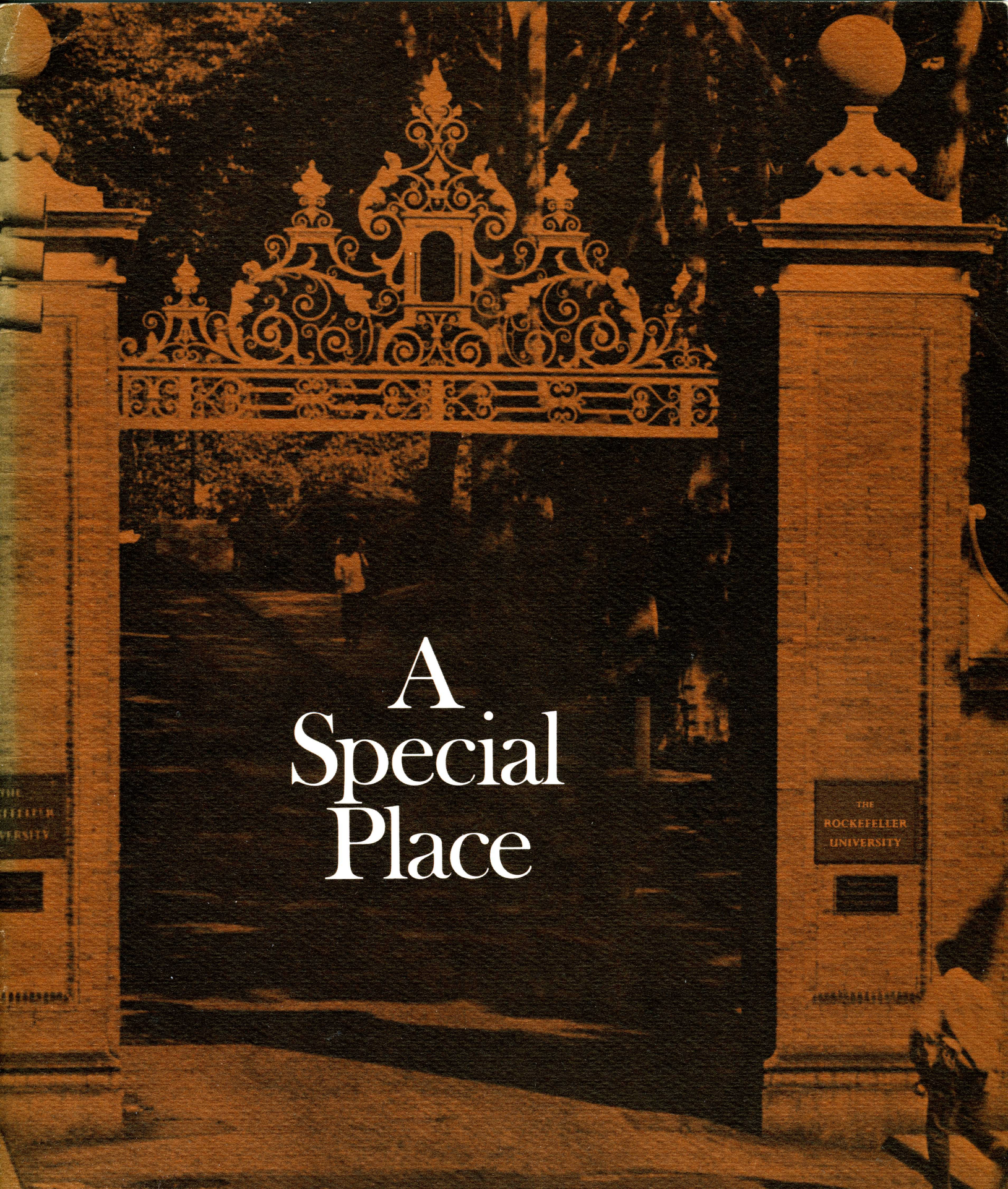
1982

A Special Place

The Rockefeller University



A Special Place

Scientific research is one of the most enthralling pursuits that can occupy the human mind, and those who can dedicate their lifework to it are privileged indeed. But the private excitement of discovery should not obscure the enormous public stakes of the enterprise. What we learn today about the structure of DNA *and of cells and how these are knit together in a functioning organism will be indispensable tomorrow for what is indeed a war against pain, disease, and death.*

President Joshua Lederberg

THE ROCKEFELLER UNIVERSITY is engaged exclusively in scientific research and graduate education in the biomedical sciences and related behavioral and physical sciences. Compared to general purpose universities, it is not a large place. Its tree-shaded, 15-acre campus, overlooking the East River in uptown Manhattan, is the setting for a scientific community of about 1,450 people—250 regular faculty, about 200 postdoctoral fellows and research associates, 100 graduate students, and a staff of about 900, including laboratory technicians, nurses, skilled craftsmen, and other supporting and administrative personnel. Yet this cluster of buildings, reflecting the architectural styles of eight decades, contains one of the greatest concentrations of scientific talent in the world dedicated to benefiting humankind through basic research and its application to the problems of disease.

A Pioneering Venture

Founded in 1901 as The Rockefeller Institute for Medical Research, the institution has been a major force in bringing the United States to the forefront of the biological and medical sciences. The hope of the founder, John D. Rockefeller, Sr., that this pioneer venture also would serve as an example and stimulate scientific discovery elsewhere, has been realized in the establishment of a number of research centers and university-based medical research programs patterned after it. The campus is a magnet for scientists from all over the world.

View, from north, of Rockefeller University campus.

In 1910, the University opened the first hospital in the United States devoted entirely to research. This 40-bed Clinical Research Center operates in exactly the same spirit as the other University laboratories. But the investigations carried out in the Hospital laboratories are chiefly derived from problems of disease, and the scientists continuously interact with human patients. The Hospital was the first clinical research institution where human disease could be studied and treated in a setting

of rigorous, scientific inquiry. Its impact was critically important in upgrading medical education at a time when many medical colleges were no more than trade schools. Most of the medical-school leaders who moved for reform had served "apprenticeships" in clinical research at The Rockefeller Hospital. In the 1950s, the Hospital was an organizational model for the federally supported Clinical Center, with 500 beds, established by the National Institutes of Health in Bethesda, Md., as well as for the smaller clinical research centers set up, with federal funding, by more than 80 American medical schools.

For more than half a century, The Rockefeller Institute was not a degree-granting institution. But many young people at the start of their research careers came to its laboratories, either on fellowships or as junior members of the scientific staff, to work with eminent scientists and gain the skills and insights required in their chosen fields. Thousands of Ph.D.'s and M.D.'s from this country and abroad who obtained advanced training here have gone on to positions of leadership elsewhere in scientific research and education.

In 1954, the Institute became a graduate university, formally extending its educational role to provide work at the doctoral level for a small, carefully selected group of young men and women with unusual potential for distinguished scientific careers. The first Ph.D. degrees were granted in 1959. In 1965 the Institute officially changed its name to The Rockefeller University. However, in the transition from institute to university, this community of scholars has maintained the strong feeling of intimacy and the uniquely flexible organization that have always characterized its scientific and educational activities.

A Unique Structure and Spirit

The University is organized around more than 50 laboratories, a few comprising a single scholar and the rest ranging from groups of 3 to more than 35 persons. Generally a group includes a senior professor, several other faculty members, plus postdoctoral fellows and graduate fellows who share the scientific interests of the laboratory. There is no traditional departmental

structure to hinder communication or innovation. Individual investigators cross disciplinary boundaries freely and pursue overlapping interests with their colleagues in other laboratories. Simon Flexner, the Institute's first director, emphasized that the design and arrangement of the grounds and buildings should also encourage this "spirit of easy and free cooperation."

The University offers exceptional opportunity for undistracted research. Its scientists enjoy a wide freedom of inquiry based on the conviction that they work best "where research is in the air" and they can use their own imaginations, set their own directions, and rely on the observations they make from day to day to guide their efforts. The primary emphasis is on the scientific understanding of biological and physical principles–with the expectation that finding out what is not known about life processes will pave the way for practical applications. Diversity of scientific interests and independence of investigation are held together in a closely integrated scientific community by a single motivating objective that is expressed in the University's motto–*pro bono humani generis.* Out of this unique organization has come a series of achievements that, directly or indirectly, have touched the lives of people around the world and have influenced the course of some of the most important fields in modern life sciences.

A Record of Discovery

Perhaps the most revolutionary scientific discovery made at The Rockefeller was the first demonstration that the code of life is contained in DNA. This achievement, described in a paper published in 1944, actually developed from a program of research, extending over many years, on a single-celled bacterial organism, the pneumococcus. What Oswald T. Avery and his associates were seeking was knowledge to combat pneumonia. But in their efforts to analyze the chemical composition of the "factor" that could transform a harmless strain of bacteria into virulent infectious agents, they established that a nucleic acid is the stuff of the genes, thousands of which are contained in

every living cell and embody all the instructions needed to create an entire organism and keep it functioning. This fundamental insight has been called the central discovery of twentieth-century biology because of its impact on so many areas of research that are providing clues to how the cell operates, how it reproduces itself, and how it becomes diseased.

Another fundamental discovery that has stimulated work in hundreds of laboratories was made by Peyton Rous shortly after he joined the Institute in 1909 to engage in cancer research. Dr. Rous was studying tumors in rodents when a breeder of chickens brought him a hen with a subcutaneous tumor. He succeeded in transplanting bits of that malignant growth–now known to cancer investigators everywhere as "Rous sarcoma"–to fowls of the same inbred stock. This was the first avian tumor found to be transplantable. Then Dr. Rous went on to produce proof that the tumor was transmitted by a virus. This discovery–the first demonstration that an animal cancer can be caused by a virus–was greeted with skepticism, and even disbelief, by many scientists. More than 50 years later, in 1966, Dr. Rous, then 87 and still active in the laboratory, shared a Nobel Prize "for his discoveries of tumor-inducing viruses." In the years between his discovery and the invitation to Stockholm, Dr. Rous not only made many other contributions to the study of viruses and cancers, but also developed, with J. R. Turner, a practical method for preserving whole blood for transfusions. This remarkable achievement made it possible to establish the first blood bank, in World War I, and has saved countless lives since then.

Even a partial listing of research achievements mentioned in scientific surveys and histories of medicine would yield many other significant contributions by scientists at The Rockefeller, such as:

- The first isolation and successful tests of natural antibiotics.
- Advances in the science of blood groupings that eliminated the dangers of mismatches in transfusions.
- The first chemical description of immunoglobulin, one of the body's key defenses against disease.
- The development and comprehensive testing of the methadone maintenance program as an effective treatment for heroin addiction.
- The determination of the chemical structure and the laboratory synthesis of the first enzyme for which the chemical formula was established, pancreatic ribonuclease.
- The first continuous cultivation in a test tube of the parasite responsible for human malaria, a prerequisite to the development of a vaccine.
- Pioneering studies on the physiology and chemistry of vision.
- Basic contributions to a better understanding of the elementary particles that form atomic nuclei and of the forces that bind them.

Yet the total output and level of excellence of a research institution cannot be gauged by sampling achievements. The force of continual inquiry by successive generations of investigators bringing new ways of thinking and new tools of research to the study of natural processes has made the University a vital center of progress in many fields of major importance. These include the mechanisms of infection and immunity; the biology of bacteria and viruses; the clinical study of such problems in human metabolism as the role of cholesterol and the effects of diets and drugs on heart disease, obesity, and hormonal disorders; the physiological basis of behavior; and the structure and function of biologically important molecules.

View of campus from southeast, with Tower Building in foreground.

Technological Innovation

The University has also played a significant role in the development of instruments and techniques that have opened up new research frontiers and advanced the diagnosis of disease. Almost from the start, its scientists and skilled craftsmen provided leadership in the application of physical and chemical methods to the life sciences. In the Hospital's laboratories, the invention of new apparatus and the development of analytical techniques and tests laid the groundwork for medical procedures that now are standard. The late 1940s and 1950s saw the creation of several powerful methods and devices for collecting and analyzing complex biological substances that have found their way into the scientific equipment catalogues and are in common use in laboratories throughout the world.

The importance of the creative interplay between discovery and technological innovation–the laboratory and the instrument shop–is particularly well illustrated by its influence on cell biology. In the early years, the living cell was a frequent object of study here. In the 1930s, this campus became a prominent center in the development of the technology needed to culture tissues and cells in the test tube. Then, in the late thirties and early forties, a number of significant achievements took place that made possible the detailed exploration of the cellular microcosm.

A dedicated and gifted group of associates in various Univer-

sity laboratories solved many of the problems hampering the effective examination of cells at the high resolution possible under the new electron microscope. The techniques they developed for fixing specimens and cutting the infinitesimally thin cell sections required are now widely used, as are a number of instruments whose prototypes were designed and built in the University's Instrument Shop. Also, new cell fractionation techniques were introduced for simultaneously breaking up several billions of cells and isolating their parts for analysis. Mass isolation of cell components, formerly invisible but now revealed by the electron microscope, was the first step in determining their chemical composition and biological activities; this, in turn, led to an understanding of their function. That knowledge is now being applied in medicine and therapeutics. Such contributions earned for the University the description "cradle of modern cell biology." In 1974, three of its scientists received a Nobel Prize for their roles in opening up the new world of the cell.

In fact, the quality of the work carried on in the University's laboratories has been recognized again and again by the national and international scientific communities. A total of 16 Nobel Prizes—the first in 1912 and seven since 1972—have been awarded to University scientists. More than half of the University's full professors have been elected to membership in the National Academy of Sciences. Over the years, eight faculty members have received the National Medal of Science, the highest award given by the United States in science, medicine, and technology.

Research in Progress

A survey of University laboratories would show groups at work today on the broadest of fronts in experimental fields such as biochemistry, biophysics, cell biology, genetics, immunology, neurophysiology, parasitology, and virology. Another major area of research intersecting these basic interests is behavioral studies of the interactions between genetics and environment as they affect various forms of life and of the sensory, neural, and hormonal mechanisms underlying brain function and be-

Campus in spring.

havior patterns. The closely related research activities of the University Hospital span clinical studies of more than 30 diseases, largely chronic and degenerative in nature, for which there are as yet no wholly satisfactory means of prevention and treatment. The University has programs on the frontiers of mathematics and experimental and theoretical physics carried on by internationally recognized scholars.

Cell Biology Comes of Age

Any guided tour of the laboratories would show cell biology to be a major theme with multiple variations. As it has matured, cell biology has come to encompass more and more of the life sciences because it is concerned with both the chemical and the biological properties shared by all cells and the way in which each class of cells is adapted for highly specific functions. All animal and plant cells share nearly identical cellular substructures for storing and reading out genetic information, for generating chemical energy, and for manufacturing the thousands of proteins basic to life. The causes of aging, many congenital diseases, and cancer appear to be related to the breakdown of functions in these cell structures. Thanks to its long tradition of pioneering contributions to the study of the cell, the University today has the "critical mass" of instruments and corresponding human skills to exploit the full potential of modern cell biology. Priority has been placed on two lines of endeavor: efforts to increase knowledge of the basic cellular processes in depth and efforts to increase knowledge of specialized cellular processes, as in liver cells or antibody-producing cells. Considerable progress is being made along both lines, and the insights gained will continue to be applied to unsolved problems in medicine.

Insights into Cancer

Though the University has never considered itself a cancer research center, more than 15 laboratories, in the tradition of

Peyton Rous, are furnishing important insights because they are at work on projects that are proving to be directly relevant to determining the causes of this disease. The investigations include work on tumor viruses, on the structure and function of cell membranes, and on the genetic controls and immunological defenses that affect the body's natural responses to tumors.

Reproductive Biology

More than a dozen University laboratories are involved in studies designed to provide much-needed knowledge of medical, biological, and behavioral processes related to reproduction. The theme of reproductive biology has engaged faculty members and students, as well as staff members of neighboring institutions, who represent a multiplicity of professional skills. Their efforts are producing scientific findings relevant to a number of human concerns, particularly the global problem of population control.

Attacking Parasitic Disease

The many ways in which scientists can approach a problem productively are also highlighted by research on parasitic disease carried on in a number of laboratories. In only one of these is parasitology the principal interest, but all are producing knowledge basic to the conquest of such scourges as malaria, schistosomiasis, and Chagas' disease–which constitute the greatest health problems in vast areas of the world. The work ranges from the development of new chemotherapeutic agents to investigation of how large, intracellular parasites are modified by the cellular immune system. The development of the first method for continuous cultivation in vitro of the human malaria parasite has quickened hopes for a vaccine at a time when malaria is on the resurgence, and has opened up new lines of research in the entire field of parasitology.

Viruses: A Major Research Program

The biology of viruses has been a central research program at the University from the start. Among the major objects of study are the influenza viruses of man and animals and those viruses involved in parainfluenza, mumps, measles, and canine distem-

per. These viruses are responsible for diseases ranging from acute respiratory infection to persistent infections of the central nervous system that lead to chronic neurological diseases. One research objective is to increase understanding of how viruses multiply and how they cause cellular injury and disease. A number of significant findings made at the University have provided clues to possible new approaches to chemotherapy for certain virus diseases.

Another research objective of the virologists is to acquire information on cell membranes, which are crucial in most physiological processes. Viruses provide excellent models for studies of the plasma membranes of human cells.

A third area of virus research at the University is the study of interferon. Interferons are substances that cells produce as the body's first line of defense against viruses. The Rockefeller research seeks to find out how interferon inhibits cell proliferation and how its production is chemically and genetically related. The work has already furnished novel insights into the process of interferon production in the human body.

The Challenge of the Neurosciences

Among the most challenging and rapidly expanding areas of research today are the neurosciences, a vast domain where science comes up against the mysteries of the brain and nervous system. Recent studies are providing a new picture of the brain. This organ controls a vast variety of functions–from regulation of the glandular and visceral reactions essential to life up to the highest mental processes involved in scientific and artistic creativity. The University has had a strong commitment to the neurosciences ever since Herbert Gasser, neurophysiologist and Nobel laureate, succeeded Simon Flexner as head of the institution in 1935. Dr. Gasser attracted a group of distinguished neurophysiologists who expanded his work on the anatomy of nerves and the analysis of electrophysical activity within the body. This base was further broadened and strengthened by Detlev Bronk, who succeeded Dr. Gasser in 1953 and was himself a biophysicist and a major contributor to studies of the nervous

system. A number of laboratories were added, including those concerned with physiological aspects of psychology and with animal behavior.

Many of the University's laboratories are conducting investigations directly related to the neurosciences. The areas of study range from the molecular biology of brain functions to the diseases of the nervous system. One program focuses on the developmental biology of nerve cells and mechanisms of molecular recognition. The objective is to understand the events that initially shape nerve tissue in order to build a base for the comprehensive exploration of how "neural circuitry" develops. Researchers in brain chemistry are seeking to expand knowledge of the proteins of the brain. Their work is designed to develop an understanding of prenatal or postnatal biochemical changes that affect brain function. Other scientists are exploring hormonal functions and the biochemical basis of behavior, including the effects of certain drugs. One concern is how the nervous system controls reproductive behavior and the release of male and female hormones. Another area of research is the neurochemical mechanisms that govern feeding and drinking. An increasingly important line of research bears on pathological conditions that are strongly influenced by the brain in its central regulatory role, and by its responses to the stresses of life. It is no longer doubted that the mind affects the body; current research is elucidating the physiological mechanisms of such psychosomatic relations.

The Study of Animal Behavior

In 1972, the University opened its Field Research Center in Millbrook, New York. It is the headquarters for investigations in ethology, the study of animal behavior–an area of science where biology and psychology converge. On these 1,000 acres, about 90 minutes north of the Manhattan campus, ethologists, psychologists, and neurobiologists can pursue laboratory and field work on the relationships between genetic and environmental effects on the behavior of various animal species. The studies in progress are helping to resolve basic questions about

Entrance to the Hospital.

animal communication, social organization and ecology, learning, and orientation. Scientists at Millbrook frequently join forces with their colleagues in other University laboratories in projects requiring a variety of experimental approaches and knowledge from several disciplines.

During its first decade, scientists at the Center have carried out a diverse program of behavioral studies. For example, one group has used radar and weather balloons to show that migrating birds keep a correct course when flying at night between clouds. Deprived of celestial and ground cues, the migrants presumably rely on nonvisual sources. Another group has uncovered remarkable parallels in the blending of innate and experiential features that guide vocal learning in juvenile humans and birds. Students and staff associated with these two laboratories have also conducted extensive field work abroad on the significance of learned songs in the humpback whale and the occurrence of semantic communication in monkeys. A third laboratory group at the Field Center has described brain pathways for vocal control in songbirds. Such pathways show marked sexual dimorphism, dominance by the left hemisphere of the brain, sensitivity to gonadal hormones, and a positive relation between size of cell nuclei used in song learning and how much song is learned.

Clinical Research

The disease research in progress at the University comes to a focus in its Clinical Research Center. As already noted, the Hospital laboratories concentrate on problems peculiar to human beings and most appropriately investigated in human patients. The areas of study span a variety of genetic disorders, including the porphyrias; immunological diseases, such as

rheumatoid arthritis, systemic lupus erythematosus, and lymphatic leukemia; infectious diseases, such as rheumatic fever, gonorrhea, and meningitis; the crippling disease of the nervous system, multiple sclerosis; endocrine-related cancer; dermatologic disorders; obesity; diabetes; and arteriosclerotic heart disease. Other research interests are the widespread problems of alcoholism and narcotics addiction, nutrition, clinical pharmacology, and the area of biochemical toxicology and the impact of environmental chemicals on man.

Like their predecessors at the Hospital, today's investigators have not narrowed their perspective to particular illnesses alone. Inspired by the concept of disease as a general biological problem, they are looking ever more deeply into organic structure and function, while simultaneously seeking to put their findings together and integrate them into the complex structure of physiology and chemistry. Today, the Hospital is the largest and the only private facility in the country that is devoted exclusively to clinical investigation and is a major contributor to the fund of knowledge from which the medical science of the future will evolve.

Educational Programs

Everything that is true about the structure and style of the University with regard to research applies to its educational activities. Younger scientists taking the first step in a research career are received as colleagues in every sense of the word, and are free to move beyond their own laboratories to seek whatever advice or guidance they need in building their own bases of knowledge and research expertise. The present program for about 200 postdoctoral researchers attests to the University's continuing emphasis on providing first-rank specialized training in the biomedical and related behavioral sciences, as well as in physics and mathematics. Most of these young investigators move on to important research posts in other institutions. Many of them return from time to time to share with former colleagues the fruits of their own research or to carry out some collaborative project in one of the University

laboratories. The impact of this continuing venture in postdoctoral education is one of the University's major distinctions.

The graduate program, which admits about 20 new students each year for what is usually a five-year period of work, differs markedly from traditional patterns of predoctoral education. The laboratory, rather than the classroom, is the principal site of learning through a research-oriented and essentially tutorial program. A total of 395 Ph.D. degrees had been awarded through June 1981. Though little more than a quarter of a century old–the first class graduated in 1959– the University's "experiment" in producing leaders in science has been recognized as a success by scientists and educators, as well as by independent national evaluations of the quality of doctoral graduates in the biomedical sciences, which place the University's alumni at the top. In the spring of 1980, of 371 graduates surveyed, 91 percent were engaged in full-time research or teaching. Of this group, 83 (22 percent) had reached the rank of full professor or the equivalent, 89 (24 percent) were associate professors, and another 85 (23 percent) had become assistant professors. Two graduates have won the Nobel Prize.

Responding to a need for educational innovation to enhance the integration of scientific and medical interests, the University, in 1972, started an experimental joint M.D./Ph.D. program with Cornell University Medical College designed for a small number of candidates strongly motivated toward a research career in the basic or clinical biomedical sciences. On completion of their studies, candidates receive the Ph.D. degree from Rockefeller and the M.D. degree from Cornell. The extraordinarily high quality of applicants gives promise of the program's success.

The Finances of Discovery

The concept of a coherent research community dedicated to discovery, *pro bono humani generis,* was basic to the motivation of the Institute's founder. John D. Rockefeller, Sr. provided a financial base, which, with subsequent additions from other family sources, enabled the institution to operate entirely from

endowment income for more than fifty years. By the late 1950s, however, it became evident that the scope of the University's work and its importance to society had grown beyond the point where it was either practical financially or appropriate in principle to depend on such a limited base of private support. Thus federal support was accepted and, because of the high quality of research on campus, grew fairly rapidly in pace with the University's programs. By the late 1960s, inflationary pressures, constantly spiraling energy costs, and other economic concerns sharpened the necessity to develop an entirely new constituency of private donors if the University were to maintain the free spirit and flexible structure that made it a major contributor to the improvement of the human condition.

Need for Continuity

For the past ten years, a major effort has been made to make the University fiscally stable and to preserve its distinction. This effort has included substantial cuts in institutional expenses and the launching of the University's first fund-raising venture. Today, the annual operating budget is in hard-won balance at a level of about $55 million. Federal support (of hundreds of individual projects) accounts for half of the budget; private sponsorship by individuals, foundations, and corporations for one-quarter; and endowment income accounts for the remaining quarter.

What federal funding neglects is the need for continuity in long-range research programs and for flexibility to explore new fields. To assure these essentials for creative science, private support is indispensable. The University is now engaged in a ten-year Development Program that is seeking $150 million from private sources for endowment, operating funds, and facilities. In effect, it is looking to the private sector to help sustain freedom of inquiry and path-breaking investigations by investing in this special place.