which is available at no charge in print and on the Internet (www.hhmi.org/labmanagement). As evidence of the need for such a course within the scientific community, some 10,000

copies of the book have been distributed and the course (in its entirety or by individual chapters) has been downloaded electronically more than 110,000 times.



CAREER AWARDS IN THE BIOMEDICAL SCIENCES

The ribosome is a submicroscopic bundle of proteins and RNA in living cells that translates the genetic code to make useful proteins. **Rachel Green**, **Ph.D.**, of Johns Hopkins University School of Medicine, is deciphering how the ribosome catalyzes and coordinates the complex molecular events of translation. Her studies may reveal important details that affect the workings of other protein-making units, like the spliceosome and telomerase. Since ribosomes are the target of many antimicrobial drugs, including erythromycin and chloramphenicol, Dr. Green's studies may yield vital information for drug development.



Brendan P. Cormack, Ph.D., of Johns Hopkins University School of Medicine (and Dr. Green's husband), focuses on the molecular mechanisms underlying the host-pathogen relationship for fungal pathogens, particularly the *Candida* species, which infects mucosal tissue. Infection with *Candida* is especially dangerous to people with weakened immune systems; *Candida* can easily run riot through the body and precipitate a life-threatening crisis. Dr. Cormack's research is centered on *Candida glabrata*, the most frequently isolated fungal species in U.S. hospital intensive care units. Dr. Cormack and his team are illuminating the unique way *C. glabrata* adheres to its mammalian host's epithelial cells and are looking for the genes responsible for the fungus's special virulence.

INFECTIOUS DISEASES

—Dr. Victoria McGovern:

It's remarkable how many times the Fund and I crossed paths. In college, during a sophomore mycology course, I got fascinated with the pathology of *Histoplasma* infections, and I sought out Bill Goldman, who was to become one of the first BWF Scholars in Mycology,



Infectious Diseases: Victoria P. McGovern, Ph.D., senior program officer (left), and Jean A. Kramarik, senior program associate.

and I worked with his group through the rest of my undergrad years. In grad school, I regularly attended a journal club and always sat behind Steve Hajduk, who went on to be named a Parasitology Scholar and is now a member of my advisory committee on disease pathogenesis. The club presented each and every new paper from John Boothroyd back when he was a Parasitology Scholar, and he later chaired my advisory committee on parasitology. We also heard about the work of BWF Parasitology Scholar Nina Agabian, everything she did with RNA trans-splicing. So I was very aware of the Fund, which was always acknowledged at the back of the really exciting papers. Then, to wrap it up, as a postdoc I worked with Jim Oliver on the response of *Vibrio vulnificus*, a deadly human pathogen, to environmental shifts, and Jim eventually served as a Wellcome Visiting Professor in Microbiology. Small world, isn't it?

During my postdoc, I got interested in science policy and began working with a loose-knit group of early career scientists on issues related to the stability of scientific careers, providing input into the mid-1990s discussions that laid the groundwork for recent improvements in postdoctoral compensation and for the increasing acceptance of "alternative careers" for scientists. That was fun: going to meetings in Washington, D.C.—at the American Association for the Advancement of Science, at the National Academy of Sciences, places that I knew mattered for deciding how American science gets done—and learning how the process works. It was such an exciting time, and it really got me going in a new direction, as far as my reading and thinking went. I became one of the first correspondents for *Science*'s *Next Wave* and learned some excellent things that way. I'd written for newspapers and other publications before, but somehow I'd forgotten how great writing is for asking some of the awkward questions postdocs just can't ask. And all of these activities opened doors over the next few years, helping me get more opportunities beyond the lab—college teaching and more writing assignments—and eventually bringing me to the attention of the Fund. When a spot on the staff opened up, I joined as a program officer for infectious diseases, a Fund program that I'd admired for so long. Can you imagine? I could have a role in the best science, and also keep working on scientific workforce policy. This is such a great job.

When I came to the Fund, I took over three of our oldest program areas, parasitology, pharmacology, and toxicology, and one of our newest, mycology. I also took over handling our interest in seeing the newly emerging field of genomics brought to bear on some difficult diseases caused by eukaryotes—malaria, Chagas' disease, African sleeping sickness, leishmania, aspergillosis, histoplasmosis, cryptococcosis, and other diseases you'd really rather not get. The toxicology and pharmacology programs were retired after our 2000 terrain mapping to provide more dollars for new efforts, including an expanded program in infectious diseases.

Jean Kramarik, a microbiologist and toxicologist who'd spent most of her career as a lab manager, soon joined me as my program associate. Jean and I complement each other well. With her organizational and people skills, she's been able to streamline our grants management, and, even better, she's gotten awardees well acquainted with the hows and whys of our system, which puts serious emphasis on awardee progress reports. She and I both spend a good bit of our time getting to know our awardees, working with our advisory committees, and keeping up with our fields.

The Infectious Diseases program really harks back to Henry Wellcome's passionate interest in tropical diseases, an interest that was reflected at his companies and at BWF. One activity that directly celebrates this legacy is our joint program with the Wellcome Trust; this is the only program our organizations run together. This initiative has provided \$26 million to support collaboration among researchers in the United States, Canada, the United Kingdom, and developing countries to study diseases afflicting the developing world. One significant aspect of the program is a commitment to train scientists on-site in developing nations.

Another international collaboration that BWF has helped support, the *Plasmodium* falciparum Genome Project, also has proved fruitful and exciting. Begun in 1997, this team effort ended in 2002 with the sequencing of the genome of the most dangerous form of the parasitic mosquito that causes malaria. This was a remarkable project—it started before any whole organism had been completely sequenced, back when even the project to sequence the bacteria *Escherichia coli* looked like it was on the rocks. And there were known problems with manipulating Plasmodium DNA, whose chemical structure makes it behave, physically, in some *really* inconvenient ways. The project's funders made a leap of faith—faith in the malaria research community and in the researchers, inside and outside of malaria, who were developing these sequencing technologies-that we could work together to overcome these problems. And we did. So, today, malaria's got something unique-"the malaria triad." We've got in hand the complete sequence of an important pathogen, its human host, and its vector, the mosquito, which was sequenced with private and public funds and also completed in 2002. What a fantastic thing! Having all three genomes sequenced opens up the pathway for developing a truly integrated understanding of how this parasite works, "from the cradle to the grave," and it's ours!

In formal terms, BWF's current Infectious Diseases program is a continuation and expansion of the Fund's 25 years of direct investment in this field. The Fund's early award program in parasitology helped draw the emerging "new biology" into research on parasitic disease, an area that was having a hard time jumping into the then-new molecular paradigms. Sam Katz and Trudy Elion, both on BWF's board when the Fund received its endowment from the Wellcome Trust, were very interested in seeing us press ahead in this area. As part of this effort, we initiated in the mid-1990s a parallel program in mycology to use the parasitology program's strategy to bring new thinking into this field, which was lagging compared to other areas of infectious disease.

In 2000, the Fund decided to extend its interests in infectious diseases into virology and bacteriology, and we launched the Infectious Diseases program. Under this program, we offer Investigators in Pathogenesis of Infectious Disease awards. As the name suggests, these



Dr. Gail Cassell joined the Fund's board in 1999 and served as its chair from 2003 to 2004.

awards are meant to encourage the study of infectious *disease* itself, as a phenomenon, rather than the study of individual diseases. Fund board members George Miller and Gail Cassell were both enthusiastic about seeing us take on a broader view of this field, and they've helped us a great deal in shaping the program and getting the word out about how and why we changed gears in this area. The new program also shifts BWF's focus more completely in a career development direction—through it we're encouraging investigators early in their careers, at the assistant professor level, to study the host/pathogen interface using new tools from genomics, immunology, and other areas.

The terrorist attacks of 9/11 and subsequent anthrax attacks have focused a lot of scientific attention and money

on bioterrorism and biodefense, and the Fund has carefully not duplicated these efforts. In considering where we can make a difference, BWF has been reorienting our program to big picture issues. One of the questions we've been asking is: How can we help the research community in infectious diseases think more about the phenomenon of infection rather than about this bug or that bug?

This field has tended to move bug by bug. Say you have two bacteria that evolutionary scientists believe are separated by an itty bitty micro-hair, and one causes a terrible gut disease and another a horrifying lung disease. Well, you can study all day long about how particular bugs work, and you can learn great things that way—scientists have been doing that for decades. But a lot of the damage that happens in infectious diseases and in autoimmune diseases is actually caused by the devastating power of your immune system turning on you, and not by the pathogens themselves. So if instead of asking how does this particular pathogen do things to you, we ask: What triggers damage? What is pathogenesis? How does this interaction with another organism turn into such a big problem for the human body? Then, maybe we'll learn a whole lot more about preventing or stopping infectious diseases.

Our program has proved remarkably competitive, funding at about the 10 percent rate. We're looking for people who truly are asking questions about pathogens in contexts relevant to the human host. This might mean, for example, looking at cell-cell interactions, what happens when the pathogen collides with a host immune cell, or how it crosses an epidermal layer; or working on how host genetics plays out in its interaction with a pathogen; or studying chronic diseases like atherosclerosis or peptic ulcer that are turning out to have infectious roots; or even developing novel animal models that will provide better insights into what happens when host and pathogen worlds collide. I'm looking forward to seeing how the applications evolve over the next few years, with so much interesting work going on in understanding biofilms in the body—what organisms are there, how do they get established, how do they behave. There's so much natural history that we don't understand, and it's all going on inside us. My favorite gee whiz fact these days is that the microbes outnumber us 100 to one within ourselves: for every human cell in a body, there are 100 cells that aren't human. With that in mind, have we ever asked the right questions about the nature of human health? I'm looking forward to seeing the right questions coming in, though, and I'm thinking they'll be rolling in soon.

Jean and I put a lot of effort into developing tools to help our awardees get on a great career trajectory. We've brought together our awardees in 1998, 2001, and 2004. The 2004 meeting was especially exciting, because for the first time we really did reach across the entire BWF family, bringing in researchers—current and past awardees and advisory committee members—from across the Fund's programs to talk about looking at pathogenesis from new angles. Board members Gail Cassell, Jerry Straus, Phil Gold, and Mary-Lou Pardue all were part of that, and they've had some excellent insight into how we can ask new kinds of questions in this field. We heard some terrific ideas, and hope that the future includes developing loose networks to foster new work around some of the really novel ones.

We've also been developing resources to help trainees navigate their careers, especially in nuts-and-bolts areas like grant writing, public speaking, and teaching. We're finding that our awardees come in with varied preparation in these areas. So we're working here at the Fund and with outside organizations to try to put together materials that will help our awardees—and their trainees—by giving them a starting point for filling some of these gaps.



INVESTIGATOR IN PATHOGENESIS OF INFECTIOUS DISEASE

Certain bacteria, like *Escherichia coli*, which triggers traveler's diarrhea and kills infants in underdeveloped areas, and *Pseudomonas aeruginosa*, which colonizes immunocompromised patients, appear to infect humans by way of little sacs of toxins. These tiny sacs, carried along the outer membrane of the bacteria, burst into host cells upon close contact. **Margarethe J. Kuehn, Ph.D.**, of Duke University Medical Center, is examining the genetic, biochemical, and functional features that

mark bacterial vesicle production. Her lab is identifying genes essential to the production process, specific proteins carried in the blisters, and molecules that ease the vesicles' way into host tissue. Her work suggests that enterotoxin, a major virulent factor of *E. coli*, facilitates entry of the sacs into human colorectal cells. With insights provided by Dr. Kuehn's studies, scientists may develop more targeted therapies for important human pathogens.

INTERFACES IN SCIENCE and TRANSLATIONAL RESEARCH

-Dr. Nancy Sung:

I was a postdoctoral fellow at the University of North Carolina-Chapel Hill Lineberger Comprehensive Cancer Center in 1997 when I heard that BWF was hiring staff to put its new programs in place. My doctoral research had focused on understanding the ways that tumor viruses subvert cellular machinery after infection and the conditions under which the viruses could contribute to initiation or growth of cancer. During my postdoc, I began to appreciate clinical research, as I was using biopsies from patients with nasopharyngeal cancer to look for both lesions in the cellular DNA and differences among strains of the Epstein Barr virus, which is found in every patient with this disease. I also began to collaborate with a biostatistician in an



Interfaces in Science and Translational Research: Nancy S. Sung, Ph.D., senior program officer (right), and Debra A. Vought, senior program associate.

attempt to identify meaningful patterns in the huge volume of DNA sequence data that we obtained from patients in the regions of China where nasopharyngeal cancer is endemic. In addition, I organized an international collaboration in order to help move this work forward.

These factors—the evolution of my basic molecular research into more clinical and interdisciplinary approaches, and my discovery that I really enjoyed connecting people and working at the "big picture" level—made the prospect of working at BWF attractive. I wrestled with leaving the bench, because I'd been on an academic career path. But my budding interest in making a career shift was nurtured by Joseph Pagano, my graduate advisor and a BWF board member, who felt that this opportunity would be a great fit for both me and the Fund. I also recall being impressed with BWF as an organization, for its keen perception of the areas of science most in need of support and for the professionalism of its staff.

So, I took the leap. Shortly after I joined the Fund, we were fortunate to find Debra Vought, whose freshly minted master's degree in microbiology and superb organizational and communications skills made her a perfect program associate. Debi handles many of the important details of running our programs and is our primary "face" to our awardee community.

We have responsibility for two program focus areas, which are vastly different
and yet have one common thread: both bridge scientific universes. The first focus area, Interfaces in Science, seeks to bridge biology, on the one hand, and the physical, chemical, and computational sciences, on the other. Biology and the physical/computational sciences represent immensely different cultures, separated by a seemingly uncrossable chasm. Our program attempts to help bridge this chasm by creating a cadre of well-trained people who speak both the language of biology and the language of math and physics. In pursuit of that goal, we awarded grants, typically providing \$2.5 million over five years, to a total of 10 institutions to establish interdisciplinary training programs. These awards—made in 1996, 1998, and 2000—departed from the Fund's usual practice of funding individual scientists. The aim, instead, was to create the "habitats" necessary to nurture a new kind of scientist.

BWF also views these institutional programs as "experiments" for testing new models of scientific training. We didn't prescribe the elements of the training programs, but said, "You tell us how you think it will work, given your scientific and institutional environment." We funded programs that had a high level of scientific rigor and that seemed to have most thoughtfully addressed the culture barriers between scientific disciplines. Many of the program graduates are still in training; thus, it is too early to formally evaluate the impact of these programs. Some important principles have emerged, however, and they subsequently have served as the philosophical basis for other funding agencies as they have built similar programs—roughly 10 years after BWF first fielded its experiment—to support interdisciplinary training at the interfaces of science.

As in BWF's other programs, we have made it a priority to get to know the students and fellows, by convening them at regular intervals so that they can share their work with each other, build networks, and discuss career concerns. Debi provides the personal touch. She routinely goes the extra mile to communicate with our awardees, building relationships that help to convince them that although BWF has high expectations, we really are on their side.

Several years into this program, the Fund recognized that top research universities were stepping up their efforts to create improved habitats for interdisciplinary scientists and federal agencies were increasing their funding for interdisciplinary training. For these reasons, BWF returned to its core strategy of supporting individual scientists rather than providing more training grants. In 2001, the Fund launched the Career Awards at the Scientific Interface program, which is patterned on the Career Awards in the Biomedical Sciences program. In the interface program, however, applicants must have doctoral training in a physical/computational discipline and be applying their expertise to an important biological question. They apply as postdocs and can take the award with them to another institution for a faculty position. So far, we've made 26 awards to investigators working in a diverse range of fields, including genomics, neuroscience, cellular networks, pattern formation, single molecule studies, and imaging, among others. They've rapidly moved into faculty positions at top universities, and are disproving the old critiques—"neither fish nor fowl"; "a mile wide and an inch deep"—leveled at interdisciplinary training. We trust that these awardees will distinguish themselves just as awardees in BWF's flagship career-development program have done.

The second program focus area that Debi and I administer bridges the laboratory bench and the patient bedside. The Clinical Scientist Awards in Translational Research program traces its roots to the Fund's first competitive award program, in clinical pharmacology. In the mid-1990s, the National Institutes of Health (NIH) and other organizations began paying increased attention to the movement—or, more properly, the lack of movement—of bench research into clinical studies. The United States makes huge investments in basic science, but the results often aren't translated quickly enough into improved human health. A big part of the problem is that the people arguably best suited to the task, physicians trained as scientists, face major disincentives to building careers in academic health centers, where such translational activities often take place.

Salary is one factor. Physicians who go into private practice typically earn more money, and begin their earnings sooner, than do physicians who pursue careers in research and undertake extended scientific training. Moreover, many physician-scientists who do pursue an academic career avoid research involving patients, because funding is more difficult to get, results are slower to emerge, thus few papers are published, and promotion and tenure are less likely. So many of them, despite their clinical training, gravitate toward doing basic science, where there are more tangible rewards. Everyone recognized that something needed to be done to stabilize the careers of physician-scientists and encourage them to translate their work into clinical studies. What BWF chose to do was to fund not young scientists, as we do in our other programs, but mid-career physician-scientists who already are well-established investigators with NIH funding and a strong independent publication record. We did this because we noticed that the generation of people who could mentor younger physician-scientists was disappearing—they were falling out of the system and leaving their research careers. We wanted to identify those individuals who chose to stay, who were achieving success, and who would be enthusiastic mentors to the next generation. In the first six years of the program, we've given out 52 awards.

The program is highly competitive. Ideally, we look for people with great science based on clinical insight, who will be ready to launch a clinical study within the five-year grant period. Equally important is the mentoring capacity. We look for people who have what we call the "mentor phenotype," meaning they attract young scientists, then guide and inspire them. How do we recognize it? We look for people whose trainees are listed as first authors on papers coming out of the lab and whose trainees go on to good jobs and stay in research. Some scientists have a clear track record of reproducing themselves in younger people, as opposed to those who really don't view developing their people as a primary role. Not coincidentally, as more women have come into science, mentoring has received a lot more attention, and mentors are expected to be much more nurturing.

In all of our focus areas, we try to target programs in a way that will have the greatest impact on the career development of our awardees. But we don't stop there. We also design a constellation of activities around those programs that will enhance the environment in which those people work, and address any barriers to their success. To that end, BWF has supported a number of policy activities related to the conduct of clinical research and career development of clinical investigators, notably the Clinical Research Roundtable of the Institute of Medicine. BWF also has worked with a number of professional societies to include career development modules at their annual meetings.

Because most of the issues surrounding clinical research are systemic and cannot

be solved by the Fund alone, we've also been active in working with other funders who share our interests. We're now formalizing the Health Research Alliance, a new consortium of private foundations and voluntary health agencies that support biomedical and health research. BWF has provided leadership for this effort, and we have taken the important step of providing manpower to move this effort forward by hiring Kathryn Ahlport as its program manager. Kate came to us with a background in health philanthropy and public health, along with great experience in entrepreneurial consensus-building. Our hope is that within two years the Health Research Alliance will be an independent organization with a broad support base among foundations and voluntary health agencies, whose mission is to improve communication, foster collaboration, and enhance the overall effectiveness of grantmakers in supporting biomedical and health research. The ethos at BWF—promulgated by our president, Queta Bond—has been to seek likeminded partners, with a spirit of generosity and shared credit, and to collaborate whenever possible to accomplish our goals.

CAREER AWARD AT THE SCIENTIFIC INTERFACE



Michael B. Elowitz, Ph.D., of Rockefeller University, is taking a new approach to biological research in his effort to understand how genes work together. He not only looks at gene networks in nature, but also builds models of gene systems in the lab. Scientists studying diseases have long concentrated on factors outside the genetic network that impact genes' ability to direct protein production. Dr. Elowitz's focus is inside the system. He wants to see how well genes express themselves when left on their own. To that end, Dr. Elowitz and colleagues designed their own genetic

system, putting two virtually identical copies of a gene onto a single DNA chromosome in the bacterium *Escherichia coli*. The sole distinction was that each gene produced a different colored protein. Because the two genes shared the same environment, they could be expected to produce equal amounts of protein. But they didn't, demonstrating that cells intrinsically possess a degree of randomness or unpredictability, in scientists' parlance "noise," that results in fluctuating gene expression.

CAREER AWARD AT THE SCIENTIFIC INTERFACE



With the advances in molecular genetics and the development of mouse models of human disease, there has been increasing interest in the imaging of live mice as a way to follow disease progression and to assess the potential of new drugs. However, applying the nuclear medicine methodology of imaging the distribution of radioactivetagged tracers is difficult because of the animal's small size and low blood volume. **Todd E. Peterson, Ph.D.**, of Vanderbilt University, is working to enhance instrumentation and techniques for high-resolution small-animal imaging. One route

he is pursuing is to use silicon strip detectors, which have spatial resolution that is at least an order of magnitude better than scintillation detectors used in other nuclear imaging systems.



CLINICAL SCIENTIST AWARDS

Brian J. Druker, M.D., of the Oregon Health & Science University, helped bring a revolutionary type of cancer drug to the market that has brightened the outlook of patients with chronic mylogenous leukemia. Unlike traditional chemotherapy, the new drug, marketed under the name Gleevec, targets the genetic abnormality that causes the cancer and leaves healthy cells alone, thereby causing far fewer side effects. Many of the patients who have received the drug since its 2001 approval by the Food and Drug Administration have achieved remission of the disease.



Using highly sophisticated robotic, fiberoptic, and chip technologies, **Thomas J. Hudson, M.D.**, conducts a million DNA tests a week in his lab at McGill University, looking for the genes involved in common complex diseases, including lupus, inflammatory bowel disease, coronary artery disease, diabetes, and asthma. Dr. Hudson predicts that within five years, asthma researchers will have identified 90 percent of the genes implicated in asthma—a major step toward developing targeted treatments for the disease.



Science Education: D. Carr Thompson, senior program and communications officer (left), and Melanie B. Scott, senior program associate and database specialist.

SCIENCE EDUCATION

-D. Carr Thompson:

In my biased opinion, science education is the most rewarding of the Fund's program areas. One of our primary goals is to develop the careers of young scientists—and this includes growing the minds of students, from their early years onward, who will become the future scientists, mathematicians, and engineers of America. To help fill the educational pipeline with students interested in becoming scientists, we reach into the primary and secondary schools to nurture students' enthusiasm for science and expose them to the scientific process.

I have a personal interest in this. I've always loved math. As a young girl growing up in eastern North Carolina, I wasn't encouraged to pursue a career in math or science; my two daughters were guided differently. They participated in science and math enrichment activities after school throughout their primary and secondary school years. One daughter has gone on to earn a bachelor's degree in mathematics and is now in a Ph.D. program in applied mathematics; the other is majoring in physics. Melanie Scott, who wears two hats at the Fund, working with me in the science education program area and serving as BWF's database specialist, attributes her undergraduate degree in chemistry to the science enrichment experiences she took advantage of in secondary school. So it's great that BWF is helping direct more students toward science and mathematics careers.

The Student Science Enrichment Program (SSEP), which we began in 1996, is the Fund's first competitive award program to target individuals at the K-12 level. The awards enable students at middle- and high school levels to take part in inquiry-based learning, an educational approach that effectively reaches students in ways that keep them interested and help them learn. Since schools have standard courses of study that must be followed in the classroom, our program fosters educational activities outside the classroom, including after school hours or during vacations. These "add on" programs often prove pivotal in reinforcing what is learned in the classroom. In order to reach all of the stakeholders in the education process, we make SSEP grants available to universities and colleges, private and public schools, museums, and nonprofit community groups, such as the Girl Scouts and 4H clubs. In these programs, students meet scientists, conduct laboratory experiments, keep journals that improve their writing skills, and work with high-technology tools—anything that's aligned with the state's standard course of study and will get the students involved with doing science in innovative and creative ways.

As in every Fund program, we pay close attention to evaluation. We want to learn what works and what doesn't. Based on nearly a decade of experience, we've identified a number of factors that help drive successful science enrichment programs. The list includes having curriculum appropriate for the designated students, providing "minds-on" as well as hands-on activities, involving scientists and teachers, giving students ample opportunities to discuss and present their work to others, requiring programs to reach out to a broad pool of applicants, and building on-going relationships with students. We regularly convene directors of the organizations that win SSEP grants and teach them how to evaluate their programs and improve activities. We also teach them to use data-driven research in writing grant proposals for additional support to continue their activities.

The SSEP is restricted to North Carolina, because the Fund's resources are

modest and we really wanted to do something for our home state. We make grants totaling approximately \$2 million annually, and to date, we've invested more than \$10 million in programs across the state. Nearly 24,000 students have participated in our programs. As a measure of success, more than 45 percent of these students say their experience encouraged them to view science as a career option. They also say they would refer the programs to their friends—a real compliment coming from teenagers!

BWF's experience in investing in science enrichment activities also made us aware early on that many factors outside the classroom control what is taught in the classroom. Consequently, we partner with other organizations to further develop the science, mathematics, and technology education infrastructure across North Carolina. Together with the Public School Forum of North Carolina, we helped create the N.C. Institute for Education Policymakers, the first such initiative in the United States. Newly elected state board of education members and state legislators who are involved with education, or allocations committees and the like, participate in this institute to learn about the past 15 or so years of education policymaking in North Carolina. They get a better understanding of what policies were created, what impact those policies had, and who the key players were. By all accounts, this institute has helped to break down barriers among North Carolina policymakers. Looking beyond our borders, the institute has been replicated in other states, including Georgia and South Carolina, and colleagues in England have developed a similar institute there.

We also take these policy leaders on study programs to explore model educational systems in other countries to get ideas for improving North Carolina's educational system. I recall our trip to England in March 1999. The legislators were trying to determine what policies to put in place regarding parental choice and school accountability. England had used a national voucher program for more than a decade, and our legislators learned about the results. They came away convinced that our state should not adopt a voucher program, but should consider other options to promote school choice, such as charter schools. North Carolina now has roughly 100 of these schools across the state.

In other partnering ventures, the Fund has looked to the informal learning community

as an effective resource for improving science learning. There are more than 20 science museums and aquariums across the state, and these facilities reach both students and adults, providing a continuum of learning. To enhance the learning opportunities provided by these museums, the Fund provided an endowment to create the Grassroots Science Museum Collaborative to coordinate hands-on science learning. It's the first such museum collaborative in the United States and is now funded by the state.

The North Carolina School of Science and Mathematics (NCSSM) offers gifted secondary school students a high-quality residential learning environment. The Fund has partnered with the school to create the Education Future Center, which focuses on developing distance-learning programs for teachers and students across the state. Many areas in North Carolina lack the financial resources to provide schools with enough teachers in advanced subjects such as physics, chemistry, biology, or mathematics. The Future Center fills that gap by using teleconferencing to bring to the schools high-level courses taught by NCSSM faculty through satellite sites called cyber campuses. More students across the state are now receiving top-quality instruction and curriculum to help them advance and prepare for college.

North Carolina has a wealth of scientists and educators who have an interest in pre K-12 education. Annually, BWF and North Carolina State University's Science House bring together university scientists, educators, community leaders, and program directors of pre K-12 science outreach programs. Participants summarize their experiences, identify areas of success, and create a collective vision for expanding outreach programs and disseminating their results.

There are many ongoing efforts to improve science and mathematics education across the state. To direct, manage, and align North Carolina's myriad programs and activities, the Fund in 2002 created the North Carolina Science, Mathematics, and Technology Education Center, or the SMT Center, as we call it. Headed by Sam Houston, a longtime educator and community leader, the center is dedicated to systematically improving performance in science, mathematics, and technology pre K-12 education in North Carolina so that all students will have the necessary knowledge and skills to have successful careers, be good citizens, and advance the economy of the state. He recently hired Lisa Rhoades as his program associate. The SMT Center has launched several initiatives to improve science teaching and learning. The Teacher Link Program, for example, connects area scientists with teachers to provide them with up-to-date scientific content and boost their expertise in teaching inquiry-based science. Melanie Scott works closely with Dr. Houston on this project. With scientists and teachers working together in such efforts, one important aim is to develop science content that meets the federal mandates set forth by the No Child Left Behind legislation. The participating scientists serve as mentors in helping teachers to conduct classroom experiments that put students in the role of scientists. North Carolina lags behind many other states in implementing inquiry-based learning, and this program is helping us to move forward.

The success of this and other projects has been impressive. We can't wait to see what happens next. Growing the Fund's science education program has been a great experience.

STUDENT SCIENCE ENRICHMENT PROGRAM



The Mentor Center at the **Shodor Education Foundation** is a year-round program that pairs 60 middle- and high school students with scientists practicing in the field of computational science. Using computer modeling, Shodor teaches students how science and mathematics relate to their everyday lives and then matches them with scientist mentors for hands-on science exploration. Some of these students become Shodor interns and help both scientists

and educators develop and update Web-based instructional materials—available to educators nationwide—in science and mathematics. Shodor received a Student Science Enrichment Program grant to fund the Mentor Center and since has received a grant from the National Science Foundation (NSF) for \$2.8 million to open a new pathway to the National Science Digital Library, which is NSF's online library of resources for science, technology, engineering, and mathematics education. "This NSF grant is a good example of leveraging BWF's support to take high-quality education materials developed by students and teachers from across our local area to the national level," says BWF President Dr. Enriqueta Bond.



CHAPTER 6

Behind the Scenes

As the Fund has grown, so has its need for a good organizational support system—in administration, finance, and communications. Under Dr. Bond's leadership, the Fund developed sturdy organizational legs to support its day-to-day work.

Martie Nolan, one of the original cast of Fund veterans, now is senior manager of facility and administrative services. Under her management, the Fund added computer systems, network services, and other key technologies, such as a new grants management database that eased tracking of grant applications, awardees, and funding. When the Fund built its new headquarters, Nolan worked with the architects, interior design team, and building contractor, and helped decide how office and meeting space would be allocated.



Above: Administration staff—From left, Martie Nolan, Betsy Stewart, Glenda Oxendine, and Brent Epps. Facing page: Interior gardens of the Fund's headquarters.

Three additional employees manage the flow of information and materials. Secretary/receptionist Betsy Stewart is on the front line, handling visitors and incoming phone calls, as well as providing secretarial support for staff. Glenda Oxendine, document/ Web specialist, has developed processes for producing electronic documents, such as board minutes and PowerPoint presentations, and manages the Fund's website. Brent Epps covers records retention, recycling, and minor office maintenance.

Over the years, the Fund has increasingly emphasized its role as convener—of biomedical researchers, policymakers, and health care funders. Planning and organizing approximately 20 meetings a year is the domain of Catherine Voron, meeting professional, and Barbara Evans, administrative meeting assistant. The Fund hosts meetings not only at its headquarters in Research Triangle Park, but also across the United States and occasionally in Canada and the United Kingdom, sometimes with as many as 150 participants.

To accommodate its variety of meetings, the Fund's building was designed to provide ample and efficient space for convening groups. Meeting rooms, which range up to 1,500 square feet in size, have media capabilities and offer laptop connectivity at each seat. Even the spacious and well-lit corridors connecting the meeting rooms can be used for exhibitions.



Meetings staff-From left, Catherine Voron and Barbara Evans.



Finance Staff-From left, Kenneth Browndorf, Jennifer Caraballo, and Scott Schoedler.

Without sound financial management, however, none of the Fund's programs and activities would be possible. Scott Schoedler, vice president for finance, oversees the Fund's investment strategy and works closely with its financial advisory committee to ensure that investments are performing as they should. He also handles the Fund's human resources function, including staff pension and health insurance plans. Kenneth Browndorf joined the financial team in 1995 and now serves as senior asset and accounting manager. Jennifer Caraballo is the staff accountant.

As in all modern organizations, technology underpins every aspect of the Fund's work. Wendell Jones, technology coordinator, and Sam Caraballo, systems and Web engineer, are responsible for keeping the technology infrastructure up-to-date and functioning at peak performance, maintaining the diverse software systems used throughout the Fund, and training staff members in how to use new technological tools as they become available.

"Keeping up with the rate of technological change has sometimes been a challenge," Jones and Caraballo say. "But as a 'close follower' of the leading edge of change, the Fund has never had to pull a technological system out of service once it has been fitted into our



Technology staff—From left, Sam Caraballo and Wendell Jones.

operations." The Fund's latest innovation: implementing an electronic system for receiving and processing grant applications. Applicants will be able to submit their materials directly via the Internet, and Fund staffers will no longer have to process volumes of printed material by hand—no small task given the hundreds of applications received each year. Debra

Holmes, program assistant, who is responsible for entering grant applications into the current database system, will work closely with the technology staff on implementing the new online application system.

Following the Fund's first terrain mapping, Dr. Bond and the Board of Directors recognized the need to open the books for public scrutiny of the Fund's programs and expenditures and the importance of communicating to its various audiences. The Fund's key objectives are attracting top-notch applicants to its competitive award programs, publicizing the accomplishments of its award recipients, and drawing attention, and hopefully more funding, to the underfunded areas of science that it supports.

To build a customized communications program, the Fund worked with several outside consultants, including



Debra Holmes tracks grant applications for all programs.

Betsy Turvene, an experienced science editor and former colleague of Dr. Bond's at the National Academy of Sciences, and Tom Burroughs, a longtime science journalist, who later joined the Fund as communications manager. Together with Carr Thompson, the Fund's senior program and communications officer, they created a unified look for the Fund's printed materials. "This new look included the introduction of BWF as the Fund's acronym and a new 'banner' logo that combines the Fund's full name with a stylized version of the eye of Horus," Thompson says, "These features were meant to establish an easily recognizable public signature for the Fund. We wanted our publications to stand out in ways that would attract attention among our various target audiences, including the scientific, philanthropic, and policymaking communities, as well as the media and the general public."



THE EYE OF HORUS

From its inception, the Burroughs Wellcome Fund has used the eye of Horus as its insignia. In Egyptian mythology, Horus fought with Set, the demon of evil, and lost an eye, which was miraculously restored. Consequently, the eye of Horus became a symbol of health and strength. Ancient Egyptians wore the eye of Horus as an amulet to confer on the wearer good health and the strength of

the noonday sun. Over the years, BWF's logo has had several incarnations. The first duplicated a design crafted for the Wellcome Historical Medical Museum in London. Since then, the Fund's emblem has become progressively simpler and more stylized.



Recognizing that both the scientific and journalistic communities were moving rapidly into an electronic world, BWF began using the Internet as a major communications tool. In 1996, the communications and programs staff launched the Fund's first home page on the World Wide Web. BWF's website offered program information, annual reports, and news about awardees. Since then, the website has undergone several redesigns and the addition of a searchable awardee database. Mirinda Kossoff, the Fund's communications manager until April 2005, moved BWF further into the electronic arena by converting its quarterly printed newsletter, *FOCUS*, into an email newsletter, which also can be accessed from the website.

Another element of BWF's communications strategy has been to support outside organizations in their efforts to boost science communication. BWF provided pioneering support to the American Association for the Advancement of Science (AAAS) to develop and implement its *Science's Next Wave* website, which provides career-related information, news summaries, and other updates tailored for young scientists. Recognizing, too, the importance of communicating science to the public, BWF has supported the Council for the Advancement of Science



Communications—Mirinda Kossoff.

Writing's annual New Horizons in Science Briefing, which introduces hot topics and new developments in science to journalists from across the United States and Canada. Through AAAS, the Fund also supports newspaper and magazine internships in science writing for scientists who want to write about science for the public or pursue careers in science journalism.

Vol. 1, No. 1 Summer 1988

ON THE BURROUGHS WELLCOME FUND



People in The News 3 ELCOME TO FOCUS FOCUS is the first newsletter published by The Burroughs Wellcome Fund, a nonprofit foundation dedicated to providing financial aid for the advancement of medical knowledge by research, and for other scientific, scholarly and educational purposes. The objective of this newsletter is to inform you of research supported by our foundation and to spotlight grantees who are

health through their research. The Fund's mission is best explained by Fund President George H. Hitchings, Ph.D.: "Our purpose is to identify and support underfunded areas of research where advances may improve the health of mankind. The Fund has modest means, but at the right moment, its help can change the course of a scientist's work or inspire an emerging field of research."

working to improve public

HE BURROUGHS WELLCOME FUND: 33 YEARS OF GIVING Thirty-three years ago, The

Burroughs Wellcome Fund began with a vision to improve public health through medical research and education.

The years have shown us how modest, timely support can aid the course of a scientist's work. The Fund's emphasis on people who pioneer new areas of medicine comes from a tradition of Burroughs Wellcome philanthropy.

In 1880 two American pharmacists, Silas Burroughs from New York and Henry Wellcome, born in Wisconsin and raised in Minnesota, founded their pharmaceutical company in London. The company prospered using new medical discoveries and technologies to produce and standardize pharmaceuticals. The compressed tablet, then a novelty, became a specialty of Burroughs Wellcome Co. Wellcome coined the word "Tabloid" as the Company's trademark for compressed medicines.

Sir Henry Wellcome survived his partner and built their pharmaceutical firm into an international enterprise now consolidated as The Wellcome Foundation, Ltd. His will, set up in 1936, created The Wellcome Trust which required dividends from the international Wellcome companies be distributed to support medical research, museums and libraries worldwide.

To continue Wellcome's philanthropic tradition in the United States, The Burroughs Wellcome Fund was created in 1955. It is supported exclusively by Burroughs Wellcome Co., a research-based pharmaceutical firm located in Research Triangle Park, N.C. In its 33 years, The Fund has given over \$30 million in grants to U.S. medical institutions and nonprofit organizations.

The chart on page 2 shows the relationship between the various "Wellcome" entities.

WELLCOME PHILAN-THROPY: WHAT THE FUND SUPPORTS

The Fund does not attempt to compete with government and other funding agencies. Instead, our support goes to underfunded areas of research and has had a significant impact in attracting individuals to various fields. During the 1987/88 fiscal year ending April 30, The Fund granted \$4.25 million to more than 153 researchers, students and teachers.

The Fund's major grant programs are described in the following sections.

Scholar Awards

The Fund provides annual awards in these six areas: (1) clinical pharmacology-the action of therapeutic agents in humans; (2) pharmacoepidemiology-assessing the safety and effectiveness of drugs in large populations; (3) immunopharmacology of allergic diseases-underlying mechanisms of allergic responses; (4) molecular parasitologyprevention and treatment of parasitic diseases; (5) toxicology-effects of drugs and environmental pollutants on human health; and (6) innovative methods in drug designimproved understanding of the basis of drug design.

Each of these awards is for \$300,000 payable over five years. Outside scientific advisory committees review applications. "Being a true innovator takes more than intelligence and hard work. Those are givens. What we wish to see in today's outstanding young researchers is creativity, originality, a unique way of looking at problems. And they must have tenacity, belief in their vision, and the will to pursue it."

-Dr. George H. Hitchings (1988), Nobel laureate and former BWF president

These words still ring true as the Fund celebrates our 50th anniversary and looks to the years ahead. Our mission is clear. We will support creative young scientists who are using innovative approaches and state-of-the-art tools to pursue challenging scientific questions. And we will encourage and educate more young people to become the next generation of scientists, and the next after that.

More than a century after two enterprising young Americans set in motion their pioneering partnership, the Burroughs Wellcome Fund remains committed to the belief that supporting the best and the brightest scientists offers the fullest promise for improving human health today and into the future.

-Dr. Enriqueta C. Bond, BWF president

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ing signed by all of the Incorporators and t red filed with the minutes of the meeting. Chairman reported that the Certificate of Inbeen filed in the Department of State of the ork on the 24th day of May, 1955 at 10 o'clow f such Certificate of Incorporation was order serted in the minute book as part of the reco eeting.

Chairman presented to the meeting the signed ion of Iris B. Evans as an Incorporator and